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Gastrointestinal Symptoms and Belly Pain During the Phases of the Menstrual Cycle in Healthy Young Females

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GASTROINTESTINAL SYMPTOMS AND BELLY PAIN DURING THE PHASES OF THE MENSTRUAL CYCLE IN HEALTHY YOUNG FEMALES

by

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ABSTRACT

There are significant differences between the incidence of gastrointestinal (GI) symptoms between males and females. A recent review found that females report having more severe GI health problems compared to males. One explanation for the higher reporting rates of GI symptoms in females could be attributed to menstrual cycle influences rather than GI processes.

This research aims to examine the relationship between how gastrointestinal (GI) symptoms experienced by women covary with the different stages of the menstrual cycle. A secondary purpose is to determine the moderating effect of health anxiety on the severity of menstrual and GI symptoms.

Responses were collected and analyzed from 531 eligible participants using an anonymous online survey. The survey encompassed the GI-PROMIS scales, Health Anxiety Inventory, Pain Map, a Physiological profile assessment, and demographic items. Participants were placed into one of three groups relating to their phase in the menstrual cycle.

It was hypothesized that higher GI symptom levels and higher belly pain ratings would be observed during the Menstrual and Luteal groups compared to the Follicular groups. These differences will be observed after controlling for levels of health anxiety. Individuals with greater menstrual and premenstrual symptoms are hypothesized to indicate increased pain in the Hypogastric region, which includes the female reproductive organs.

There were no significant **multivariate** differences between the groups on the GI PROMIS scales or the Pain Map, which indicates that when these variables were used together, they did not discriminate between the phases of menstrual cycle in healthy young women with

regular 28-day periods. That the Menstrual group reported significantly higher Belly Pain scores and higher Pain ratings at the hypogastric region (Region H) compared to the other two groups suggests that increased GI PROMIS Belly Pain T-score elevations are likely to originate from the hypogastric region (Region H) and are related to the menstrual cycle. Additionally, the results showed that health anxiety is a significant moderating variable in women's reporting of GI symptoms and Pain ratings, which suggests a possible mechanism for the previously documented sex differences in GI symptom reporting.

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TABLE OF CONTENTS

LIST OF FIGURES

Figure **Page**

LIST OF TABLES

INTRODUCTION

There are significant differences between the incidence of gastrointestinal (GI) symptoms between males and females. A recent review found that females report having more severe GI health problems compared to males (Vivier, 2019). However, no study has distinguished between pain due to GI, menstrual, or general bodily symptoms in females. One explanation for the higher reporting rates of GI symptoms in females could be attributed to menstrual cycle influences rather than GI processes.

Sex Differences between Male and Female GI pain

For many chronic pain disorders, including Functional Gastrointestinal Disorders (FGIDs), the prevalence is significantly higher in women than in men (Unruh, 1996). Epidemiological evidence has shown that females are more likely than men to report symptoms of pain of any duration and severity (Unruh, 1996). In fact, laboratory studies have shown that when both men and women are exposed to the same experimental noxious stimuli (pressure and electrical stimulation), females reported higher levels of pain (Fillingim and Maixner, 1995; Berkley, 1997; Riley et al., 1998). A meta-analysis of pain studies showed that women were, on average, more sensitive to pain and had less pain tolerance than men (Riley et al., 1998).

Irritable Bowel Syndrome (IBS) is a specific chronic pain condition with documented sex differences. Up to twice as many females are affected compared to males (Drossman et al., 2002). In one study that measured the development of post-infectious IBS after gastroenteritis, females demonstrated a disproportionate development of IBS symptoms. Three months

following the gastroenteritis, 77% of females had developed IBS symptoms, such as abdominal pain, bloating, and cramping, while only 36% of males had developed IBS (Gwee et al., 1999). In a study that evaluated GI symptoms amongst young adults with an approximately 1:1 ratio of males to females, the percentage of females that made up the population of mild and moderate GI health groups were 77.1% and 84%, respectively (Vivier, 2019). However, it is interesting to note that prior to puberty, boys' and girls' gastrointestinal disorders occur with similar prevalence (Walker, 1999). Thus, one may postulate that the possible explanation for sex differences in FGIDS is the psychological and biological changes associated with puberty. One of the central changes during puberty for females is menarche and the emergence of a regular menstrual cycle.

Not only are there sex-based differences in the prevalence of FGIDS, but there are also differences in the variation of GI symptom patterns. In populations of women and men with equal levels of IBS severity, chronicity, and psychological distress, women have greater extraintestinal symptoms compared to men, such as chronic pain and headaches (Lee et al., 1999). In a large survey of college students, women reported significantly more gastrointestinal symptoms, such as abdominal pain and bloating, compared to men (Taub et al., 1995). In a community sample of IBS patients, women reported more constipation, while men reported more diarrhea (Talley, 1991).

Although sex-based differences in GI symptomology is evident, it is possible that external psychosocial factors play a role in the disparity between sexes. These variables include higher levels of health anxiety in females or possible willingness to disclose GI as well as other

physical and emotional symptoms (Fillingim & Maixner, 1995). Lastly, there may be inherent and subtle sex biases in the Rome criteria for diagnosis of FGIDs (Smith et al.,1991).

Physical Symptoms Associated with GI Health

The physical symptoms and diagnoses associated with gastrointestinal health have been extensively researched. GI symptoms are caused by pathologies including gastroesophageal reflux disease (GERD), gastritis, peptic ulcer disease, gastroenteritis, gastric and esophageal cancer, functional dyspepsia, and diabetes mellitus (Wallander, 2007). In 1985, the physical symptoms associated with IBS included abdominal pain, constipation, and diarrhea (Svedland, 1985) and it also was associated with symptoms of abdominal distension and hard stool (Thompson, 1984). Another diagnostic category of great interest at that time was peptic ulcers. Peptic ulcers were associated with symptoms of stomach pain, heartburn, belching, and nausea (Sjoudin, 1985). In 1988, the first patient-subjective rating scale of gastrointestinal symptoms was created for patients with IBS and peptic ulcer disease, titled the Gastrointestinal Symptom Rating Scale (GSRS). This scale was created because, at the time, clinicians had relied solely on pathophysiological symptoms while patient reports and symptom ratings were not emphasized (Svedlund, 1988). GSRS included patient ratings of abdominal pains, heartburn, acid regurgitation, sucking sensations in the epigastrium, nausea, vomiting, borborygmus, abdominal distension, eructation, increased flatus, decreased passage of stools, increased passage of stools, loose stools, hard stools, and urgent need for defecation (Svedlund, 1988).

Traditionally, theories of GI disorders hypothesized that symptoms occur due to abnormal functioning of the GI tract rather than structural or biochemical issues, so symptoms

can go undetected in medical tests. More recently, theories recognize a more complex picture leading to the development of the construct of Functional Gastrointestinal Disorders (FGIDs). FGIDs are disorders of the gut-brain axis characterized by a variety of recurring GI symptoms. Symptoms may be caused by a combination of the following factors: motility disturbance, visceral hypersensitivity, altered mucosal and immune function, altered gut microbiota, and altered central nervous system processing. (Drossman, 2016, p. 1268). FGIDs affect all parts of the GI tract. Accordingly, they are broken down into categories for disorders of the esophagus, stomach, duodenum, bowels, gallbladder, sphincter of Oddi, anus, and rectum. There are over 30 FGIDs; however, the most common FGIDS include Irritable Bowel Syndrome (IBS), functional dyspepsia, and functional abdominal pain. FGIDs are diagnosed based on the presence of symptoms, using the Rome IV Criteria (Schmulson & Drossman, 2017).

In 1994, The Rome Foundation made the first effort to create a comprehensive diagnostic and classification tool for all the FGIDs, by publishing the Rome I criteria. Rome criteria is notable for shifting the FGID diagnostic methods from physiologically-based to symptom-based. Rome criteria classified all FGIDs into six domains based on primary symptom types and severity (Refer to Table 1).

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, 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)

The Rome criteria has evolved over the years. Most recently, in 2016, the Rome IV criteria was published. A notable change in the Rome IV was shifting away from the use of the term "FGID" and instead referring to FGIDs as *Disorders of Gut-Brain Interaction* (DGBI) (Schmulson & Drossman, 2017). This change in terminology was made to reflect the research indicating the existence of bidirectional communication between the gut and the brain.

In the late 1970s, epidemiological researchers discovered the importance of evaluating psychological and social factors in relation to biological factors when determining the etiology of illnesses and predicting illness behaviors. This eventually became known as the biopsychosocial model of illness. This played out in the context of GI health as well. Researchers discovered there was a significant comorbidity of GI symptoms with psychological distress in both clinical and non-clinical populations. For example, in studies investigating IBS patients receiving treatment and non-clinical IBS patients, researchers found that higher levels of psychosocial distress enabled symptom severity and illness behaviors (Drossman, 1988; Whitehead et al.,

1988). Stress can cause changes in the gut flora and affect the bidirectional communication between the central nervous system and the gut (De Palma et al., 2014; Mayer et al., 2015). This stress can induce bloating, gas, and discomfort (Carabotti et al., 2015).

Conducting a formal assessment of specific GI symptoms helps to gain accuracy, so the National Institute of Health (NIH) created the PROMIS-Gastrointestinal Symptom Scales; these scales are patient-reported outcomes on the severity of each unique gastrointestinal symptom. These include scales on Belly Pain, Bowel Incontinence, Constipation, Diarrhea, Disrupted Swallowing, Gas and Bloating, Nausea and Vomiting, and Reflux.

In summary, the physical symptoms and psychosocial factors associated with GI disorders have been thoroughly studied since the 1970s and numerous assessment and diagnostic tools have been constructed. The construct of DGBIs was developed to accurately study GI symptoms, and the continuously evolving development of the Rome criteria has been offered as a more effective and reliable diagnostic approach.

Physical Symptoms Associated with the Menstrual Cycle

Decades of research on the physical symptoms related to the menstrual cycle have helped to establish common patterns of menstrual-cycle-related physiological changes (Kiesner et al., 2016). The menstrual cycle encompasses both somatic and affective symptoms (Negriff et al., 2009). Historically, clusters of menstrual cycle symptoms have been diagnosed as dysmenorrhea (pain) and premenstrual syndrome (PMS) (Negriff et al., 2009).

Menstruation is the discharge of blood from the uterine lining that is regulated by hormone levels, such as progesterone, luteinizing hormone, and follicle-stimulating hormone on

a cyclic basis. The cycle is made up of three main phases: the follicular phase, ovulatory phase, and luteal phase, in that sequence specifically. The follicular phase is subdivided into the menses and the proliferative period. The median length of a menstrual cycle is 28 days, while most females' cycles range from 25 to 30 days (Reed & Carr, 2018). The variability in the cycle lengths is due to varying lengths of the follicular phase, which can range from 10 - 16 days (Reed & Carr, 2018). The luteal phase, on the other hand, maintains a constant length of 14 days in almost all women (Reed & Carr, 2018).

A series of studies surveyed women about their menstrual cycle, providing important insight into the relationship between changes in the menstrual cycle and associated physical symptoms. Research has shown that cognitive, affective, and physical symptoms fluctuate according to the phases of the menstrual cycle (Ross & Coleman & Stojanovska, 2003; Van de Akker, 1985). However, there are inconclusive findings about the pattern of symptom changes through the stages of the menstrual cycle.

In a study by Ross, Coleman, and Stojanovska (2003), 181 women from the general population, with a mean age of 30, completed a modified Menstrual Distress Questionnaire survey every day for 70 days. The symptom subscales included negative affect, cognitive symptoms, behavior changes, somatic symptoms, autonomic reactions, and fluid retention. Only the subscales of somatic symptoms, fluid retention, and negative affect showed cyclicity, while the subscales for behavior change, cognitive symptoms, and autonomic reactions were not consistent. All symptoms were generally at their lowest level during the follicular phase and increased premenstrually, with the greatest change occurring during the premenstrual period. Symptom severity did not change significantly between the premenstrual period and menses.

However, somatic symptoms were significantly higher in the menstrual phase compared to the premenstrual phase, while fluid retention was higher premenstrually.

In another study by Van de Akker and Steptoelo (1985), 185 women completed a modified version of the Menstrual Distress Questionnaire (MDQ) every day for 35 days. The women were employees and students at a medical school and hospital, with ages ranging from 16 to 35. The mean age was about 23. Results showed that most symptoms peaked menstrually, with the exceptions of weight gain, cold sweats, depression and painful breasts, which all peaked premenstrually. Boyle and Grant's (1992) study utilized the MDQ to survey symptoms from 103 young women and found that symptoms of pain, autonomic reaction, fluid retention, and behavior changes peaked menstrually rather than premenstrually. On the other hand, negative affect was highest premenstrually.

GI Symptoms Associated with the Menstrual Cycle

Only two studies were found which examined the relationship between specific GI symptoms and the menstrual cycle. The first of these was Bernstein et al. (2012), who conducted a study where 268 women with Inflammatory Bowel Disease (IBD) were compared with a healthy cohort of women after completing a retrospective survey on their GI symptoms. They concluded that perimenstrual GI symptoms were common in both healthy women and women with IBD, indicating that GI symptoms vary uniquely with the menstrual cycle phases.

Bernstein et al. (2014) conducted a retrospective study surveying 156 healthy women (Mean age: 32.3) on their emotional and GI symptoms over their past three menstrual cycles. A unique questionnaire was developed to assess the range of GI symptoms and emotional

symptoms. The survey assessed seven GI symptoms specifically: abdominal pain, diarrhea, constipation, nausea, vomiting, bloating, and pelvic pain. Of these participants, 73% experienced at least one GI symptom in the premenstrual phase, while 69% reported at least one GI symptom in the menstrual phase. Abdominal pain, diarrhea, and bloating were the most commonly experienced GI symptoms. Overall, the prevalence of each GI symptom was similar across both phases. The authors concluded that more research is needed to precisely "quantify the prevalence or nature of these symptoms, or to consider associated factors," (Bernstein et al., 2014).

However, the studies that did focus on the relationship between GI symptoms and menses investigated only an incomplete range of GI symptoms or investigated individuals who had a diagnosed GI disorder. Therefore, a limited amount of research has been done investigating how the complete range of GI symptoms varies along the phases of the menstrual cycle in an otherwise healthy cohort of women.

PURPOSE STATEMENT

The objective of this study was to examine the relationship between gastrointestinal (GI) symptoms experienced by women during different stages of the menstrual cycle. The menstrual phase is defined by the 7-day period that a female is undergoing menses. The follicular phase is defined as the seven days following the end of the menstrual phase. The luteal phase is defined as the 14-day period starting after the end of the follicular phase.

Additionally, I examined the role of health anxiety as a moderating variable of GI symptoms' severity. This cross-sectional study collected information through an online survey from a large population of undergraduate females. The following research questions were answered: (1) Do GI symptoms occur more predominantly during a specific phase of the menstrual cycle? (2) To what extent does health anxiety moderate the degree of GI symptoms? By investigating the relationship between GI symptoms and the menstrual cycle, we hoped to acquire a greater understanding of which specific GI symptoms are commonly associated with each stage of the menstrual cycle. Investigating whether there is a relationship between health anxiety and GI symptoms at a particular stage of the menstrual cycle (i.e., premenstrually and during menses) may help explain why some women have more severe GI problems and dysmenorrhea.

HYPOTHESIS

Based on the literature review, the primary hypothesis was that there would be higher GI symptoms as measured by the PROMIS-GI scales during the menstrual and luteal phases of the menstrual cycle compared to the follicular phase. Women were assigned to one of three groups. Their average level of symptoms on PROMIS-GI were compared. It was predicted that women in the luteal phase would demonstrate higher GI and belly pain symptoms. Health anxiety was included in the analyses as a covariate to examine whether it is a significant moderator in this relationship. I hypothesized that higher levels of health anxiety will be associated with higher GI symptom severity, higher belly pain scale scores, and increased intensity of symptoms throughout all the phases of the menstrual cycle.

Exploratory analyses examined intercorrelations between the different dependent measures. Individuals that have higher GI symptom severity were hypothesized to have higher belly pain reporting across the entire abdomen region. Individuals that reported greater menstrual and premenstrual symptoms were hypothesized to indicate increased pain in the Hypogastric region, which includes the female reproductive organs.

METHODS

The online survey included 131 questions assessing FGID symptoms and health anxiety. The survey also included demographic items such as age, gender, race, and ethnicity. Additionally, there was a physical assessment of participants' typical menstrual cycle patterns. The survey took about 30 minutes to complete. Two validity check questions were also included in the questionnaire as a determining variable for respondent data elimination or retention. 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) developed the Patient Reported Outcomes Measurement Information System (PROMIS®) Gastrointestinal Symptom Scales (PROMIS-GI) in 2014. The PROMIS-GI scales have been validated as an effective measure of a broad range of GI symptoms within the general and clinical populations. (Shah, Almario, Speigel, & Chey, 2018; Spiegel et al., 2014). The PROMIS-GI symptom scales may be effective in identifying clinical thresholds for action (Spiegel et al., 2014). The PROMIS-GI scales have been concluded to have good psychometric measures, such as internal construct validity (Spiegel et al., 2014). The PROMIS-GI scales evaluate eight GI symptom domains: abdominal pain (6 items), gas/bloating (12 items), diarrhea (5 items), constipation (9 items), bowel incontinence (4 items), gastroesophageal reflux (GER) (13 items), disrupted swallowing (8 items), and nausea/vomiting (4 items). Scores will be calculated by pre-determined algorithms available via the PROMIS website. Individuals' scores are provided as a T-score metric. The higher the T-score, the greater the severity of the symptom.

T-scores will be 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).

Abdominal Pain Scale. The pain scale used here (refer to Figure 1) is an adaptation of the numeric rating scale that is commonly used in many medical specialties (Williamson & Hoggart, 2005). Individuals are asked to report their pain on a scale from 0 to 10, with 0 representing least pain and 10 representing the most pain possible. The abdominal regions were graphically divided into nine regions and individuals provided a numeric rating for each region. This was facilitated by a drawing of the abdomen with a 3 x 3 grid drawn on top of the image. This will allow for differentiation of different types of belly pain: menstrual cramps or gastrointestinal issue.

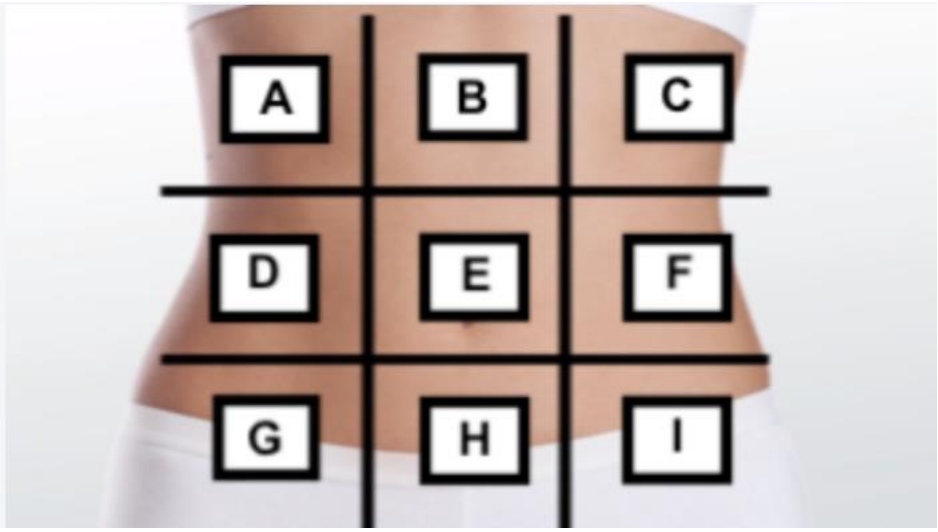


Figure 1: Abdominal Pain Scale

The abdomen can be divided into nine regions for purposes of clinical research and practice. Table 2 below provides details on the medical terminology and associated organs for each region in the Abdominal Pain drawing.

Table 2: Identification of 9 Clinical Subdivisions of the Abdominal Region

	Region	Location	Included Organs
A	Right Hypochondriac	Upper row, right	Liver, Gallbladder, Right Kidney, Small Intestine
B	Epigastric	Upper row, middle	Stomach, Liver, Pancreas, Duodenum, Spleen, Adrenal Glands
C	Left Hypochondriac	Upper row, left	Spleen, Colon, Left Kidney, Pancreas
D	Right Lumbar	Middle row, right	Gallbladder, Liver, Right Colon
E	Umbilical Region	Center	Umbilicus, Jejunum, Ileum, Duodenum
F	Left Lumbar	Middle row, left	Descending Colon, Left Kidney
G	Right Iliac	Lower row, right	Appendix, Cecum
H	Hypogastric Region	Lower row, middle	Urinary Bladder, Sigmoid Colon, Female Reproductive Organs
I	Left Iliac	Lower row, left	Descending Colon, Sigmoid Colon

Health Anxiety Assessment

Short Health Anxiety Inventory. The Health Anxiety Inventory was developed in 2002 in order to measure healthy anxiety and the cognitive factors associated with hypochondriasis independent of physical health status (Abramowitz, Deacon, & Valentiner, 2007). The original

Health Anxiety Inventory has 64 items, with each item on a four-point Likert scale (Solkovskis et al., 2002). An abbreviated 18-item scale was also constructed, termed the Short Health Anxiety Inventory (SHAI) (Solkovskis et al., 2002). There are three factors in the SHAI that assess the perceived likelihood of becoming ill, body vigilance, and the perceived severity of becoming ill (Abramowitz, Deacon, & Valentiner, 2007). The SHAI is often preferred in research and clinical settings because it has comparable validity and reliability to the original Health Anxiety inventory (Abramowitz, Deacon, & Valentiner, 2007). The SHAI was determined to have good psychometric properties, including reliability and convergent, divergent, predictive, construct, and criterion validity (Abramowitz, Deacon, & Valentiner, 2007). The first 14 items on the SHAI represent the main section of the SHAI (Solkovskis et al., 2002). Each item is scored on a scale of 0 – 3 and the items are totaled to create a score (Solkovskis et al., 2002). For the purpose of this study, only the first 14 items of the SHAI were used. Higher scores indicate higher levels of health anxiety (Solkovskis et al., 2002).

Demographic Assessment

Demographic information collected in this study included standard items, such as age, gender, race/ethnicity, marital status, and college status. Additionally, a physiological profile assessment was collected to assess the pattern of the menstrual cycle in each participant, such as if and when GI symptoms occur in relation to their menstrual cycle, and if they have any diagnosed conditions or contraceptive use.

Participants

Undergraduates enrolled in introductory psychology courses at a large, public university in the southeastern United States were recruited to participate in this study for course credit. Introductory psychology is a required course for all programs at this university, which ensures that a diverse range of majors and backgrounds were represented in the undergraduate population. Eligibility criteria excluded vulnerable populations and required participants to be biologically female, between the ages 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 of the university.

PROCEDURE

Data was collected from June 22, 2020 until December 3, 2020. Participants completed the survey by logging into SONA, an online research system in which students can participate in research studies in order to receive course credit while remaining anonymous to the researcher. SONA connects participants to the Qualtrics surveys and stores their responses. The study closed after 717 individuals responded to the survey.

Data Cleaning

The dataset was reviewed prior to data analysis. Participants were removed using the following exclusion criteria:

1. Report of last period starting more than 28 days prior which indicates an irregular cycle (n = 146).
2. Endorsement of one or more validity check item (n = 15).
3. Failure to complete survey (n = 18).
4. Outside 18 - 25 age range (n = 1).
5. Inconsistent reporting regarding their period start and end dates (n = 6).
6. Pregnancy (n = 0).

Additionally, mean substitution was utilized to fill in missing responses for 25 participants on the GI-PROMIS Gas and Bloating T-scores, two participants on the Pain Map-Region C, and one participant for the item “How much do you weigh, in pounds?” After these steps for data cleaning, the final sample size was 531 participants.

Group Assignment

Participants were then categorized into one of three groups based on their answer to the survey question, "How many days ago did your most recent period start?" If they answered “0 - 7 days ago”, they were operationally defined as in the Menstrual group. If the participant answered “8 - 14 days ago” they were assigned to the Follicular group. If the response was “15 - 28 days ago”, they were assigned to the Luteal group. This group assignment was based on the traditional phases of the menstrual cycle as described by Fehring, Schneider, and Raviele (2006).

Participant Demographics

Using the criteria described above to classify participants into one of three groups, the Menstrual group totaled 126 participants, the Follicular group had 150 participants, and the Luteal group represented 255 women.

The average age of the participants was 19.1 years, SD = 1.6 years. The average BMI of the participants was 23.8 kg/m^2, SD = 5.1 kg/m^2. There were no significant differences between the groups on these two variables. There was a diverse spread of participants across race and college status. Ninety-eight percent of the women were not married. The demographic descriptions for each group are listed in Table 3 below. A chi-square analysis revealed no significant differences between the three groups of participants on any categorical variable.

Table 3: *Participants' gender, race, marital status, and college status by Group*

Variables	Menstrual (N=126)		Follicular (N=150)		Luteal (N=255)	
	N	%	N	%	N	%
Race*						
White	78	14.7	79	14.9	133	25.0
Black	15	2.8	26	4.9	42	7.9
Hispanic/Latino	25	4.7	51	9.6	77	14.5
Asian/Pacific Islander	12	2.3	14	2.6	21	4.0
Native American	1	0.2	0	0	2	0.4
Other	5	0.9	6	1.1	14	2.6
Marital status						
Not married	124	23.4	147	27.7	251	47.3
Married	2	0.4	3	0.6	4	0.8
College status						
Freshman	76	14.3	88	16.6	156	29.4
Sophomore	20	3.8	23	4.3	32	6.0
Junior	16	3.0	19	3.6	40	7.5
Senior	14	2.6	19	3.6	27	5.1
Unclassified	0	0	1	0.2	0	0

* Race frequency values are not additive because participants selected multiple racial identifications

RESULTS

All statistical analyses were conducted on SPSS version 26. Means and standard deviations for the measures are presented by group in Table 4.

Table 4: *Mean and Standard Deviations of GI PROMIS scales by Group*

GI-PROMIS Measure	Menstrual (N=126)		Follicular (N=150)		Luteal (N=255)	
	Mean	SD	Mean	SD	Mean	SD
Belly Pain	55.452	9.891	53.473	9.484	52.794	10.322
Nausea	53.192	8.750	51.203	8.413	51.875	8.581
Diarrhea	46.796	7.555	46.428	8.006	46.287	7.268
Constipation	49.572	7.771	49.228	7.619	49.938	7.301
Gas	55.944	5.851	54.840	7.508	54.829	6.912
Swallow	48.063	7.123	46.625	6.023	47.496	6.544
Reflux	45.074	8.071	44.367	6.834	45.515	7.245

A MANCOVA was conducted on the seven GI PROMIS scales with the three Menstrual groups as a fixed factor and the SHAI score as a covariate. No significant multivariate main effect for group was obtained, indicating that the GI PROMIS measures were not significantly distinguishable between the three groups. However, a significant multivariate main effect was obtained for the SHAI covariate ($F(7, 521) = 17.830$, $p = 0.000$, Pillai's $V = .193$, partial $\eta 2 = .193$, power = 1.0), which demonstrates that the SHAI scores had a significant effect on the GI PROMIS scores across all three groups.

Next, the tests of between-subjects effects were reviewed for the seven GI PROMIS subscales with the three groups as a fixed factor and the SHAI scores as a covariate. These were planned comparisons since differences between the groups on the GI PROMIS Scales was a central purpose of this study. The Belly Pain GI subscale demonstrated a significant difference

between the three groups (F (2, 527) = 3.253, p = 0.039, partial η2 = 0.012, power = .619). Further planned comparisons revealed that there was a significant difference between the Menstrual and Luteal groups on the GI PROMIS Belly pain scores (p = 0.012). Review of Table 4 indicates that the Menstrual group had higher GI PROMIS Belly Pain than the Luteal group. No other contrasts were significant.

The SHAI scores were a significant covariate for each of the seven PROMIS GI scales, illustrated in Table 5. This indicates that SHAI was a significant moderator for women's reporting of their GI pain symptoms across all seven PROMIS GI subscales. Additionally, a Bivariate correlation test was performed to indicate the direction and strength of the relationship between SHAI scores and GI PROMIS scale T-scores. This is demonstrated in Table 6.

Table 5: *SHAI covariance with the GI PROMIS scale T-Scores*

GI PROMIS T-Scores By Scale	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared	Observed Power
Belly Pain	4933.329	1	4933.329	54.435	.000	.094	1.000
Constipation	2093.915	1	2093.915	39.916	.000	.070	1.000
Diarrhea	1496.953	1	1496.953	27.577	.000	.050	.999
Gas and Bloating	2006.957	1	2006.957	46.381	.000	.081	1.000
Nausea	3961.603	1	3961.603	59.888	.000	.102	1.000
Swallow	1210.341	1	1210.341	29.789	.000	.054	1.000
Reflux	3515.397	1	3515.397	74.346	.000	.124	1.000

Table 6: *SHAI correlation with the GI PROMIS scale T-Scores*

	Belly Pain T score	Constipation T score	Diarrhea T score	Gas T score	Nausea T score	Swallow T score	Reflux T Score
Pearson Correlation	.305	.264	.223	.284	.317	.229	.350
Sig. (2-tailed)	.000	.000	.000	.000	.000	.000	.000

Next, I turned to the analysis of the Pain Map by group. The means and standard deviations for the nine pain ratings are presented by group in Table 7.

Table 7: *Mean and Standard Deviations of Pain Map regions by Group*

Pain Map Region	Menstrual (N=126)		Follicular (N=150)		Luteal (N=255)	
	Mean	SD	Mean	SD	Mean	SD
A – Right Hypochondriac	0.587	1.161	0.827	1.574	0.839	1.705
B – Epigastric	1.016	1.711	1.040	1.806	1.231	2.138
C – Left Hypochondriac	0.714	1.528	0.691	1.331	0.830	1.683
D – Right Lumbar	1.262	1.911	1.300	2.154	1.228	2.039
E – Umbilical Region	2.333	2.626	2.393	2.664	2.373	2.751
F – Left Lumbar	1.397	2.016	1.260	2.128	1.322	2.098
G – Right Iliac	2.460	2.957	1.987	2.642	1.929	2.733
H – Hypogastric	4.198	3.145	3.687	3.028	3.094	3.153
I – Left Iliac	2.413	2.935	1.900	2.564	1.859	2.721

A MANCOVA was performed using the nine ratings from the Pain Map with the three groups as a fixed factor and the SHAI score as a covariate. No significant multivariate effect was obtained by group, which indicates that the Pain Map ratings were not significantly affected by the three groups. However, a significant multivariate effect was obtained for the SHAI covariate ($F (9, 519) = 5.253$, $p = .000$, Pillai's $V = .083$, partial $\eta 2 = .083$, power = 1.0), which

demonstrates that the SHAI scores had a significant effect on the Pain Map ratings across all three groups.

Next, the tests of between-subjects effects as planned comparisons were reviewed for the nine Pain Map regions with the three groups as a fixed factor and the SHAI scores as a covariate. The Pain Map rating for Region H demonstrated a significant difference between the three groups ($F(2, 527) = 5.679$, $p = 0.004$, partial $\eta 2 = 0.021$, power = .862). Further planned comparisons revealed that there was a significant difference between the Menstrual and Luteal groups on the Pain Map ratings for Region H ($p = 0.001$). Review of Table 7 indicates that the Menstrual group had higher Pain rating at the hypogastric (Region H) compared to the Luteal group. No other contrasts were significant.

The SHAI scores were a significant covariate for each of the 9 Pain Map regions as illustrated in Table 8. This indicates that SHAI was a significant moderator for women's reporting of their belly pain severity across all nine belly pain map regions. Additionally, a Bivariate correlation test was performed to indicate the direction and strength of the relationship between SHAI scores and the Pain Map region scores. This is demonstrated in Table 9 below.

Table 8: *SHAI covariance with the Pain Map Region Scores*

Pain Map by Region	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared	Observed Power
A – Right Hypochondriac	16.534	1	16.534	6.916	.009	.013	.747
B – Epigastric	65.908	1	65.908	17.838	.000	.033	.988
C – Left Hypochondriac	35.749	1	35.749	15.200	.000	.028	.973
D – Right Lumbar	41.140	1	41.140	10.030	.002	.019	.885
E – Umbilical Region	189.170	1	189.170	27.296	.000	.049	.999
F – Left Lumbar	33.888	1	33.888	7.879	.005	.015	.800
G – Right Iliac	126.031	1	126.031	17.013	.000	.031	.985
H – Hypogastric	228.074	1	228.074	24.530	.000	.044	.999
I – Left Iliac	119.873	1	119.873	16.550	.000	.030	.982

Table 9: *SHAI correlation with the Pain Map Region Scores*

	A	B	C	D	E	F	G	H	I
Pearson Correlation	.114	.180	.167	.137	.222	.121	.176	.210	.174
Sig. (2-tailed)	.009	.000	.000	.002	.000	.005	.000	.000	.000

Exploratory analyses were conducted comparing participants who reported having received a medical FGID diagnoses with those who did not. This was conducted on all participants without regard to whether they had reported a period starting in the last 28 days. This resulted in a total of 677 participants who were assigned to a FGID group or Non-FGID group. Women who self-reported a diagnosis of IBS, Crohn's Disease, IBD, or Ulcerative Colitis

were placed in the FGID group (n = 31) and the remaining women were placed in the non-FGID group (n = 646).

The means and standard deviations for the GI-PROMIS measures are presented by FGID group in Table 10.

Table 10: *Mean and Standard Deviations of GI PROMIS scales by Group (FGID and Non-FGID)*

GI-PROMIS Measure	FGID (N=31)		Non-FGID (N=646)	
	Mean	SD	Mean	SD
Belly Pain	62.116	8.531	53.176	9.8986
Nausea	53.548	8.624	51.924	8.501
Diarrhea	51.197	8.584	46.005	7.393
Constipation	55.826	6.630	49.595	7.393
Gas	59.716	6.867	54.886	6.847
Swallow	48.868	6.465	47.375	6.615
Reflux	49.868	8.472	44.743	7.210

A MANCOVA was conducted on the seven GI PROMIS scales with the two groups (FGID and Non-FGID) as a fixed factor and the SHAI score as a covariate. There was a significant multivariate main effect for group ($F (7, 668) = 5.054$, $p = 0.000$, Pillai's $V = .050$, partial $\eta 2 = .050$, power = 0.997). This indicates that the GI PROMIS scales were able to discriminate between participants with FGIDS and without FGIDS. A significant multivariate main effect was also obtained for the SHAI covariate ($F (7, 668) = 22.368$, $p = 0.000$, Pillai's $V = .190$, partial $\eta 2 = .190$, power = 1.0).

The tests of between-subjects effects were reviewed for the seven GI PROMIS subscales with the two groups (FGID and Non-FGID) as a fixed factor and the SHAI scores as a covariate. Five of the seven GI PROMIS subscales demonstrated significant differences between groups: Belly Pain, Constipation, Diarrhea, Gas, and Reflux. The values are shown in Table 11 below.

For these five GI PROMIS subscales, the FGID group reported higher symptom severity scores compared to the non-FGID groups, as seen in Table 10.

Table 11*: Main Effect of Group (FGID and Non-FGID) on Individual GI PROMIS scale T-Scores*

GI PROMIS T-Scores By Scale	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared	Observed Power
Belly Pain	1446.630	1	1446.630	16.167	.000	.023	.980
Constipation	708.798	1	708.798	13.972	.000	.020	.962
Diarrhea	477.813	1	477.813	9.042	.003	.013	.851
Gas and Bloating	367.821	1	367.821	8.451	.004	.012	.827
Reflux	329.547	1	329.547	7.106	.008	.010	.759

The SHAI scores were a significant covariate for each of the seven PROMIS GI scales and FGID group, as illustrated in Table 12. This demonstrates that SHAI was a significant moderator for women of both the FGID and non-FGID groups in the reporting of their GI pain symptoms across all seven PROMIS GI subscales.

Table 12: *SHAI covariance with the GI PROMIS scale T-scores & Group (FGID and Non-FGID)*

GI PROMIS T-Scores By Scale	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared	Observed Power
Belly Pain	5072.056	1	5072.056	56.683	.000	.078	1.000
Constipation	2382.801	1	2382.801	46.969	.000	.065	1.000
Diarrhea	1845.145	1	1845.145	34.917	.000	.049	1.000
Gas and Bloating	2316.240	1	2316.240	53.216	.000	.073	1.000
Nausea	4655.639	1	4655.639	71.009	.000	.095	1.000
Swallow	1749.974	1	1749.974	42.540	.000	.059	1.000
Reflux	4428.838	1	4428.838	95.497	.000	.124	1.000

In addition, I analyzed the difference in Pain Map scores by group (FGID and Non-FGID). The means and standard deviations for the 9 pain regions are presented by group in Table 13.

Table 13: *Mean and Standard Deviations of Pain Map regions by Group (FGID and Non-FGID)*

Pain Map Region	FGID (N=31)		No FGID (N=646)	
	Mean	SD	Mean	SD
A – Right Hypochondriac	1.065	2.081	0.728	1.515
B – Epigastric	2.097	3.113	1.014	1.807
C – Left Hypochondriac	0.960	2.121	0.744	1.536
D – Right Lumbar	1.355	2.138	1.201	2.028
E – Umbilical Region	4.871	2.790	2.195	2.612
F – Left Lumbar	1.903	2.599	1.269	2.086
G – Right Iliac	2.484	2.839	2.077	2.784
H – Hypogastric	5.161	2.782	3.435	3.170
I – Left Iliac	3.000	3.141	2.011	2.759

A MANCOVA was performed using the 9 ratings from the Pain Map with the two FGID groups as a fixed factor and the SHAI score as a covariate. There was a significant multivariate effect obtained by FGID group ($F(9, 666) = 4.378$, $p = .000$, Pillai's $V = .056$, partial $\eta 2 = .056$, power = .998). Also, there was a significant multivariate effect obtained for the SHAI covariate ($F(9, 666) = 6.360$, $p = .000$, Pillai's $V = .079$, partial $\eta 2 = .079$, power = 1.0).

The test of between-subjects effects for the 9 pain map regions and the FGID groups demonstrated that there is a significant difference in regions B, E, and H. The values are listed in Table 14. The results indicate that the FGID group experienced more pain in the Epigastric region (Region B), Umbilical region (Region E), and Hypogastric region (Region H) compared to the non-FGID group.

Table 14: *Main Effect of Group (FGID and Non-FGID) on Pain Region Ratings*

Pain Map By Region	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared	Observed Power
B – Epigastric	21.747	1	21.747	6.291	.012	.009	.707
E – Umbilical Region	156.652	1	156.652	23.699	.000	.034	.998
H – Hypogastric	47.020	1	47.020	4.938	.027	.007	.602

The SHAI scores were a significant covariate for every individual region on the Pain Map. This is shown in Table 15 below. This demonstrates that health anxiety was a significant moderator for women of both the FGID and non-FGID groups in the reporting of their belly pain severities across all nine belly pain regions.

Table 15: *SHAI covariance with the Pain Map Region Scores*

Pain Map by Region	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared	Observed Power
A – Right Hypochondriac	13.914	1	13.914	5.876	.016	.009	.677
B – Epigastric	67.662	1	67.662	19.573	.000	.028	.993
C – Left Hypochondriac	45.361	1	45.361	18.984	.000	.027	.992
D – Right Lumbar	55.047	1	55.047	13.571	.000	.020	.957
E – Umbilical Region	177.756	1	177.756	26.892	.000	.038	.999
F – Left Lumbar	68.334	1	68.334	15.658	.000	.023	.977
G – Right Iliac	125.347	1	125.347	16.523	.000	.024	.982
H – Hypogastric	295.347	1	295.347	31.018	.000	.044	1.000
I – Left Iliac	126.408	1	126.408	16.770	.000	.024	.983

DISCUSSION

A review of the literature on the assessment of patient-reported outcomes consistently finds that women report higher levels of GI symptoms than men. Men and women differ on many biopsychosocial variables. One of the most prominent is that women experience hormonal changes in relation to their menstrual cycle. This study asks the question of whether the higher levels of GI symptoms experienced by women may be related to the different stages of the menstrual cycle. A relatively new clinical instrument, the GI PROMIS Scales were used to assess the broad range of gastrointestinal functioning in our participants. In addition, a Pain Map was used so that participants could precisely identify the regions of the abdomen where they experience pain.

Prior to analysis, participants were initially categorized into one of three groups based on the menstrual phase they reported. They were placed into a Menstrual group if they were in the 7-day window that the woman reported menstruating, the Follicular group if they were in the 7-day period following the end of the menstruation, and the Luteal group if they reported they were in the 14-day period following their follicular phase.

Given the literature review, it was hypothesized that there would be higher GI symptoms in the Menstrual group and Luteal group versus the Follicular group. However, this hypothesis was not supported because no significant **multivariate** differences between the groups on the GI PROMIS scales or the Pain Map were observed. This means that when these variables were considered together, they did not discriminate between the phases of menstrual cycle in healthy young women with regular 28-day periods. However, a significant difference between the

Menstrual and Luteal groups was observed on selected pain measures in the planned comparisons. The Menstrual group reported higher Belly Pain T scores compared to the Luteal group. This was the only difference between the groups on any GI PROMIS scale.

This difference may be explained in part by a review of the Pain Map analyses, which found that women in the Menstrual group reported significantly higher pain in the hypogastric region (Region H) compared to women in the Luteal group. The hypogastric region is associated with the female reproductive organs that are most often implicated in menstrual pain. With these two findings in mind, one can infer that the increased GI PROMIS Belly Pain T score elevations are likely to originate from the hypogastric region (Region H) and are related to the menstrual cycle. Fortunately, these symptoms are easily discriminated from other significant GI symptoms because of their specific location and periodicity.

Thus, only minor differences in the GI PROMIS scales were observed across groups. Furthermore, the influence of the menstrual cycle on these measures was easy to discriminate from gastrointestinal symptoms and probably pain due to menstrual cramping. These results demonstrate that except for one GI PROMIS score – Belly Pain, the GI PROMIS subscales did not vary significantly with the phases of the menstrual cycle. Taken together, the findings indicate that the PROMIS GI scales appear to be relatively unaffected by physical symptoms arising from the menstrual cycle in women.

A secondary hypothesis was that health anxiety would be significantly correlated with higher GI PROMIS symptom severity and higher belly pain scores across all the phases of the menstrual cycle. The statistical analyses showed that all the PROMIS GI scales, as well as all the Pain map regions, covaried significantly with the Short Health Anxiety Inventory, as evidenced

by Tables 5 and 8. This indicates that health anxiety is a significant moderating variable in women reporting of GI symptoms and Pain ratings, suggesting a possible mechanism for the previously documented sex differences in GI symptom reporting.

Additionally, the results of the exploratory analyses suggest that there are significant differences between the FGID and non-FGID groups on the GI PROMIS scales and Pain Map ratings, with FGID groups reporting more GI symptoms and greater Abdominal Pain experienced. The FGID disorders encompass gastroduodenal disorders, bowel disorders, and centrally mediated disorders, to name a few. The increased severity noted in the FGID group for the Constipation, Diarrhea, and Gas subscales is attributed to bowel disorders. The increased Belly Pain scores in the FGID groups in conjunction with the Pain Map analysis suggest that the belly pain experienced from these FGID diagnoses is localized to the middle column of the abdomen (epigastric region, umbilical region, and hypogastric region). These findings support the utility of the GI PROMIS scales in the diagnoses of FGID disorders, because it is expected that FGID groups will report significantly higher GI symptom severity compared to non-FGID groups.

Limitations

One limitation of this study was that the classification of women into one of the three menstrual phase groups was entirely based on women's self-report of the start and end date of their most recent period. This introduces the possibility of participant recall error. Another limitation was that women were filtered out and placed into one of three groups assuming that every woman had a 28-day menstrual cycle. Women were excluded from the study if they

reported a period length greater than 28 days. This is a possible source of error because not all women have a regular, 28-day menstrual cycle, so some participants may have been erroneously excluded from data analyses, while some participants may have been placed into the wrong group.

Clinical Implications

This study supports the utility of the GI PROMIS scales in assessing gastrointestinal symptom severity, given that the results from this study showed that the GI PROMIS scales were relatively unaffected by the physical symptoms arising during the different phases of the menstrual cycle. The exploratory analyses yielded a significant difference between the FGID and non-FGID groups on the GI-PROMIS scales, which further validates the use of the GI-PROMIS scales in diagnosing FGIDs.

This study suggests that researchers and clinicians should factor in a woman's menstrual cycle when interpreting belly pain symptoms. The results showed that women in the menstrual phase reported belly pain symptoms originating in the hypogastric region, suggesting that their reported belly pain symptoms may be in part due to menstrual pain. Given that the GI PROMIS Belly Pain scale does not provide specific location information, I encourage clinicians to utilize a pain map diagram to further localize the regions of belly pain to distinguish between menstrual cycle-related pain and GI pain.

The findings also highlight that health anxiety plays a significant role in the severity of GI symptoms. Clinicians may consider factoring in health anxiety in the diagnosis and treatment

of their patients. If necessary, clinicians can refer patients to the appropriate mental health practitioners to help patients manage their health anxiety.

Future Directions

Several studies have been published suggesting women experience higher levels of health anxiety. This suggests a possible mechanism for sex differences in GI symptom reporting. Future work should therefore include health anxiety as a moderator in studies with men.

Given the cross-sectional design of this study, a more reliable marker of determining women's current menstrual phase would be optimal for future studies, such as obtaining blood samples. Additionally, the cross-sectional design of this study did not facilitate any conclusions to be made on the direction of GI symptom variations between the different menstrual cycle phases. A future study may utilize longitudinal GI symptom reporting to address that.

These results may not be generalizable for women above the age 18-25, so this study needs to be replicated with older women.

Despite the limitations of this study, this research provides the first investigation into quantifying the associations of a full range of GI symptoms across the phases of the menstrual cycle. The results of this study are that the GI symptoms do not vary significantly across the phases of the menstrual cycle. In fact, the reporting of GI pain in women in any phase of the menstrual cycle is highly influenced by health anxiety, which provides a possible explanation for the sex-based differences in GI pain between men and women.

APPENDIX

APPENDIX A: IRB EXEMPT DETERMINATION LETTER

UNIVERSITY OF CENTRAL FLORIDA

Institutional Review Board
FWA00000351
IRB00001138, IRB00012110
Office of Research
12201 Research Parkway
Orlando, FL 32826-3246

EXEMPTION DETERMINATION

June 18, 2020

Dear Jeffrey Cassisi:

On 6/18/2020, the IRB determined the following submission to be human subjects research that is exempt from regulation:

Type of Review:	Initial Study
Title:	Gastrointestinal Symptoms and Belly Pain during the Phases of the Menstrual Cycle in Otherwise Healthy Young Females: A Cross-sectional Study
Investigator:	Jeffrey Cassisi
IRB ID:	STUDY00001918
Funding:	None
Grant ID:	None
Documents Reviewed:	• Explanation of Research, Category: Consent Form; • Measures used in the survey, Category: Survey / Questionnaire; • Request for Exemption, Category: IRB Protocol;

This determination applies only to the activities described in the IRB submission and does not apply should any changes be made. If changes are made, and there are questions about whether these changes affect the exempt status of the human research, please submit a modification request to the IRB. Guidance on submitting Modifications and Administrative Check-in are detailed in the Investigator Manual (HRP-103), which can be found by navigating to the IRB Library within the IRB system. When you have completed your research, please submit a Study Closure request so that IRB records will be accurate.

If you have any questions, please contact the UCF IRB at 407-823-2901 or irb@ucf.edu. Please include your project title and IRB number in all correspondence with this office.

Due to current COVID-19 restrictions, in-person research is not permitted to begin until you receive further correspondence from the Office of Research stating that the restrictions have been lifted.

Sincerely,

Kamille C. Birkbeck

Kamille Birkbeck
Designated Reviewer

APPENDIX B: DEMOGRAPHICS QUESTIONNAIRE

Start of Block: Demographics

D1 Month of your birth?

▼ January (1) ... December (12)

D3 Year of your birth

▼ 1995 (1) ... 2002 (8)

D4 Are you between the age of 18 and 25?

- Yes (1)
- No (2)

D5 What is your gender identity?

- Male (1)
- Female (2)
- Other (3) _____

D6 What is your biological sex?

- ○ Male (1)
- ○ Female (2)

D7 What is your racial or ethnic identification? (fill in all that apply)

- ☐ American Indian or other Native American (1)
- ☐ Asian or Pacific Islander (2)
- ☐ Black or African American (3)
- ☐ Caucasian (other than Hispanic) (4)
- ☐ Mexican-American (5)
- ☐ Puerto Rican (6)
- ☐ Other Hispanic (7)
- ☐ Other (8)

D8 What is your marital status?

- Not married (1)
- Married (2)
- Divorced (3)
- Separated (4)
- Widowed (5)

D9 What is your classification in college?

- Freshman/first-year (1)
- Sophomore (2)
- Junior (3)
- Senior (4)
- Graduate Student (5)
- Unclassified (6)

End of Block: Demographics

APPENDIX C: PHYSIOLOGICAL PROFILE QUESTIONNAIRE

Start of Block: Physiological Profile

P1 How tall are you?

Feet

▼ 4 Ft (4) ... 7 Ft (7)

P2 Inches

▼ 0 (0) ... 11 (11)

P3 How much do you weigh, in pounds (lbs)?
If you have a scale, go ahead and weigh yourself.

_____

P4 Are you currently pregnant?

- ○ Yes (1)
- ○ No (2)

Skip To: End of Survey If Are you currently pregnant? = Yes

P5 When was the date of the start of your last period? Be as accurate as possible.

Month (1)	▼ January (1) ... Click to write Scale Point 31 (31)
Day (2)	▼ January (1) ... Click to write Scale Point 31 (31)
Year (3)	▼ January (1) ... Click to write Scale Point 31 (31)

JS

P6 What was the date of the end of your last period? Be as accurate as possible.

Month (1)	▼ January (1) ... Click to write Scale Point 31 (31)
Day (2)	▼ January (1) ... Click to write Scale Point 31 (31)
Year (3)	▼ January (1) ... Click to write Scale Point 31 (31)

X→

P7 How many days ago did your most recent period start?

▼ 0 (0) ... Other (100)

P8 If your previous answer was "Other", write in the number of days since your most recent period started.

_____

P9 For the past 6 months, has your period been regular?

- ○ Yes (1)
- ○ No (2)

X→

P10 Are you currently on any birth control method?

- ○ Pill (1)
- ○ IUD (2)
- ○ Shot (3)
- ○ Implant (4)
- ○ Spermicide (5)
- ○ Patch (6)
- ○ I am not on any birth control (7)

X→

P11 Are you receiving medical treatment for any of the following? Select all that apply.

- ☐ Ulcerative Colitis (1)
- ☐ Irritable Bowel Syndrome (IBS) (2)
- ☐ Gastritis (3)
- ☐ Crohn's Disease (4)
- ☐ Stomach Ulcers (5)
- ☐ Inflamatory Bowel Disease (6)
- ☐ Functional Dyspepsia (7)
- ☐ Premenstrual Syndrome (PMS) (8)
- ☐ Dysmenorrhea (9)
- ☐ Amenorrhea (10)
- ☐ Menorrhagia (11)
- ☐ Other (12) _____

P12 Do you experience gastrointestinal symptoms when you are on your period?

- ○ Yes (1)
- ○ No (2)

Skip To: P14 If Do you experience gastrointestinal symptoms when you are on your period? = No

P13 If yes, can you describe the symptoms you experience? (ex. belly pain, nausea, constipation)

_____

_____

P14
Do you experience gastrointestinal symptoms when you are NOT on your period?

- Yes (1)
- No (2)

Skip To: End of Block If Do you experience gastrointestinal symptoms when you are NOT on your period? = No

P15 If yes, can you describe the symptoms you experience? (ex. belly pain, nausea, constipation)

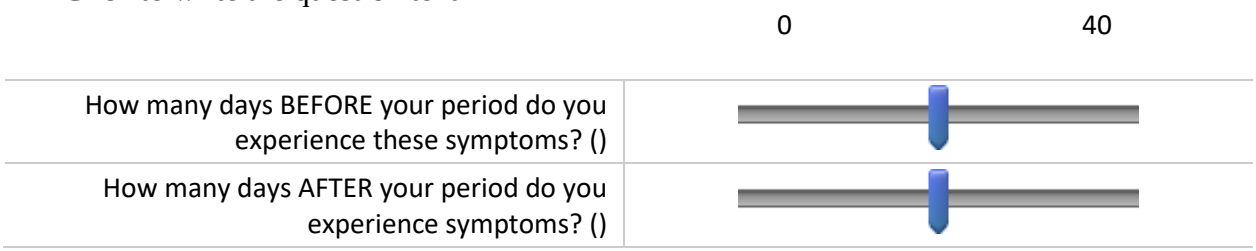
_____

_____

P16 When in the menstrual cycle do you experience gastrointestinal symptoms?

- 1 week before my period (1)
- 1 week after my period (2)
- 2 weeks after my period (3)

P17 Click to write the question text



End of Block: Physiological Profile

REFERENCES

Abramowitz, J. S., Deacon, B. J., & Valentiner, D. P. (2007). The Short Health Anxiety Inventory: Psychometric Properties and Construct Validity in a Non-clinical Sample. *Cognitive therapy and research*, *31*(6), 871–883. https://doi.org/10.1007/s10608-006-9058-1

Berkley K. J. (1997). Sex differences in pain. *The Behavioral and brain sciences*, *20*(3), 371–513. https://doi.org/10.1017/s0140525x97221485

Bernstein, M.T., Graff, L.A., Targownik, L.E., Downing, K., Shafer, L.A., Rawsthorne, P., Bernstein, C.N. and Avery, L. (2012), Gastrointestinal symptoms before and during

menses in women with IBD. Aliment Pharmacol Ther, 36: 135-144. doi:10.1111/j.1365-2036.2012.05155.x

Bernstein, M. T., Graff, L. A., Avery, L., Palatnick, C., Parnerowski, K., & Targownik, L. E. (2014). Gastrointestinal symptoms before and during menses in healthy women. *BMC women's health*, *14*, 14. https://doi.org/10.1186/1472-6874-14-14

Boyle, Gregory J. & Grant, Amanda. (1992). Prospective versus retrospective assessment of Menstrual cycle symptoms and moods: Role of Attitudes and beliefs. Journal of Psychopathology and Behavioral Assessment. 14. 307-321. 10.1007/BF00960776.

Carabotti, M., Scirocco, A., Maselli, M. A., & Severi, C. (2015). The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems. *Annals of gastroenterology: quarterly publication of the Hellenic Society of Gastroenterology*, *28*(2), 203.

De Palma, G., Collins, S. M., Bercik, P., & Verdu, E. F. (2014). The microbiota–gut–brain axis in gastrointestinal disorders: stressed bugs, stressed brain or both? *The Journal of physiology*, *592*(14), 2989-2997.

Drossman, D. A. (1988). Irritable bowel syndrome: A multifactorial disorder. *Hospital Practice*, *23*(9), 119-133.

Drossman, D. A., Camilleri, M., Mayer, E. A., & Whitehead, W. E. (2002). AGA technical review on irritable bowel syndrome. *Gastroenterology*, *123*(6), 2108–2131. https://doi.org/10.1053/gast.2002.37095

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

Fehring, R. J., Schneider, M., & Raviele, K. (2006). *Variability in the Phases of the Menstrual Cycle. Journal of Obstetric, Gynecologic & Neonatal Nursing, 35(3), 376–384.* doi:10.1111/j.1552-6909.2006.00051.x

Gwee, K. A., Leong, Y. L., Graham, C., McKendrick, M. W., Collins, S. M., Walters, S. J., Underwood, J. E., & Read, N. W. (1999). The role of psychological and biological factors in postinfective gut dysfunction. *Gut*, *44*(3), 400–406. https://doi.org/10.1136/gut.44.3.400

Kiesner, J., Mendle, J., Eisenlohr-Moul, T. A., & Pastore, M. (2016). Cyclical symptom change across the menstrual cycle: Attributional, affective, and physical symptoms. *Clinical Psychological Science*, *4*(5), 882–894. https://doi.org/10.1177/2167702616635031

Logue, C. M., & Moos, R. H. (1986). Perimenstrual symptoms: Prevalence and risk factors. *Psychosomatic Medicine*, *48*(6), 388–414. https://doi.org/10.1097/00006842-198607000-00002

Mari-Ann Wallander, Saga Johansson, Ana Ruigómez, Luis Alberto García Rodríguez, Roger Jones, Dyspepsia in general practice: incidence, risk factors, comorbidity and mortality, *Family Practice*, Volume 24, Issue 5, October 2007, Pages 403–411, https://doi.org/10.1093/fampra/cmm050

Mayer, E. A., Berman, S., Chang, L., & Naliboff, B. D. (2004). Sex-based differences in gastrointestinal pain. *European Journal of Pain*, *8*(5), 451–463. https://doi.org/10.1016/j.ejpain.2004.01.006

Mayer, E. A., Tillisch, K., & Gupta, A. (2015). Gut/brain axis and the microbiota. *The Journal of clinical investigation*, *125*(3), 926-938.

Negriff, S., Dorn, L. D., Hillman, J. B., & Huang, B. (2009). The measurement of menstrual symptoms: factor structure of the menstrual symptom questionnaire in adolescent girls. *Journal of Health Psychology, 14(7), 899–908.* doi:10.1177/1359105309340995

Riley, J. L., 3rd, Robinson, M. E., Wise, E. A., Myers, C. D., & Fillingim, R. B. (1998). Sex differences in the perception of noxious experimental stimuli: a meta-analysis. *Pain*, *74*(2-3), 181–187. https://doi.org/10.1016/s0304-3959(97)00199-1

Ross, C., Coleman, G., & Stojanovska, C. (2003). *Prospectively reported symptom change across the menstrual cycle in users and non-users of oral contraceptives. Journal of Psychosomatic Obstetrics & Gynecology, 24(1), 15–29.* doi:10.3109/01674820309042797

Salkovskis, P. M., Rimes, K. A., Warwick, H. M., & Clark, D. M. (2002). The Health Anxiety Inventory: development and validation of scales for the measurement of health anxiety and hypochondriasis. *Psychological medicine*, *32*(5), 843–853. https://doi.org/10.1017/s0033291702005822

Schmulson, M. J., & Drossman, D. A. (2017). What Is New in Rome IV. *Journal of neurogastroenterology and motility*, *23*(2), 151–163. https://doi.org/10.5056/jnm16214

Sjoudin, I., Svedlund, J., Dotevall, G., & Gillber, R. (1985) Symptom Profiles in Chronic Peptic Ulcer Disease, Scandinavian Journal of Gastroenterology, 20:4, 419-427, DOI: 10.3109/00365528509089674

Spiegel, B. M., Hays, R. D., Bolus, R., Melmed, G. Y., Chang, L., Whitman, C., Khanna, P. P., Paz, S. H., Hays, T., Reise, S., & Khanna, D. (2014). Development of the NIH Patient-Reported Outcomes Measurement Information System (PROMIS) gastrointestinal

symptom scales. *The American journal of gastroenterology*, *109*(11), 1804–1814. https://doi.org/10.1038/ajg.2014.237

Svedlund, J., Sjoudin, I., Dotevall, G., & Gillber, R. (1985). Upper Gastrointestinal and Mental Symptoms in the Irritable Bowel Syndrome. *Scandinavian Journal of Gastroenterology*, 20:5, 595-601, DOI: 10.3109/00365528509089702

Svedlund, J., Sjödin, I. & Dotevall, G. (1988). GSRS—A clinical rating scale for gastrointestinal symptoms in patients with irritable bowel syndrome and peptic ulcer disease. *Digest Dis Sci* 33, 129–134. https://doi.org/10.1007/BF01535722

Taub, E., Cuevas, J. L., Cook, E. W., 3rd, Crowell, M., & Whitehead, W. E. (1995). Irritable bowel syndrome defined by factor analysis. Gender and race comparisons. *Digestive diseases and sciences*, *40*(12), 2647–2655. https://doi.org/10.1007/BF02220455

Thompson W. G. (1984). Gastrointestinal symptoms in the irritable bowel compared with peptic ulcer and inflammatory bowel disease. *Gut*, *25*(10), 1089–1092. https://doi.org/10.1136/gut.25.10.1089

Unruh A. M. (1996). Gender variations in clinical pain experience. *Pain*, *65*(2-3), 123–167. https://doi.org/10.1016/0304-3959(95)00214-6

Van den Akker, O., & Steptoe, A. (1985). The pattern and prevalence of symptoms during the menstrual cycle. *The British Journal of Psychiatry, 147(2), 164–169.* doi:10.1192/bjp.147.2.164

Vivier, Helize, "Determining Common Patterns of Gastrointestinal Health in Emerging Adults: A Latent Class Analysis Approach" (2019). Honors Undergraduate Theses. 461. https://stars.library.ucf.edu/honorstheses/461

Walker L. S. (1999). Pathways between recurrent abdominal pain and adult functional gastrointestinal disorders. *Journal of developmental and behavioral pediatrics : JDBP*, *20*(5), 320–322. https://doi.org/10.1097/00004703-199910000-00005

Whitehead, W. E., Bosmajian, L., Zonderman, A. B., Costa Jr, P. T., & Schuster, M. M. (1988). Symptoms of psychologic distress associated with irritable bowel syndrome: comparison of community and medical clinic samples. *Gastroenterology*, *95*(3), 709-714.

Williamson, A., & Hoggart, B. (2005). Pain: a review of three commonly used pain rating scales. *Journal of clinical nursing*, *14*(7), 798–804. https://doi.org/10.1111/j.1365-2702.2005.01121.x