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The Relationship Between Gastrointestinal Disease and Post-Traumatic Stress Disorder in United States Military Veterans

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The Relationship Between Gastrointestinal Disease and Post-Traumatic Stress Disorder in United States Military Veterans

by

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The Relationship Between Gastrointestinal Disease and Post-Traumatic Stress Disorder in United States Military Veterans

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Abstract

This study examined relationship between gastrointestinal disease (GI Disease) and post-traumatic stress disorder (PTSD) in United States Military Veterans. Based upon literature and clinical practice data sources from the US Veterans Administration, GI disease and PTSD were hypothesized to be positively correlated in Veterans. The *specific aims* of the study were to determine the frequency with which: 1) GI Disease and PTSD are diagnosed co-morbidities; 2) a diagnosis of GI Disease accompanies a diagnosis of PTSD; and, 3) a diagnosis of PTSD accompanies a diagnosis of a GI Disease. The *methodology* was a retrospective, correlational design using data collect from the Department of Veteran's Affairs Patient Database. *Findings* were that PTSD is bi-directionally correlated with the GI diseases of gastroesophageal reflux disease (GERD), peptic ulcer disease, functional dyspepsia, Crohn's disease, diverticular disease, and irritable bowel syndrome (IBS), and the symptoms of constipation and nausea/vomiting within Veterans who served during wartime periods. The study also found that PTSD is not correlated with ulcerative colitis in Veterans.

TABLE OF CONTENTS

List of Tables and Figures

List of Abbreviations

Corporate Data Warehouse (CDW)

Data Access Request Tracker (DART)

Department of Veterans Affairs (VA)

Gastroesophageal reflux disease (GERD)

Gastrointestinal (GI)

Institutional Review Board (IRB)

Irritable bowel disease (IBD)

Irritable bowel syndrome (IBS)

National Data Systems (NDS)

National Institute of Mental Health (NIMH)

Peptic ulcer disease (PUD)

Period of Service (POS)

Post-traumatic stress disorder (PTSD)

Standardized Query Language (SQL) (pronounced “sequel”)

Tennessee Valley Healthcare System (TVHS)

Veterans’ Health Administration (VHA)

Abstract

This study examined relationship between gastrointestinal disease (GI Disease) and post-traumatic stress disorder (PTSD) in United States Military Veterans. Based upon literature and clinical practice data sources from the US Veterans Administration, GI disease and PTSD were hypothesized to be positively correlated in Veterans. The *specific aims* of the study were to determine the frequency with which: 1) GI Disease and PTSD are diagnosed co-morbidities; 2) a diagnosis of GI Disease accompanies a diagnosis of PTSD; and, 3) a diagnosis of PTSD accompanies a diagnosis of a GI Disease. The *methodology* was a retrospective, correlational design using data collect from the Department of Veteran's Affairs Patient Database. *Findings* were that PTSD is bi-directionally correlated with the GI diseases of gastroesophageal reflux disease (GERD), peptic ulcer disease, functional dyspepsia, Crohn's disease, diverticular disease, and irritable bowel syndrome (IBS), and the symptoms of constipation and nausea/vomiting within Veterans who served during wartime periods. The study also found that PTSD is not correlated with ulcerative colitis in Veterans.

Chapter One: Introduction

Introduction

Chapter One provides an introduction exploring the relationships between GI Disease and PTSD. The study problem is presented. Then an overview of the background and significance of the problem, statement of purpose and goals, research questions and aims, theoretical framework, study variables, and definition of terms are highlighted. In the Chapter's conclusion, an overview of the quantitative research methodology, data collection and analysis, and a brief overview of the study findings are presented.

Statement of the Problem

GI Disease, such as Irritable Bowel Syndrome (IBS), has been associated with anxiety and depression in numerous studies (Addolorado, et al., 2008; Haug, Mykletun, & Dahl, 2002). Post-traumatic stress disorder (PTSD), which can occur after experiencing or witnessing a traumatic life event (e.g. serving during wartime periods), has also been associated with symptoms of anxiety and depression. In the researcher's clinical experience, GI Disease and PTSD often occur together as co-morbidities. Logically, the *research question* arises regarding whether gastrointestinal disease (i.e., GI Disease) is linked to traumatic life events (i.e., PTSD). The *problem* of this study was to determine the relationship between GI Disease and PTSD in US military Veterans who have served during wartime periods.

Background and Significance of the Problem

Background

Post-Traumatic Stress Disorder (PTSD).

In the United States, the accepted standard of diagnosis for mental health disorders is the Diagnostic and Statistical Manual of Mental Disorders (DSM-5, 2013). PTSD was categorized in prior versions as an anxiety disorder until 2013 [American Psychiatric Association (APA), 2000]. Subsequently the revised DSM-5 reclassified PTSD under "Trauma- and Stressor-Related Disorders" (APA, p. 271). However, since Veteran records for this study were reviewed from as far back as 1999, many Veteran's diagnosis of mental illness may be based on the prior version, the DSM-IV-TR (APA, 2000), and possibly even the DSM-IV (APA, 1994).

The DSM-5 expands the criterion set for PTSD, to allow the traumatic event to include learning that a traumatic event occurred to a close relationship and "experiencing repeated or extreme exposure to aversive details of the traumatic events," (APA, 2013, p.271). This updated diagnostic criterion allows for more cases of PTSD diagnosis than under the former DSM-IV (APA, 1994) and DSM-IV-TR (APA, 2000). It is assumed that the healthcare provider used the most up-to-date version of the DSM available at the time of diagnosis.

Gastrointestinal Disease (GI Disease).

GI Disease is traditionally accepted as those diseases of the gastrointestinal tract, to include the esophagus, stomach, small intestine, large intestine and rectum, and the accessory organs of digestion, the liver, gallbladder, and pancreas (National Institute of Diabetes and Digestive and Kidney Diseases, 2018). For the purposes of this study, GI Disease was limited to those diseases that have had more than 500,000 ambulatory care visits annually in the United States, i.e. peptic ulcer disease, gastroesophageal reflux disease, diverticular disease, ulcerative colitis, Crohn's disease, irritable bowel syndrome,

chronic constipation, and functional dyspepsia. Additionally, the study limited GI disease to those of the GI tract, so that disorders of the liver, gallbladder, and pancreas were not included. Diseases with an identifiable non-GI cause, such as cancer, infection, hepatitis, and acute injury or hernia, were not included for the purposes of this study. Finally, this study distinguished between *functional GI Disease* (e.g. IBS, chronic constipation, and functional dyspepsia), and *structural GI Disease* (e.g. PUD, GERD, diverticular disease, ulcerative colitis, and Crohn's Disease).

Studies have shown that participants with gastrointestinal disorders such as Irritable Bowel Syndrome (IBS), (Ford, Miller, Eastwood, & Eastwood, 1987), and nonulcer dyspepsia (Locke, Weaver, Melton, & Talley, 2004) also reported the presence of anxiety and depression. Additionally, a study of 117 patients with IBS found that the presence of chronic life stressors was a predictor for lack of improvement in symptoms of IBS (Bennett, Tennant, Badcock, & Kellow, 1998). In Veterans, Maguen, et al, 2014, found that 20% of those returning from Iraq and Afghanistan had a gastrointestinal disease. Additionally, those Veterans with a mental health diagnosis were twice as likely to be diagnosed with gastrointestinal disease (Maguen, Madden, Cohen, Bertenthal & Seal, 2014). Most significantly, in a group of 21,264 African Americans, researchers selected all the individuals with IBS from this population (8.2%) and found those with IBS were significantly more likely to be diagnosed with PTSD (Iorio, Makipour, Palit, & Friedenburg, 2014).

The brain-gut connection. Commonly known as the brain-gut connection or the brain-gut axis is the communication link between the Enteric Nervous System (ENS) and the Central Nervous System (CNS). The ENS consists of millions of nerve cells that line

the GI tract from the esophagus to the rectum. The CNS consists of the brain and spinal cord and has long been thought to control the body and the mind. More recently, it has been discovered that the two systems communicate and interact with each other to effect both gut function and mood (Rhee, Pothoulakis, & Mayer, 2009). A main component of this connection is the vagus nerve, which oversees multiple systemic bodily functions in addition to facilitating communication between the gut and the brain. Research has identified the vagus nerve as a potential target for intervention in psychiatric illness, as stimulation of the nerve has been shown to trigger fibers in the gut that affect symptoms of mood and anxiety (Breit, Kupferberg, Rogler, & Hasler, 2018). Several other factors are also known to influence this system, including the stress response of the hypothalamic-pituitary-adrenal axis, the presence of corticotrophin releasing factor (CRF), and the presence of gut microbial (Bonaz & Bernstein, 2013).

The Corticotropin-releasing Factor (CRF). CRF, a hormone released during stress, increases colonic motility and induces fecal excretion. CRF antagonists have shown promising results in reducing anxiety and depression scores in some patients with depression. It has been suggested that this antagonist may also prove therapeutic in the treatment of mental health symptoms that occur in patients with IBS (Tache, Martinez, Million, and Wang, 2001). CRF is partially responsible for initiating a signaling cascade in the hypothalamic-pituitary-adrenal axis. When studied in mice, administration of CRF as well as urocortin peptides triggered anxiety-like behaviors, and "stimulated colonic secretion, intestinal motility, and visceral sensitivity," according to Fichna & Storr (2012). Similar elevated levels of CRF were found in the thalamus of neonatal rats experiencing separation from their mothers. (Fichna & Storr, 2012). Recent studies have

demonstrated “increased influence” from the thalamus to the middle/inferior frontal gyrus and insula in cases of PTSD (Zhang, Chen, Long, Cui, & Chen, 2016). This initial research into the circuit of CRF to thalamus may explain a connection between PTSD and GI symptoms but warrants further study before conclusions may be made.

Measurement of Colonic Pressure.

Rao, Hatfield, Suls, and Chamberlain (1998) used pressure sensors in the gut to measure colonic pressure activity during and after both psychological and physical stressors. While colonic motor activity was increased in both stressors, the activity ceased immediately after the end of the physical stressor but persisted long after the end of the psychological stressor. Rao, et al, 1998 suggested that psychological or emotional stress may contribute to the symptomology of functional GI disease.

While this study provided a wealth of knowledge regarding the relationship between stress and GI disease, the researchers only studied acute exposure to stress. Research is beginning to suggest potential mechanisms for functional GI diseases, especially IBS. These models propose a complex interaction of neural and immune systems. Animal models use chronic stress to trigger these systems, which have replicated symptoms of stress-disorders (Mayer & Collins, 2002).

The Gap

The research has long shown a relationship between GI symptoms and both stress and anxiety, (Ford, et al., 1987; Locke, et al., 2004; Rao, et al., 1998). There are also several studies that suggest a link between PTSD and GI Disease (Savas, et al, 2008; Maguen, et al, 2013), which warrants further research on the relationship between GI

Disease and PTSD in U.S. Military Veterans. The current research does not fully explore whether GI disease and PTSD accompany each other in Veterans. The literature does not state the risk of developing GI disease in Veterans diagnosed with PTSD. Conversely, the literature does not state the risk of PTSD diagnosis in those Veterans diagnosed with GI disease.

The Significance

This research is *significant*, because a correlation between GI disease and PTSD will enable providers to improve screening for co-occurring disease. This study utilized national data from the Department of Veterans Affairs patient records to examine the relationship between GI disease and military-related PTSD. By exploring GI disease as a potential predictor of PTSD, this study fulfills the National Institute of Mental Health's (NIMH) first aim or research priority, which is to "identify mechanisms that confer vulnerability to psychiatric illness" (2018, "Areas of High Priority," para. 4). A positive correlation between GI Disease and PTSD will provide information for future research that will address the second aim or priority of NIMH, which is to "develop early interventions for reducing the severity and incidence of psychopathology," (NIMH, 2018, "Areas of High Priority," para. 4).

Statement of Purpose, Goals, and Objectives

The Purpose

The *overall purpose* of this study is to determine if GI Disease is a predictor of PTSD in Veterans who have served during wartime periods.

The Goals

The *long-term goal* is to identify predictors of PTSD in Veterans who have served during wartime periods, in order to develop strategies to prevent new cases of PTSD from occurring.

The Objectives

The *overall objective* of this study is to determine the relationship between GI Disease and PTSD in Veterans who have served during wartime periods. This study was designed to use national data from the Department of Veterans Affairs to identify in populations of Veterans, who have served during wartime periods, those who have PTSD and/or GI Disease. GI Diseases include:

- Structural or motility diseases, e.g. gastroesophageal reflux disease (GERD), diverticular disease, inflammatory bowel disease (IBD), peptic ulcer disease (PUD), Crohn's disease, and ulcerative colitis; OR
- Functional diseases, e.g. functional dyspepsia, chronic constipation, and irritable bowel syndrome (IBS);

Completion of these objectives are expected to reveal the following outcomes in the Veteran population who have served during wartime periods:

- Beginning knowledge of the relationship between GI Diseases and PTSD,
- Additional knowledge that will aid in the formulation of future research regarding relationships between GI Disease and PTSD.

The Research Questions, Specific Aims, and Hypotheses

The *central hypothesis* is that in United States Veterans who have served during wartime periods, GI Disease and PTSD are positively correlated. The *rationale*

underlying the proposed research is that Veteran patients with co-occurring GI Disease and PTSD are frequently identified and documented in the researcher's clinical practice, but the relationship has yet to be fully explored in the literature. If such a relationship is identified, intervention strategies may be developed to identify risk factors and/or prevent or reduce the symptoms of these co-occurring morbidities.

Research Question, Specific Aim, and Hypotheses 1

Specific Aim 1.

Specific Aim 1 is: To determine the frequency with which GI Disease and PTSD are diagnosed co-morbidities in Veterans who have served during wartime periods.

Research Question 1.

Research Question 1 is: In Veterans who have served during wartime periods, what is the frequency with which GI Disease and PTSD are diagnosed co-morbidities?

Research Hypothesis 1.

Research Hypothesis 1 is: In Veterans who have served during wartime periods, GI Disease and PTSD are frequently diagnosed co-morbidities.

Research Question, Specific Aim, and Hypothesis 2

Specific Aim 2.

Specific Aim 2 is: To determine the frequency with which a diagnosis of functional or structural GI Disease accompanies a diagnosis of PTSD in Veterans who have served during wartime periods.

Research Question 2.

Research Question 2 is: In Veterans who have served during wartime periods, what is the frequency with which a diagnosis of functional or structural GI Disease accompanies a diagnosis of PTSD?

Research Hypothesis 2.

Research Hypothesis 2 is: In Veterans who have served during wartime periods, a diagnosis of functional or structural GI Disease frequently accompanies a diagnosis of PTSD.

Research Question, Specific Aim, and Hypothesis 3

Specific Aim 3.

Specific Aim 3 is: To determine the frequency with which a diagnosis of PTSD accompanies a diagnosis of functional or structural GI Disease in Veterans who have served during wartime periods.

Research Question 3.

Research Question 3 is: In Veterans who have served during wartime periods, what is the frequency with which a diagnosis of PTSD accompanies a diagnosis of functional or structural GI Disease?

Research Hypothesis 3.

Research Hypothesis 3 is: In Veterans who have served during wartime periods, a diagnosis of PTSD frequently accompanies a diagnosis of functional or structural GI Disease.

Statement of the Theoretical Framework

The Transactional Model of Stress and Coping (TMSC Model)

The *theoretical framework* for this study was the Transactional Model of Stress and Coping (TMSC Model), which allows for the evaluation of coping after a stressful event (Glanz, Rimer, & Viswanath, 2008). In the model, a transaction is a stressful event between the person and the environment. In the case of PTSD, transactions could be not only the initial stressor or trauma, but the daily reminders of the trauma, or triggers, that bring on flashbacks and nightmares, causing the individual to relive the initial trauma (Gieselmann, Elberich, Mathes, & Pietrowsky, 2020). According to the TMSC Model, when a person is exposed to a stressor, the risk of harm is assessed, a response termed the primary appraisal; subsequently, capacity to change the situation is determined, a response termed the secondary appraisal. The ability to cope with the stressor leads to several outcomes, which include impacts on emotional well-being, functional status, and health behaviors (Glanz, et al, 2008,).

TMSC Model: Coping Strategies

Individuals use coping strategies after the primary and secondary appraisals, and these coping efforts fall into two categories: problem management and emotional regulation. However, some coping strategies that individuals use may not always be beneficial in the long term, such as avoidance and denial, symptoms also associated with PTSD. Glanz et al. (2008, p. 217), suggests a relationship between coping strategies and traumatic events by stating, “When a stressor is perceived as highly threatening and uncontrollable, a person may be more likely to use disengaging coping strategies,” such as distancing, cognitive and behavioral avoidance, and distraction. Gieselmann, et al,

applied the model to conceptualize nightmare distress while testing tools to measure reactions to nightmares. The authors recognize that in addition to just noting the presence of a symptom, such as nightmares, it is important for clinical providers to note the reaction to that symptom. In their results, they determined that the Cognitive Appraisal of Nightmares tool was best for physiological and emotional consequences related to nightmares (2020).

Research on Stress and Coping Strategies

Resilience.

Conceptually aligned with the TMSC Model is the newer concept of *resilience*, which is conceptually defined as "an individual's ability to adapt and recover from stressful situations, trauma, and hardship" (Thompson & Dobbins, 2018, p. 24). Emerging research is focusing on building resilience through existing coping strategies, such as mindfulness training, cognitive-behavioral methods of managing stress and reducing anxiety, and specialized trainings such as pre-deployment stress briefings.

Resilience is a concept that is still difficult to operationally define or measure, but greater resilience is thought to be a preventative factor for development of PTSD (Thompson & Dobbins, 2018). In a study on resilience and psychological well-being in women with IBS, researchers used the Connor-Davidson Resilience Scale to measure resilience. When compared to healthy women, those with IBS had lower scores of resilience and components of positive relations with others, environmental mastery, purpose in life and acceptance, suggesting that these factors may be involved in the symptoms and exacerbation of IBS (Shahdadi, Balouchi, & Shaykh, 2017).

Physical Health.

Similarly aligned with the TMSC Model, several studies have shown an impact of stress and coping strategies on physical health. For example, the stress hormone cortisol has been associated with shorter survival time in breast cancer (Sephton, Sapolsky, Kraemer, & Spiegel, 2000). Hocking and Lochman (2005), conducted a review using the TMSC Model to identify factors that improved outcomes in children with sickle cell disorder and insulin-dependent diabetes. The identified the variables of maternal adjustment, social support, child coping methods, behavioral competence and adaptive behavior skills as having an impact on child adjustment and health outcomes (Hocking & Lochman, 2005).

In summary, the Review of Literature supports the use of the TMSC Model as the framework to investigate the relationship between PTSD and gastrointestinal disease. Specifically, the Review supports the exploration of whether there is a relationship between the coping strategies that are evidence of a diagnosis of PTSD and corresponding morbidity involving gastrointestinal symptoms.

The Study Variables

Comparisons were conducted with Veteran subjects diagnosed with PTSD and functional GI Disease (e.g. IBS, chronic constipation, and functional dyspepsia), or structural GI Disease (e.g. PUD, GERD, diverticular disease, IBD, ulcerative colitis, and Crohn's Disease). The two major categorical variables, GI Disease and PTSD, were compared in the following manner:

- Specific Aim 1: GI Disease and PTSD is compared as independent variables.

- Specific Aim 2: GI Disease, the independent variable, is compared to PTSD, the dependent variable.
- Specific Aim 3: PTSD, the independent variable, is compared to GI Disease, the dependent variable.

Independent Variables

The i*ndependent variables* are the presence or absence of GI Disease and the presence or absence of PTSD.

Dependent Variables

The *dependent variables* are also the presence or absence of GI disease and the presence or absence of PTSD. Since the research objective is bi-directional, these variables serve as both independent and dependent variables.

Confounding Variables

The *confounding variables* include age, ethnicity, gender, and period of service. These demographic data are descriptive variables reported by Veterans enrolling in Veterans Affairs healthcare services.

Definition of Relevant Terms

Post-Traumatic Stress Disorder (PTSD)

Conceptual Definition.

Post-traumatic stress disorder is conceptually defined as a mental illness that occurs after witnessing or experiencing a particularly disturbing, upsetting, or painful experience (American Psychiatric Association, 2013). The disorder is identical in every Veteran, just as the triggering trauma is not the same for every individual. Some of the

core symptoms that define the disorder are nightmares, flashbacks, intrusive memories of the traumatic event, and alterations in mood, emotions, sleep, and daily functioning (American Psychiatric Association, 2013).

Operational Definition: Diagnostic Indicators of PTSD.

A diagnosis of PTSD, under the DSM-5 (2013), is operationally defined via specific indicators under Criteria A-H:

- Criterion A conceptually defined a traumatic event as: "Exposure to actual or threatened death, serious injury, or sexual violence."
- Criterion B requires evidence of one or more intrusion symptoms, operationally defined as intrusive and distressing memories, nightmares, dissociative reactions, psychological distress at exposure to cues of the trauma, and/or physiological distress at exposure to cues.
- Criterion C requires evidence of one avoidance symptom, operationally defined to include either avoidance of distressing memories, thoughts or feelings about the trauma; and/or avoidance of external reminders, such as people, places, conversations, activities, and/or situations.
- Criterion D requires evidence of two or more cognitive and mood related symptoms, operationally defined to include memory loss of the event, negative beliefs, distorted cognitions about the cause or consequences of the event, negative emotional state, diminished interest in activities, detachment, and/or inability to experience positive emotions.

- Criterion E requires evidence of two symptoms of alterations in arousal or reactivity, operationally defined to include irritable behavior or angry outbursts, reckless behavior, hypervigilance, exaggerated startle response, difficulty concentrating, and/or sleep disturbance.
- Criteria F requires evidence that the disturbance persist longer than one month.
- Criteria G requires that the condition causes clinically significant distress or impairment to the individual.
- Criteria H states that the condition cannot have been caused by a medical condition or substance use (American Psychiatric Association, 2013, p. 271).

In order to receive a diagnosis of PTSD under the DSM-5, an individual must meet all criteria A-H.

Alignment Between Indicators of PTSD and TMSC Coping Strategies.

These diagnostic criteria and indicators for PTSD align conceptually with the TMSC Model because:

- Criterion A conceptually defines a traumatic event as a highly threatening stressor, and;
- Criteria B and H operationally defines criteria and indicators of PTSD as specific coping strategies (dissociative reactions and avoidance).

Functional Gastrointestinal Disease

Conceptual Definition.

Functional GI diseases are conceptually defined as a set of illnesses of the stomach and bowel that do not have a physiological identifiable cause and disrupt the functioning of the individual.

Operational Definition: Diagnostic Indicators.

Functional GI Disease is operationally defined as diagnosed IBS, chronic constipation, and functional dyspepsia. This group of illnesses is diagnosed using the Rome Criteria, which is based on symptomology, with no identifiable change in the body or structure of the organs (Drossman, 2016).

Structural/Motility Gastrointestinal Disease

Conceptual Definition.

Structural and motility GI diseases are conceptually defined as a set of illnesses of the stomach and bowel that have an identifiable physiologic cause and disrupt the functioning of the individual.

Operational Definition: Diagnostic Indicators.

Structural or motility diseases are operationally defined as diagnosed GERD, PUD, IBD, ulcerative colitis, diverticular disease, and Crohn's disease. This group of illnesses is diagnosed based on a change in physiology of the organ at the macro- or micro-level, or altered motility relating to muscle activity (Drossman, 2016).

Demographic Data

The demographic data are confounding variables conceptually defined in the following manner:

1. *Gender* is conceptually defined as the sex determined at the Veteran's birth, as listed on their birth certificate.
2. *Period of service* is conceptually defined as the wartime period in which the Veteran served. Rates of PTSD development vary based on the period of service, with 15% of Vietnam Veterans, 12% of Gulf War Veterans, and 11-20% of Operations Iraqi Freedom (OIF) and Enduring Freedom (OEF) Veterans developing the disorder, (US Department of Veterans Affairs, 2018). The VA operationally defines periods of service as the following wartime periods:
    - "Mexican Border Period (May 9, 1916 – April 5, 1917 for Veterans who served in Mexico, on its borders, or adjacent waters);
    - World War I (April 6, 1917 – November 11, 1918);
    - World War II (December 7, 1941 – December 31, 1946);
    - Korean Conflict (June 27, 1950 – January 31, 1955);
    - Vietnam era (February 28, 1961 – May 7, 1975 for Veterans who served in the Republic of Vietnam during that period; otherwise August 5, 1964 – May 7, 1975)
    - Gulf War (August 2, 1990 – through a future date to be set by law or Presidential Proclamation)" (U.S. Department of Veterans Affairs, 2018).

When classifying patients in their medication record, there are many options that the Department of Veterans Affairs utilizes for Period of Service, several of which apply to non-Veteran patients such as active duty military personnel or foreign dignitaries making use of the VA for their medical care. This study included patients with the following classifications: Korean, Persian Gulf War, Post-Korean, Post-Vietnam, Pre-Korean, Spanish American, Vietnam Era, World War I, and World War II.

Overview of Research Methodology

The Design

This project is a retrospective, correlational study using a large data set.

Theoretical Framework

The TMSC Model was utilized as the framework to investigate the relationship between PTSD and GI Disease. According to the TMSC Model, when a person is exposed to a stressor, the risk of harm is assessed, a response termed the primary appraisal; subsequently, capacity to change the situation is determined, a response termed the secondary appraisal. The ability to cope with the stressor leads to several outcomes, which include impacts on emotional well-being, functional status, and health behaviors (Glanz, Rimer, & Viswanath, 2008).

The Variables

Comparisons were conducted with Veteran subjects diagnosed with PTSD and functional GI Disease (e.g. IBS, chronic constipation, and functional dyspepsia), or

structural GI Disease (e.g. PUD, GERD, diverticular disease, IBD, ulcerative colitis, and Crohn's Disease).

The two major categorical variables, GI Disease and PTSD, were compared in the following manner:

- Specific Aim 1: GI Disease and PTSD is compared as independent variables.
- Specific Aim 2: GI Disease, the independent variable, is compared to PTSD, the dependent variable.
- Specific Aim 3: PTSD, the independent variable, is compared to GI Disease, the dependent variable.

Descriptive Data

The interaction between the two categorical variables produced nominal level data. Descriptive statistics (i.e. means, percentages, histograms, and contingency tables), is used to describe the data. These descriptive statistics were utilized to compare the group demographics (i.e. age, gender, ethnicity, and period of service).

Overview of Design: Data Collection and Data Analysis

Data Collection

Institutional Review Board (IRB Approval).

Approval was sought from the Institutional Review Board (IRB) at University of Texas Medical Branch, in Galveston, TX, and then the IRB at the Department of Veterans Affairs, in Nashville, TN, known henceforth as the Tennessee Valley Healthcare System (TVHS). The TVHS IRB automatically forwarded the application to the local Research and Development Committee, which is also in Nashville. The

Research & Development Committee determined the alignment of the research with the goals and regulations of the institution.

The Data Request and Protection.

Once approved by the TVHS IRB and the Research and Development Committee, a specific data request was sent to the office of National Data Systems, who manage the CDW. This is done via a Data Access Request Tracker, or DART application. The DART application contains the same information as the IRB and is reviewed by privacy and security officers within the NDS. The office of NDS created a cohort of VHA patients that met the researcher's ICD 9 & 10 criteria. The cohort was accessed by the researcher using Microsoft SQL Server, which is only accessible via a remote workspace with VHA identification card and login. The researcher used Standardized Query Language (SQL) to query the data and then transfer the saved tables to SAS 9.4 software, also located on the VHA remote workspace, for data analyzation. VHA security measures prevented data from being removed from this remote workspace in order to protect the privacy of the participants.

Inclusion Criteria.

Data requested included demographic information (age, gender, ethnicity, and period of service) and specific diagnoses and date of diagnosis for all Veterans from 1999 to present day who have either a GI Disease or PTSD diagnosis. GI Disease include only diseases with greater than 500,000 annual ambulatory care visits in the United States, to include: peptic ulcer disease, gastroesophageal reflux disease, diverticular disease, inflammatory bowel disease, ulcerative colitis, Crohn's disease, irritable bowel

syndrome, constipation, nausea/vomiting, and functional dyspepsia (Everhart & Ruhl, 2009; Kozma, Barghhout, Slaton, Frech, & Reeder, 2002).

Diagnostic Information.

This diagnostic information was determined using diagnostic codes that have been used by the Department of Veterans Affairs since establishment of the database in 1999. This includes ICD-9 and ICD-10 codes, which providers enter into the charting system at each patient encounter. In the VHA system providers made the transition from ICD-9 to ICD-10 gradually during the 2015 calendar year. Codes were not necessarily in the currently used coding format (ICD-10), since patients have died or otherwise stopped seeking care before coding was updated. For example, in order to obtain all cases of PTSD, the data request pulled the ICD-9 Code of 309.81 Posttraumatic Stress Disorder and the ICD-10 codes of F43.10 Posttraumatic Stress Disorder, unspecified, F43.11 Posttraumatic stress disorder, acute, and F43.12 Posttraumatic stress disorder, chronic (Centers for Disease Control, 2013).

Data Analysis

SAS 9.4 software was utilized to statistically analyze and interpret the frequency data. Descriptive statistics, including means, percentages, histograms and contingency tables was used to describe and explain the data outcomes. Chi-Square and contingency tables were used to examine the relationships between the categories and sub-categories of GI Disease and PTSD, as well as differences among categories of demographic data, (e.g. age, gender, ethnicities, period of service, and functional verses structural GI diseases).

Overview of Study Findings

Study findings revealed that PTSD is bi-directionally correlated with the GI Diseases of gastroesophageal reflux disease, peptic ulcer disease, functional dyspepsia, Crohn's disease, diverticular disease, and irritable bowel syndrome, as well as the GI symptoms of constipation and nausea/vomiting. The study also found the PTSD was not correlated with the GI disease of ulcerative colitis. Functional diseases of IBS and functional dyspepsia had a stronger correlation with PTSD than the structural GI diseases.

Summary of Chapter One

Chapter One introduced this quantitative study, which explored the relationship between GI Disease and PTSD in Veterans who served during wartime periods. The statement of the study problem is presented. Then the background and significance of the problem, statement of purpose and goals, research questions and aims, theoretical framework, study variables, and definition of terms were provided. Finally, the Chapter offered an overview of research methodology, data collection and analysis, and a brief overview of study findings.

Plan for Remaining Chapters

Chapter Two provides a detailed review of the literature on GI Disease and PTSD. Chapter Three discusses the application of the quantitative research design. Chapter Four presents the study findings. Chapter Five presents the conclusions, discussion, and recommendations relative to the study findings.

References

Addolorado, G., Mirijello, A., D'Angelo, C., Leggio, L., Ferrulli, A., Abenavoli, L., … Gasbarrini, G. (2008). State and trait anxiety in patients affected by gastrointestinal diseases: Psychometric evaluation of 1641 patients referred to an internal medicine outpatient setting. *International Journal of Clinical Practice, 62*, pp. 1063-1069. doi: 10.1111/j.1742-1241.2008.01763.x

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders 5th ed.* Arlington, VA: American Psychiatric Association.

American Psychiatric Association (APA). (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., Text Revision). Arlington, VA: American Psychiatric Association.

Bennett, E. J., Tennant, C. C., Badcock, C. A., & Kellow, J. E. (1998). Level of chronic life stress predicts clinical outcome in irritable bowel syndrome. *Gut, 43*, pp. 256-261.

Bonaz, B. L., & Bernstein, C. N. (2013). Brain-gut interactions in inflammatory bowel disease. *Reviews in Basic and Clinical Gastroenterology and Hepatology, 144*, pp. 36-49.

Breit, S., Kupferberg, A., Rogler, G., & Hasler, G. (2018). Vagus nerve as modulator of the brain-gut axis in psychiatric and inflammatory disorders. *Front Psychiatry 9*, pp. 44.

Centers for Disease Control and Prevention. (2013). ICD-10-CM official guidelines for coding and reporting. Retrieved from: http://www.cdc.gov/nchs/data/icd9/icd10cm_guidelines_2014.pdf

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

Everhart, J. E. & Ruhl, C. E. (2009). Burden of digestive diseases in the United States part I: Overall and upper gastrointestinal diseases. *Gastroenterology. 136*, pp. 376-386.

Fichina, J., & Storr, M.A. (2012). Brain-gun interactions in IBS. *Frontiers in Pharmacology, 3*, pp. 1-12. doi:10.3389/fphar.2012.00127

Ford, M. J., Miller, P. M., Eastwood, J., & Eastwood, M. A. (1987). Life events, psychiatric illness, and the irritable bowel syndrome. *Gut.28*, pp. 160-165.

Gieselmann, A., Elberich, N., Mathes, J., & Peitrowsky, R. (2020). Nightmare distress revisited: Cognitive appraisal of nightmares according to Lazarus' transactional model of stress. *Journal of Behavior Therapy and Experimental Psychiatry, 68* doi:10.1016/j.jbtep.2019.101517

Glanz, K., Rimer, B. K., &Viswanath, K. (2008). *Health Behavior and Health Education*. San Francisco, CA: Jossey-Bass.

Haug, T. T., Mykletun, A., & Dahl, A. A. (2002). Are anxiety and depression related to gastrointestinal symptoms in the general population? *Scandinavian Journal of Gastroenterology, 37*, pp. 294-298.

Hocking, M.C., & Lochman, J.E. (2005). Applying the transactional stress and coping model to sickle cell disorder and insulin-dependent diabetes mellitus: Identifying psychosocial variables related to adjustment and intervention. *Clinical Child and Family Psychology Review, 8,* pp. 221-246. doi: 10.1007/s10567-005-6667-2

Iorio, N., Makipour, K., Palit, A., & Friedenberg, F. K. (2014). Post-traumatic stress disorder is associated with irritable bowel syndrome in African Americans. *Journal of Neurogastroenterology & Motility, 20*, pp. 523-530. doi:10.5056/jnm14040.

Kozma, C. M., Barghhout, V., Slaton, T., Frech, F., & Reeder, C.E. (2002). Office-based physician visits: A comparison of irritable bowel syndrome with other gastrointestinal disorders using national ambulatory medical care survey data. *Practical Gastroenterology, XXVL,* pp. 58-68.

Locke, G. R., Weaver, A. L., Melton, L. J., & Talley, N. J. (2004). Psychosocial factors are linked to functional gastrointestinal disorders: A population based nested case-control study. *American Journal of Gastroenterology, 99*, pp. 350-357. doi:10.1111/j.1572-0241.2004.04043.x

Maguen, S., Madden, E., Cohen, B., Bertenthal, D., & Seal, K. (2014). Association of mental health problems with gastrointestinal disorders in Iraq and Afghanistan Veterans. *Depression & Anxiety, 31*, pp. 160-165. doi: 10.1002/da.22072

Mayer, E. A., & Collins, S. M. (2002). Evolving pathophysiologic models of functional gastrointestinal disorders. *Gastroenterology, 122*, pp. 2032-2048.

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). (2018). *Digestive diseases,* para 1. Retrieved from https://www.niddk.nih.gov/health-information/digestive-diseases

National Institute of Mental Health. (2018). Division of Translational Research. Retrieved from https://www.nimh.nih.gov/about/organization/dtr/index.shtml

Rao, S. C., Hatfield, R. A., Suls, J. M., & Chamberlain, M. J. (1998). Psychological and physical stress induce differential effects on human colonic motility. *American Journal of Gastroenterology, 93*, pp. 985-990.

Rhee, S. H., Pothoulakis, C., & Mayer, E. A. (2009). Principles and clinical implications of the brain-gut-enteric microbiota axis. *Nature Reviews Gastroenterology & Hepatology, 6,* pp. 1-19.

Sephton, S.E., Sapolsky, R.M., Kraemer, H.C., & Spiegel, D. (2000). Diurnal cortisol rhythm as a predictor of breast cancer survival. J*ournal of the National Cancer Institute, 92,* pp. 994-1000. doi:10.1093/jnci/92.12.994

Shahdadi, H., Balouchi, A., & Shaykh, A. (2017). Comparison of resilience and psychological wellbeing in women with irritable bowel syndrome and normal women. *Mater Sociomed, 29(2),* pp. 105-108. doi: 10.5455/msm.2017.29.105-108

Tache, Y., Martinez, V., Million, M., & Wang, L. (2001). Stress and the gastrointestinal tract III: Stress-related alterations of gut motor function: role of brain corticotropin-releasing factor receptors. *American Journal of Gastrointestinal & Liver Physiology, 280,* pp. G173-G177.

Thompson, S.R., & Dobbins, S. (2018). The applicability of resilience training to the mitigation of trauma-related mental illness in military personnel. *Journal of the American Psychiatric Nurses Association, 24*, pp. 23-34. doi:10.1177/1078390317739957

U.S. Department of Veterans Affairs. (2017). About VHA. Retrieved from https://www.va.gov/health/aboutvha.asp

U.S. Department of Veterans Affairs. (2018). Eligible wartime periods. Retrieved from https://www.benefits.va.gov/pension/wartimeperiod.asp

U.S. Department of Veterans Affairs. (2018). How common is PTSD? Retrieved from https://www.ptsd.va.gov/public/ptsd-overview/basics/how-common-is-ptsd.asp

Zhang, Y., Chen, H., Long, Z., Cui, Q., & Chen, H. (2016). Altered effective connectivity network of the thalamus in post-traumatic stress disorder: a resting-state FMRI study with granger causality method. *Applied Informatics, 3*, pp. 1-8.

Chapter Two: Review of Literature

Introduction

Chapter Two provides a review of literature related to GI Disease and PTSD. The Chapter begins with a theoretical and historical overview of literature regarding GI Disease and PTSD, including related research studies. The literature review also explores related variables, e.g. prevalence, demographics, and risk factors. Finally, the variables were defined, the gaps in the literature were identified, and the rationale for the study was discussed.

Review of Literature: Theoretical and Historical

Posttraumatic Stress Disorder (PTSD)

PTSD was first identified in the Civil War era, and early names for the disorder include "nostalgia," "Soldier's heart," and "irritable heart." By World War I, it was beginning to gain more awareness as "war neuroses" and soldiers were beginning to receive official diagnoses of "shell shock." Around the time of World War II, this diagnosis changed to "combat stress reaction," or in layman's terms "battle fatigue." The first Diagnostic and Statistical Manual of Mental Disorders was published in 1952 by the American Psychiatric Association and included "gross stress reaction." The disorder did not get its present-day name of post-traumatic stress disorder until the 3rd edition of the DSM, published in 1980 after research into military personnel from the war in Vietnam was available (U.S. Department of Veterans Affairs, 2019).

As the disorder has evolved over the years, the symptoms of PTSD have also been more clearly identified. In order to be diagnosed with PTSD in the present day, the individual must meet seven criteria, labeled A-G, first of which being that they must have been exposed to a traumatic event. This event could be the experience or threat of death,

injury, or sexual violence to oneself, or witnessing these events happening to someone else. The diagnosis of PTSD, may include any combination of the following symptoms:

- intrusive memories,
- recurrent dreams,
- psychological and physiological stress at exposure to the trauma,
- avoidance of memories or reminders of the trauma,
- amnesia of the trauma,
- negative beliefs about oneself or the world,
- distorted cognitions,
- negative emotional state,
- diminished interest or pleasure in activities,
- detachment,
- inability to experience positive emotions,
- irritable behavior,
- reckless behavior,
- hypervigilance,
- being easily startled,
- difficulty concentrating, and
- difficulty sleeping (American Psychiatric Association, 2013).

Gastrointestinal Disease (GI Disease)

The Gastrointestinal Tract.

The gastrointestinal (GI) system is comprised of the gastrointestinal tract and accessory organs, i.e. the tongue, salivary glands, liver, pancreas, and gallbladder. This

study has focused on the GI tract only. The GI tract is essentially a long, muscular tube that stretches from the mouth to the anus. Food is first ingested through the mouth and mechanically processed by the teeth and tongue. The digested product will then travel through the esophagus, stomach, small intestine, and large intestine. The small intestine is comprised of layers of mucosa, submucosa, muscularis externia, and the serosa, which allow for absorption of nutrients, secretion of enzymes, and movement of food through the GI tract. The submucosa and muscularis externa layers contain sensory neurons and motor neurons, through which the enteric nervous system and autonomic nervous system coordinate the muscles' movement of the digested food through contractions known as peristalsis (Martini, Nath, & Bartholomew, 2017).

The physiology of digestion.

The stomach secretes about 1500mL of gastric juice daily, keeping the contents at a pH level of 1.5-2.0. This acidic environment aids in killing harmful bacteria that enter the gut with food, breaks down plant cell walls of fruits and vegetables and connective tissues of meat, and denatures and aids in digestion of proteins. Gastric activity is regulated by the central nervous system, reflexes of the enteric nervous system, and hormones of the GI tract. After preliminary digestion is performed by the stomach, food is released into the small intestine, where 90% of nutrient absorption occurs. The small intestine contains folds, or plica circulares, which vastly increase the surface area available for absorption. From the small intestine the food enters the large intestine, which is responsible for the reabsorption of water, compacting the remaining contents into feces, and absorbing of vitamins that are the product of bacterial activity in the

stomach and small intestine. The fecal matter is then stored in the colon and moves out of the body through the rectum and anus (Martini, Nath, & Bartholomew, 2017).

The Central Nervous System and the GI tract.

The nervous system is divided into the central nervous system (CNS), consisting of the spinal cord and the brain, and the peripheral nervous system, which is further divided into the somatic nervous system and the autonomic nervous system (ANS) (Martini, Nath, & Bartholomew, 2017). As discussed later in this paper, the CNS and the ANS are important in the gut-brain axis, the communication link between the brain and GI tract (Dinan, Stilling, Stanton, & Cryan, 2015). The CNS's role in the GI tract is to prepare the tract for activity and to coordinate the movement of digested food and feces through the tract. Additionally, hypothalamic centers in the brain control hunger and satiation. Motor neurons from the parasympathetic nervous system (PNS) control smooth muscle contraction.

The CNS is more active in the stomach, but the enteric nervous system (ENS), which part of the ANS, is more active in the small intestine. The ENS contains between 200-600 million neurons (Furness, Callaghan, Rivera, & Cho, 2014), compared to the brain, which contains 100 billion neurons (Herculano-Houzel, 2009)), and assists in motility, fluid secretion, and blood flow (De Vaddera, et al., 2018). PNS activation can also produce secretion of digestive glands (including salivary glands, gastric glands, and those in the intestines, pancreas, and liver), secretion of hormones that aid in absorption of nutrients, increase in smooth muscle movement in the GI tract, and coordination of defecation (Martini, Nath, & Bartholomew, 2017).

Gastrointestinal bacteria.

The GI tract contains bacteria in quantities that are as much as ten times the number of cells in the human body, and this ecosystem can contain anywhere from 300-500 different species of bacteria. Although the GI tract is sterile within the womb, the child is immediately exposed to bacteria in the birthing process and with the ingestion of food. Due to the great variability in our exposure, each human has a unique and distinct set of bacteria within their own GI tract. Although minor changes occur with infection and diet changes, each person's distinct microbiome is thought to remain relatively stable over the course of their life. These helpful bacteria aid in protecting the body from harmful bacteria that would cause systemic infection, convert unused sugars such as lactose and alcohol into usable sources of energy, and produce their own neurotransmitters (Quigley, 2013).

Studies have shown that individuals with irritable bowel syndrome (IBS) have a fecal flora that is less diverse than those in control groups (Quigley, 2013). The addition of probiotics has been shown to reverse some of the characteristics of IBS, such as intestinal permeability (Zheng, Li, Zuo, Zhen, Yeng, & Liu, 2008), and producing visceral analgesic effects (Rousseaux, Thuru, & Gelot, 2007). One potential explanation of this process is that gut microbiota has been shown to influence the amygdala in the brain. Many brain functions that impact psychiatric symptoms such as emotional regulation and social behavior are dependent on the amygdala. This has led some to suggest the microbiota as a potential target for manipulating the amygdala, and thereby treating psychiatric illnesses such as PTSD (Cowan, Hoban, Ventura-Silva, Dinan, Clark, & Cryan, 2017).

Chronic disease of the gastrointestinal tract.

For the purpose of this study, the term "chronic disease" is operationally defined as a physiological condition of length greater than 3 months. Chronic GI Diseases encompass diagnoses such as inflammatory bowel disease, IBS, Crohn's disease, gastroesophageal reflux disease (GERD) and dyspepsia, diverticulosis and diverticulitis, and ulcerative colitis. Additionally, GI diseases are classified as either structural or functional. Structural GI Diseases include tumors and Crohn's disease, identifiable as a structural cause for the GI symptoms. Functional GI Diseases are those syndromes that present persistent GI symptoms that are abnormal functioning, but not caused by structural issues, such as IBS (UNC School of Medicine, 2017).

PTSD and GI Disease Co-Morbidities

World War II References to Co-Morbidities.

Historically, mental illness and gastrointestinal diseases as potential co-morbidities in soldiers was first recognized as early as 1945, by the Army Medical Corps in a paper titled "Psychogenic Disorders of the Upper Gastrointestinal Tract in Combat Personnel." At that time, the diagnostic label of "PTSD" did not yet exist. However, the paper described symptoms similar to those currently used to diagnose PTSD. For example, the authors discussed symptoms of "blandness of manner" and "impenetrability of defense" that mirror current descriptors of detachment and numbness. The authors also described "catastrophic dreams of frequent occurrence, obsessive visualization of past traumatic events, preoccupation with ideas of mutilation…" (Weinstein & Stein, 1945), now termed nightmares and either flashbacks or intrusive memories. Therefore, it is reasonable to conclude that the authors are speaking of soldiers that in present day would be diagnosed with PTSD.

When speaking of such soldiers, the authors made several key statements connecting PTSD to GI distress, and potentially GI Disease. *First*, "Neurotic gastrointestinal symptoms are a manifestation of, rather than a substitute for, anxiety (p. 365)." The authors then described soldiers often vomiting after the first traumatic event, i.e. being "extremely conscious of his stomach, which he endows with a set of independent feelings and attitudes (p. 366)." Without citing the source, the authors stated, "There is, in any case, considerable evidence that acute emotional changes can produce marked changes in the vascularity and secretory activity of the gastric mucosa," (Weinstein & Stein, 1945, p.367).

Civil War References to Co-Morbidities.

The authors of the 1945 paper may have been the first to identify a connection between symptoms of military trauma and GI symptoms, but this time period was not the first in which such a connection occurred. Pizarro, Silver, and Prause (2006), analyzed records from the US Pension Board examinations and military personnel records to identify physical and mental health issues in 17,700 Civil War Veterans of the Union Army. The authors noted that all recruits would have been screened for health issues prior to military service, which suggested that recruits were relatively healthy when joining the Army. The authors then transferred written exams into a database to promote standardization before attempting to analyze the data. They found that "combat exposure was related to increased self-reports of negative physical symptoms and physician-diagnosed signs of cardiac disease (e.g., arteriosclerosis), GI disease (e.g., ulcer), and mental health problems, (e.g., depression)" (Pizarro, Silver, & Prause, 2006, p.199).

Again, this time period pre-dates the diagnosis of PTSD, so only the event of combat exposure could be connected to GI and other health-related symptoms.

Follow-up Studies on Co-Morbidities.

Finally, in 1985, Goulston and other authors studied 170 Australian World War II surviving prisoners of war (POWs). The subjects were intentionally studied 40 years after the traumatic wartime event to assess the long-term effects on GI health. The subjects were compared to a control group of former soldiers who were not imprisoned as POWs. Participants completed a psychiatric interview as well as providing blood and stool samples. Even though multiple GI Diseases were identified, the only statistically significant difference was that POWs reported a higher incidence of duodenal ulcers when compared to the control group (Goulston, et al., 1985). While these earlier studies show some initial relationships between trauma and GI symptoms and disease, it is apparent that there was still much needed research in the area.

Review of Literature: Relevant Research

Veterans with PTSD

The Department of Veterans Affairs estimates 7-8% of the total U.S. population will develop PTSD in their lifetime. Furthermore, rates of diagnosed PTSD vary according to Veteran war record, at the following rate: 30% of Vietnam Veterans; 12% Gulf War Veterans; and 11-20% of Operation Iraqi Freedom and Operation Enduring Freedom Veterans (U.S. Department of Veterans Affairs, 2017). In the general adult population, 10% of women, compared to only 4 % of men, will develop PTSD in their lifetime (U.S. Department of Veterans Affairs, 2017). Since the military is mainly

comprised of men (91%), it can be inferred that the study will identify more men than women with PTSD.

A conservative estimate of the potential sample of 630,000 Veterans with PTSD is identified in Table 2.1, Estimated Demographics of Veterans with PTSD. This table was calculated based upon Veteran demographics cited above (U.S. Department of Veterans Affairs, 2017). Current numbers of Veterans with GI disease are unknown and can only be estimated based on prevalence in the general United States population. Within this project, the researcher will identify the number of Veterans with GI Disease as a co-morbidity.

Table 2.1: Estimated Demographics of Veterans with PTSD

	Total	**Men – 91%**	**Women – 9%**
White – 7%	485,100	441,441	43,659
Black – 2%	75,600	68,796	6,804
Hispanic –7%	44,100	40,131	3,969
Asian – 2%	12,600	11,466	1,134
Other – 2%	12,600	11,466	1,134
Estimated Total:	**630,000**	573,300	56,700

This is a substantial population in the United States, which can be affected by research into co-occurring PTSD and GI disease. Identification and description of the relationship between the disorder and disease is the first step that will lead to future research on predicting and preventing these conditions.

Veterans with GI Disease

Current estimates of Americans with GI disease studied in this project are as follows:

- IBS - 11% (Canavan, West, & Card, 2014),

- PUD- 10%,
- GERD - 20%,
- Diverticular disease - 35-58%, (NIDDKD, 2019),
- IBD - 1.3% - Including Crohn's disease & Ulcerative colitis - (Centers for Disease Control and Prevention, 2019),
- Chronic constipation - 2-27% (Sanchez & Bercik, 2011),
- Functional Dyspepsia – 40% (Loyd & McClellan, 2011).

There are currently no reliable estimates for prevalence of GI disease in U.S. Veterans. It is estimated that 11% of the global population has IBS (Canavan, West, & Card, 2014). Translating that estimate to the Veteran population, out of 9 million Veterans treated within the VA healthcare system, the researcher estimated a population of 990,000 Veterans from which to obtain the sample, not including the other GI diseases that would be included. However, we also know that functional gastrointestinal diseases occur more frequently in Veterans than in the average population (Riddle, et al., 2016). Therefore, the number of Veterans with GI diseases were discovered as part of this study.

Veterans with PTSD and GI Disease Co-Morbidities

Anxiety and depressive disorders have been connected to gastrointestinal symptoms in numerous studies (Addolorado, et al., 2008; Haug, Mykletun, & Dahl, 2002). Patients with PTSD can exhibit many symptoms of anxiety. These shared traits resulted in PTSD being categorized as an anxiety disorder until 2013, at which time the updated Diagnostic and Statistical Manual of Mental Disorders, 5th Edition, identified PTSD's classification as "Trauma- and Stressor-Related Disorders" (American Psychiatric Association, 2013). As PTSD is no longer classified as an "anxiety disorder,"

it is no longer appropriate to assume that PTSD and gastrointestinal symptoms are associated in the same way that anxiety disorders as are associated with gastrointestinal symptoms. This raises the question: What is the relationship between PTSD and gastrointestinal disease? The prevalence and demographic information on co-occurring GI disease and PTSD in Veterans was unknown prior and is reported as part of this study.

Psychosocial Effects on Gastrointestinal Disease

Approximately 60-70 million Americans are affected by digestive diseases (Peery, et al., Shaheen, 2013). Chronic GI Disease have a serious impact on the welfare and productivity of Americans. For example, Perry, et al., (2013) reported the symptom of abdominal pain prompted 15.9 million visits to U.S. clinics in 2012. Gastroesophageal reflux prompted 8.9 million clinic visits. In addition, there were over two million visits for each of the following symptoms: nausea, diarrhea, constipation, and vomiting (Peery, et al., 2013). Johanson and Kralstein (2007) studied 557 patients with chronic constipation; 69% of the study's participants reported some form of work or school impairment due to symptoms, and 12% reported missing time from work or school because of constipation.

Quality of Life.

Multiple studies discuss quality of life of patients with various chronic gastrointestinal disease. For example, Johanson and Kralstein (2007) found that symptoms of chronic constipation affected quality of life in 52% of survey respondents. Participants in the study rated symptoms of abdominal discomfort, infrequent bowel movements, feeling of incomplete evacuation after bowel movement, hard stool, and

straining in terms of how bothersome and level of severity of the symptoms. Moreover, 69% of the participants reported some level of work or school impairment.

Koloski, Talley, and Boyce's (2000) study of 2910 participants in Australia used a quality of life measure, which revealed that having a gastrointestinal disease was significantly associated with impairments in mental and physical functioning. Hahn, Kirchdoefer, and Mayer (1997) studied 126 patients with IBS and found that quality of life was associated with perceived symptom severity. The authors noted, "…as IBS severity increased, psychological symptom severity as part of a global measure increased" (p. 555). Additionally, Locke, Weaver, Melton, and Talley (2004) found that functional gastrointestinal diseases are linked to more psychological distress, higher interpersonal sensitivity, and greater numbers of life stress events.

The Gut-Brain Axis

The gut-brain axis is a pathway of communication that links the gut with emotional and cognitive functions in the brain (Rogers, Keating, Young, Wong, & Licinio, 2016). This axis includes a multitude of systems, such as the CNS, the neuroendocrine system, the neuro-immune system, the sympathetic and parasympathetic parts of the ANS, the ENS, and the intestinal microbiota (Dinan, Stilling, Stanton, & Cryan, 2015). Alterations on either end of the axis can affect the other end. Dinan, et al. (2015) stated "Signals from the brain can influence the motor, sensory, and secretory modalities of the gut and conversely, visceral messages from the gut can influence brain function." In mice, a high-fat diet was associated with "increased vulnerability to anxiety-like behavior," according to Rogers, et al. (2016). Additionally, these authors reported

that when mice with gastrointestinal infection and inflammation are given the bacteria *B. longum*, anxiety-like behavior normalizes (Rogers, et al, 2016).

Several factors are known to influence the gut-brain axis, including the stress response of the hypothalamic-pituitary-adrenal axis, the presence of corticotrophin releasing factor (CRF), and the presence of gut microbial (Bonaz & Bernstein, 2013).

The Corticotrophin Releasing Factor (CRF).

In a review of the current literature on stress-related alterations in gut function, Tache, Martinez, Million, and Wang, (2001), reported that CRF, a hormone released during stress, increases colonic motility and induces fecal excretion. CRF antagonists have shown promising results in reducing anxiety and depression scores in some patients with depression. The authors suggest that this antagonist may also prove therapeutic in the treatment of mental health symptoms that occur in patients with IBS (Tache, et al., 2001). CRF is partially responsible for initiating a signaling cascade in the hypothalamic-pituitary-adrenal axis.

When studied in mice, administration of CRF as well as urocortin peptides triggered anxiety-like behaviors, and "stimulated colonic secretion, intestinal motility, and visceral sensitivity," according to Fichna & Storr (2012). Similar elevated levels of CRF were found in the thalamus of neonatal rats experiencing separation from their mothers. (Fichna & Storr, 2012). Recent studies have demonstrated "increased influence" from the thalamus to the middle/inferior frontal gyrus and insula in cases of PTSD (Zhang, Chen, Long, Cui, and Chen, 2016). This initial research into the circuit of CRF to

thalamus may explain a connection between PTSD and GI symptoms but warrants further study before conclusions may be made.

Bacterial Neurotransmitters.

Initial studies reveal that some bacteria create and release neurotransmitters: "For example:

- certain *Lactobacillus* and *Bifidobacterium* species produce gamma-aminobutyric acid (GABA);
- *Escherichia*, *Bacillus*, and *Saccharomyces* produce norepinephrine (NE);
- *Candida*, *Streptococcus*, *Escherichia,* and *Enterococcus* produce 5HT;
- *Bacillus* produces dopamine DA); and
- *Lactobacillus* produces acetylcholine" (Dinan, et al., 2015).

These are the same neurotransmitters that are used in medications to treat psychiatric illness. Anxiolytics are prescribed for anxiety, such as diazepam, which act on GABA. Some antidepressants, such as venlafaxine, work on 5HT (i.e. serotonin) and norepinephrine. Antipsychotics, such as aripiprazole, act on dopamine (Stahl, 2008). Probiotic bacteria demonstrate psychotherapeutic properties of antidepressants in pre-clinical trials (Dinan, 2015).

Bacterial neurotransmitters not only affect mood and behavior but demonstrate a direct impact on the gut. Serotonin (5HT), plays a role in sensation, secretion, and gut absorption (Fichna & Storr, 2012). Use of these neurotransmitters, especially serotonin, have been used to treat functional GI Disease, which is discussed further below. It is estimated that one in eight patients with IBS is offered an antidepressant (Grover &

Drossman, 2011). Additionally, one recent study suggested that bacteria in the gut contribute to the maturation of the ENS through the release of the serotonin (De Vadder, et al, 2018).

Gastrointestinal Diseases and Life Stressors

Studies have shown that participants with gastrointestinal diseases such as IBS (Ford, et al, 1987), and non-ulcer dyspepsia (Locke, et al, 2004) also reported the presence of anxiety and depression. Levi, et al., (2006), reported that chronic life stress is the biggest predictor of IBS symptom severity. Additionally, a study of 117 patients with IBS found that the presence of chronic life stressors was a predictor for lack of improvement in symptoms of IBS (Bennett, et al, 1998). In a review of the current literature on stress-related alterations in gut function, Tache, Martinez, Million, and Wang (2001) reported corticotropin-releasing factor (CRF), a hormone released during stress, increased colonic motility and induced fecal excretion.

Colonic Pressure Activity.

Rao et al., (1998), used pressure sensors in the gut to measure colonic pressure activity during and after both psychological and physical stressors. While colonic motor activity was increased in both stressors, the activity ceased immediately after the end of the physical stressor but persisted long after the end of the psychological stressor. These researchers suggested psychological or emotional stress may contribute to the symptomology of functional GI Disease (Rao, et al., 1998). CRF antagonists demonstrate promising results in reducing anxiety and depression scores in some patients with

depression. CRF antagonists may also prove therapeutic in the treatment of mental health symptoms that occur in patients with IBS (Tache, et al., 2001).

Physical and Sexual Abuse.

One specific life stressor, that of physical and sexual abuse, has especially been shown to correlate with diagnosis of GI Disease. In one study of 206 women with GI Diseases, including both functional and structural types, 44% reported a history of physical or sexual abuse. The authors also stated: "Patients with functional disorders were more likely than those with organic (structural) disease diagnoses to report a history of forced intercourse and frequent physical abuse" (Drossman, et al., 1990, p.828). In a study that specifically reviewed patients with either IBS or IBD, 54% had a history of lifetime sexual victimization, verses five percent in controls without GI Disease (Walker, Katon, Roy-Byrne, Jemelka, & Russo, 1993). In another survey of 1,225 women, subjects with a history of childhood maltreatment were more likely to have nausea, diarrhea, constipation, and abdominal pain, in addition to a host of other physical symptoms and disabilities, compared to women without the trauma history (Walker, et al., 1999). More recent research continues to confirm this association between sexual abuse and IBS. Out of participants with either Crohn's disease, ulcerative colitis, or IBS, those with IBS reported significantly higher rates of IBS compared to the other GI diseases (Ross, 2005).

Links Between Gastrointestinal Diseases and Psychiatric Disorders

Hahn, et al (1997) was one of many studies that found an association between gastrointestinal disease and psychological symptoms or mental illness. Walker, et al., (1990) found that patients with IBS were significantly more likely to have a diagnosis of

Major Depressive Disorder, Somatization Disorder, Generalized Anxiety Disorder, Panic Disorder, and Phobic Disorder. Irwin, Falsetti, Lydiard, Ballenger, Brock, and Bener (1996) studied 50 patients with IBS and revealed that 54% met criteria for at least one psychiatric illness in their lifetime, including post-traumatic stress disorder, major depressive disorder, or substance abuse. Savas, et al., (2008) found that female Veteran participants with IBS and dyspepsia reported significantly higher levels of anxiety and depression when compared to women without GI diseases. In a systematic review of studies that analyzed co-occurring IBS and psychiatric disorders, authors concluded that gastrointestinal symptoms were not manifestations of somatization disorder, but gastrointestinal and psychiatric symptoms experienced in patients with IBS were distinct and separate disorders (Whitehead, Palsson, & Jones, 2002). In a study on anxiety and physical health conditions, any anxiety or PTSD was associated with increased risk of GI disease in older adults (El-Gabalaway, Mackenzie, Pietrzack, & Sareen, 2014).

Other studies (Savas, et al, 2008; Maguen, et al, 2013) attempted to examine the relationship between GI Diseases and mental health disorders in the U.S. Veteran population. Maguen, et al, (2013), used Department of Veterans Affairs patient data and found that IBS was associated with mental health conditions, in both genders of Veterans returning from Iraq and Afghanistan. Savas, et al, (2008) studied women Veterans with IBS and dyspepsia and revealed a high prevalence of depression, anxiety, and PTSD in this population.

Antidepressant Use in Relation to GI Disease.

Even though Whitehead, et al., (2002) categorized GI and psychiatric symptoms as separate disorders, some studies have found antidepressants, such as paroxetine

(Tabas, Beaves, Wang, Friday, Mardini, & Arnold, 2004), desipramine (Drossman, et al., 2003), and tricyclic antidepressants (Jackson, O'Malley, Tomkins, Balden, Santoro, & Kroenke, 2000), have been effective in treating functional gastrointestinal diseases (Drossman et al., 2003; Jackson et al., 2000; Tabas et al., 2004). Jackson, et al, performed a meta-analysis of 12 studies that reviewed various antidepressant effects on functional GI Diseases. These antidepressants included several tricyclics and one anti-serotonin agent (mianserin). While the authors did conclude that these medications are effective for the treatment of functional GI Diseases, they note that so far no one has shown whether this improvement is "independent of an effect of treatment on depression" (Jackson, et al, 2000).

Recent research has discovered that common antidepressants such as fluoxetine and escitalopram (Selective Serotonin Reuptake Inhibitors – SSRIs), venlafaxine and duloxetine (Serotonin & Norepinephrine Reuptake Inhibitors - SNRIs), and despiramine (a tricyclic antidepressant – TCA). Researchers administered one of these five antidepressants to mice for twenty-one days. They then analyzed their gut microbial through stool samples and assessed depressive-like behavior in the mice. Both the SSRIs and the SNRIs "reduced the richness of gut microbiota as well as increasing beta diversity." Researchers go on to explain "It is generally accepted that higher gut bacterial diversity is beneficial for individual health, and decreased microbiota richness is associated with disease states, such as irritable bowel disease or obesity (Lukic, et al., 2019, p. 12)." This is somewhat conflicting evidence on the benefit of antidepressants in the context of GI disease. Continuing their experiment, the researchers administered the bacterium *Ruminococcus flavefaciens* to mice who were on the antidepressant duloxetine.

They found that the addition of this bacterium reversed the antidepressant effects of the duloxetine. Supplementation with *Adlercreutzia equolifaciens* did not produce the same effect (Lukic, et al., 2019). Previous studies support this finding, as *Ruminococcus* has been associated with symptoms of anhedonia (Davis, et al, 2017), and prebiotics that reduced *Ruminococcus* have shown some antidepressant effects (Burokas, et al., 2017).

Review of Literature: Research Variables

Research Question 1

Research Question One is: In Veterans who have served during wartime periods, what is the frequency with which GI Disease and PTSD are diagnosed co-morbidities?

Independent Variables.

For research question one, both GI Disease and PTSD serve as independent variables.

Dependent Variables.

There are no dependent variables for research question one.

Confounding Variables.

For research question one, the confounding variables are gender, ethnicity, age, and period of service

Research Question 2

Research Question Two is: In Veterans who have served during wartime periods, what is the frequency with which a diagnosis of functional or structural GI Disease accompanies diagnosis of PTSD?

Independent Variables

For research question two, PTSD is the independent variable.

Dependent Variables

For research question two, the presence or absence of GI Disease is the dependent variable.

Confounding Variables

For research question two, the confounding variables are gender, ethnicity, age, and period of service.

Research Question 3

Research Question Three is: In Veterans who have served during wartime periods, what is the frequency with which a diagnosis of PTSD accompanies a diagnosis of functional or structural GI Disease?

Independent Variables

For research question three, functional and structural GI Diseases are the independent variables.

Dependent Variables

For research question three, the presence or absence of PTSD is the dependent variable.

Confounding Variables

For research question three, the confounding variables are gender, ethnicity, age, and period of service.

Definition of Variables

GI Disease and PTSD serve as both independent and dependent variables in this study, based on the specific research question.

Conceptual Definitions

Post-traumatic stress disorder is conceptually defined as a mental illness that occurs after witnessing or experiencing a particularly disturbing, upsetting, or painful experience. The disorder is not be identical in every Veteran, just as the triggering trauma is not the same for every individual. Some of the core symptoms that define the disorder are nightmares, flashbacks, intrusive memories of the traumatic event, and alterations in mood, emotions, sleep, and daily functioning (American Psychiatric Association, 2013).

Functional GI Diseases are conceptually defined as a set of illnesses of the stomach and bowel that do not have a physiological identifiable cause and disrupt the functioning of the individual.

Structural and motility GI Diseases are conceptually defined as a set of illnesses of the stomach and bowel that have an identifiable physiologic cause and disrupt the functioning of the individual.

Operational Definitions

PTSD, a diagnosis identified under the DSM-5 (2013), is operationally defined via specific indicators under Criteria A-H:

- Criterion A conceptually defined a traumatic event as: “Exposure to actual or threatened death, serious injury, or sexual violence.”

- Criterion B requires evidence of one or more intrusion symptoms, operationally defined as intrusive and distressing memories, nightmares, dissociative reactions, psychological distress at exposure to cues of the trauma, and/or physiological distress at exposure to cues.
- Criterion C requires evidence of one avoidance symptom, operationally defined to include either avoidance of distressing memories, thoughts or feelings about the trauma; and/or avoidance of external reminders, such as people, places, conversations, activities, and/or situations.
- Criterion D requires evidence of two or more cognitive and mood related symptoms, operationally defined to include memory loss of the event, negative beliefs, distorted cognitions about the cause or consequences of the event, negative emotional state, diminished interest in activities, detachment, and/or inability to experience positive emotions.
- Criterion E requires evidence of two symptoms of alterations in arousal or reactivity, operationally defined to include irritable behavior or angry outbursts, reckless behavior, hypervigilance, exaggerated startle response, difficulty concentrating, and/or sleep disturbance.
- Criteria F requires evidence that the disturbance persist longer than one month.
- Criteria G requires that the condition causes clinically significant distress or impairment to the individual.
- Criteria H states that the condition cannot have been caused by a medical condition or substance use (American Psychiatric Association, 2013, p. 271).

In order to receive a diagnosis of PTSD under the DSM-5, an individual must meet all criteria A-H.

Functional GI Disease is operationally defined as diagnosed IBS, chronic constipation, and functional dyspepsia. This group of illnesses is diagnosed using the Rome Criteria, which is based on symptomology, with no identifiable change in the body or structure of the organs (Drossman, 2016).

Structural or motility diseases are operationally defined as diagnosed GERD, PUD, IBD, ulcerative colitis, diverticular disease, and Crohn's disease. This group of illnesses is diagnosed based on a change in physiology of the organ at the macro- or micro-level, or altered motility relating to muscle activity (Drossman, 2016).

Confounding Variables

The *confounding variables* include age, ethnicity, gender, and period of service. These demographic data are descriptive variables reported by Veterans enrolling in Veterans Affairs healthcare services.

Gender is operationally and conceptually defined as the sex determined at the Veteran's birth, as listed on their birth certificate.

Age is operationally and conceptually defined as the number of years since the individual's birth.

Ethnicity is operationally and conceptually defined as the self-identified race of the individual.

Period of service is conceptually defined as the wartime period in which the Veteran served. Rates of PTSD development vary based on the period of service, with 15% of Vietnam Veterans, 12% of Gulf War Veterans, and 11-20% of Operations Iraqi

Freedom (OIF) and Enduring Freedom (OEF) Veterans developing the disorder, (US Department of Veterans Affairs, 2018). The VA operationally defines periods of service as the following wartime periods:

- "Mexican Border Period (May 9, 1916 – April 5, 1917 for Veterans who served in Mexico, on its borders, or adjacent waters);
- World War I (April 6, 1917 – November 11, 1918);
- World War II (December 7, 1941 – December 31, 1946);
- Korean Conflict (June 27, 1950 – January 31, 1955);
- Vietnam era (February 28, 1961 – May 7, 1975 for Veterans who served in the Republic of Vietnam during that period; otherwise August 5, 1964 – May 7, 1975)
- Gulf War (August 2, 1990 – through a future date to be set by law or Presidential Proclamation)" (U.S. Department of Veterans Affairs, 2018).

When classifying patients in their medication record, there are many options that the Department of Veterans Affairs utilizes for Period of Service, several of which apply to non-Veteran patients such as active duty military personnel or foreign dignitaries making use of the VA for their medical care. This study included patients with the following classifications: Korean, Persian Gulf War, Post-Korean, Post-Vietnam, Pre-Korean, Spanish American, Vietnam Era, World War I, and World War II.

Gaps in the Literature

The has long shown a relationship between GI symptoms and both stress and anxiety (Ford, et al, 1987; Locke, et al, 2004; Rao, et al, 1998). One study has investigated the relationship between gastrointestinal distress and the experience of

adversity in childhood. The authors define adversity as "early adverse care experiences," such as being in foster care or institutions. These experiences were associated with increased gastrointestinal symptoms in these youth. The researchers went on to follow-up with stool samples and functional magnetic resonance imaging and found that this adversity was associated with gut microbial changes and prefrontal cortex activation in response to emotional faces (Callaghan, et al., 2019). The study did not go as far as to screen the children for PTSD.

There is some research on the relationship between GI Diseases and PTSD. By definition, PTSD involves a traumatic stressor and ongoing symptoms of anxiety. Additionally, individuals often relive the traumatic stressor in the form of flashbacks and nightmares (American Psychiatric Association, 2013). Therefore, PTSD may be assumed to be a form of chronic stress.

Two studies have specifically reviewed the comorbidity of PTSD and IBS. In the *first*, authors recruited 50 participants with IBS and found that 36% of the subjects met criteria for PTSD, which was a significant result. However, this study primarily found the specific trauma that met criteria for PTSD diagnosis was physical or sexual abuse (i.e. experienced by 44% of all participants) (Irwin, et al., 1996). However, this data may or may not be generalizable to patients with military-related PTSD, as traumas experienced in the military are often from combat, rather than abuse.

In the more recent *second* study, Iorio, Makipour, Palit, and Friedenberg studied a group of 21,264 African Americans. These researchers selected all the individuals with IBS from this population (8.2%) and found those with IBS were significantly more likely to be diagnosed with PTSD (2014).

The limitation in both studies is that the subjects were all diagnosed with IBS, then a search was conducted for mental health disorders within that population. The research of Irwin, et al, (1996), Maguen, et al, (2013), and Savas, et al, (2008), mentioned throughout this paper, demonstrates the percentage of patients with IBS who have mental health disorders, but does not describe the percentage of patients with PTSD who have GI diseases. These studies do not address the question of whether GI symptoms or diseases accompany PTSD. The research also does not address whether there is a significant correlation between GI symptoms and PTSD.

Finally, there has been one study that specifically researched the association between GI disease and PTSD. In the Danish population, researchers found that among those with PTSD, risk of any GI disease was 25%, with PTSD having the strongest association with peptic ulcer (Gradus, Farkus, Svensson, Ehrenstein, Lash, & Sorensen, 2017). This study is a good start at describing the relationship between GI disease and PTSD, but generalizability is limited to the Danish population. The study does not review PTSD in the context of the United States Veteran population.

Rationale for Study

Currently, the prevalence of PTSD and GI Disease as co-occurring disorders is unknown. The current state of the science does not examine the contribution of trauma-related stressors to the symptomology of GI Diseases. Conversely, the current research also does not examine whether the presence of GI Disease is correlated with the development of psychiatric illness such as PTSD. Research is needed to describe the relationship between PTSD and GI disease before there can be progress in treatment.

Summary and Critique of Literature Review

Summary

Review of Theoretical and Historical Literature.

The co-morbid presence of GI symptoms and post-traumatic stress symptoms have been identified as early as the Civil War, pre-dating the specific diagnoses of diseases such as IBS and PTSD as we know them today. This co-morbidity of symptoms has been shown across a variety of wars, time-periods, and cultures.

Review of Relevant Research.

Research has shown an association between the gut and mental health. The CNS and ANS assist in communication between the gut and the brain through the gut-brain axis. Gut bacteria have been shown to have an influence on this communication pathway, and antidepressants have been shown to have an influence on gut bacteria. There is also some research to indicate that trauma and adversity affect gut bacteria and GI symptoms. The evidence suggests that there may be an association between GI disease and PTSD, but further research is needed to fully explore the relationship.

Review of Research Variables.

Functional GI disease, structural GI disease, and PTSD serve as both independent and dependent variables for this study. Age, ethnicity, gender, and period of service serve as confounding variables for the study.

Critique of the Review of Literature

This Literature Review did not determine the prevalence of Veterans with specific GI Diseases, e.g. peptic ulcer, gastroesophageal reflux, diverticular, inflammatory bowel, ulcerative colitis, Crohn's, irritable bowel, chronic constipation, and functional dyspepsia

diseases. The Review did not identify the prevalence of co-occurring GI Disease and PTSD within the United States Veteran population. The Review did not analyze the relationship between gender, age, ethnicity, period of service, and secondary mental illness, variables confounding the relationship of GI disease and PTSD. This study is designed to identify if GI Disease and PTSD accompany each other. Should a relationship be demonstrated, further research is needed to describe correlations and risk factors, which will then lead to prevention strategies.

Summary of Chapter

Chapter Two provided a review of literature regarding the relationship between to GI Disease and PTSD. A theoretical and historical overview of literature regarding PTSD and GI disease, including related research studies, was presented. The literature review also explored related variables, e.g. prevalence, demographics, and risk factors. Finally, the Chapter defined variables, identified gaps in the literature, and discussed the rationale for the study.

Plan for Remaining Chapters

Chapter Three discusses the application of the quantitative research design. Chapter Four presents the study findings. Chapter Five presents the conclusions, discussion, and recommendations relative to the study findings.

References

Addolorado, G., Mirijello, A., D'Angelo, C., Leggio, L., Ferrulli, A., Abenavoli, L., … Gasbarrini, G. (2008). State and trait anxiety in patients affected by gastrointestinal diseases: Psychometric evaluation of 1641 patients referred to an internal medicine outpatient setting. *International Journal of Clinical Practice*. *62*, pp. 1063-1069. doi: 10.1111/j.1742-1241.2008.01763.x

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.) Arlington, VA: American Psychiatric Association.

Bennett, E. J., Tennant, C. C., Badcock, C. A., & Kellow, J. E. (1998). Level of chronic life stress predicts clinical outcome in irritable bowel syndrome. *Gut. 43*, pp. 56-261.

Bonaz, B. L., & Bernstein, C. N. (2013). Brain-gut interactions in inflammatory bowel disease. *Reviews in Basic and Clinical Gastroenterology and Hepatology, 144*, pp. 36-49.

Burokas, A., Arboleya, S., Moloney, R. D., Peterson, V. L., Murphy, K., Clarke, G., Stanton, C., Dinan, T. G., & Cryan, J. F. (2017). Targeting the microbiota-gut-brain axis: prebiotics have anxiolytic and antidepressant-like effects and reverse the impact of chronic stress in mice. *Biol. Psychiatry 82*, pp. 472-487.

Callaghan, B. L., Fields, A., Gee, D. G., Gabard-Durnam, L., Caldera, C., Humphreys, K. L., Goff, B., Flannery, J., Telzer, E. H., Shapiro, M., & Tottenham, N. (2019). Mind and gut: Associations between mood and gastrointestinal distress in children

exposed to adversity. *Development and Psychopathology*, pp. 1-20. https//doi.org/10.1017/S0954579419000087

Canavan, C., West, J., & Card, T. (2014). The epidemiology of irritable bowel syndrome. *Clinical Epidemiology, 6,* pp. 71-80.

Centers for Disease Control and Prevention. (2019). Inflammatory Bowel Disease: Data and statistics. Retrieved from https://www.cdc.gov/ibd/data-statistics.htm

Cowan, C. S. M., Hoban, A. E., Ventura-Silva, A. P., Dinan, T. G., Clark, C., & Cryan, J. F. (2017). Gutsy moves: The amygdala as a critical node in microbiota to brain signaling. Bioessays, 40, DOI: 10.1002/bies.201700172.

Davis, D. J., Hecht, P. M., Jasarevic, E., Beversdorf, D. Q., Will, M. J., Fritsche, K., & Gillespie, C. H. (2017).Sex-specific effects of docosahexaenoic acid (DHA) on the microbiome and behavior of socially-isolated mice. *Brain Behav Immun 59*, pp. 38–48.

De Vaddera, F., Grasseta, E., Mannerås Holma, L., Karsentyb, G., Macphersonc, A. J., Olofssona, L. E., & Bäckheda, F. (2018). Gut microbiota regulates maturation of the adult enteric nervous system via enteric serotonin networks. *Proceedings of the National Academy of Sciences of the United States of America*, 115, pp. 6458-6463.

Dinan, T. G., Stilling, R. M., Stanton, C., & Cryan, J. F. (2015). Collective unconscious: How gut microbes shape human behavior. *Journal of Psychiatric Research. 63,* pp. 1-9. doi:10.1016/j.jpsychires.2015.02.021

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

Drossman, D. A., Leserman, J., Nachman, G., Li, Z., Gluck, H., Toomey, T.C., & Mitchell, C. M. (1990). Sexual and physical abuse in women with functional or organic gastrointestinal disorders. *Annals of Internal Medicine, 113,* pp. 828-833.

Drossman, D. A., Toner, B. B., Whitehead, W. E., Diamant, N. E., Dalton, C. B., Duncan, S., … Bangdiwala, S. I. (2003). Cognitive-behavioral therapy versus education and desipramine versus placebo for moderate to severe functional bowel disorders. *Gastroenterology, 125*, pp. 19-31. doi:10.1016/S00016-5085(03)00669-3.

El-Gabalaway, R., Mackenzie, C. S., Pietrzack, R. H., & Sareen, J. (2014). A longitudinal examination of anxiety disorders and physical health conditions in a nationally representative sample of U.S. older adults. *Exp Gerontol, 60,* pp. 46-56. doi: 10.1016/j.exger.2014.09.012

Fichna, J., & Storr, M. A. (2012). Brain-gut interactions in IBS. *Frontiers in Pharmacology, 3,* pp, 1-12. doi:10.3389/fphar.2012.00127.

Ford, M. J., Miller, P. M., Eastwood, J., & Eastwood, M. A. (1987). Life events, psychiatric illness, and the irritable bowel syndrome. *Gut, 28,* pp. 160-165.

Furness, J. B., Callaghan, B. P., Rivera, L. R., & Cho, H. J. (2014). The enteric nervous system and gastrointestinal innervation: integrated local and central control. *Adv Exp Med Biol: 817,* pp. 39-71. doi: 10.1007/978-1-4939-0897-4_3.

Goulston, K. J., Dent, O. F., Chapuis, P. H., Chapman, G., Smith, C. I., Tait, A. D., & Tennant, C. C. (1985). Gastrointestinal morbidity among World War II prisoners of war: 40 years on. *The Medical Journal of Australia, 143,* pp. 6-10.

Gradus, J. L., Farkas, D. K., Svensson, E., Ehrenstein, V., Lash, T. L., & Sorensen, H. T. (2017). Posttraumatic stress disorder and gastrointestinal disorders in the Danish population. *Epidemiology, 28,* pp. 354-360.

Grover, M., & Drossman, D. A. (2011). Centrally acting therapies for irritable bowel syndrome. *Gastroenterology Clin. North Am, 40*, pp. 183-206.

Hahn, B. A., Kirchdoerfer, L. J., Fullerton, S., & Mayer, E. (1997). Patient-perceived severity of irritable bowel syndrome in relation to symptoms, health resource utilization and quality of life. *Alimentary Pharmacology and Therapeutics, 11*, pp. 553-559.

Herculano-Houzel, S. (2009). The human brain in numbers: A linearly scaled-up primate brain. *Frontiers in Human Neuroscience: 3*. doi: 10.3389/neuro.09.031.2009

Hou, J. K., Kramer, J. R., Richardson, P., Mei, M., & El-Serag, H. B. (2013). The incidence and prevalence of inflammatory bowel disease among U.S. Veterans: A national cohort study. *Inflammatory Bowel Disease, 19*, pp. 1059-1064.

Iorio, N., Makipour, K., Palit, A., & Friedenberg, F. K. (2014). Post-traumatic stress disorder is associated with irritable bowel syndrome in African Americans. *Journal of Neurogastroenterology & Motility, 20,* pp. 523-530. doi:10.5056/jnm14040.

Irwin, C., Falsetti, S. A., Lydiard, R. B., Ballenger, J. C., Brock, C. D., & Brener, W. (1996). Comorbidity of posttraumatic stress disorder and irritable bowel syndrome. *Journal of Clinical Psychiatry, 57*, pp. 576-578.

Jackson, J. L., O'Malley, P. G., Tomkins, G., Balden, E., Santoro, J., & Kroenke, K. (2000). Treatment of functional gastrointestinal disorders with antidepressant medications: A meta-analysis. *The American Journal of Medicine, 108*, pp. 65-72.

Johanson, J. F., & Kralstein, J. (2007). Chronic constipation: A survey of the patient perspective. *Alimentary Pharmacology and Therapeutics, 25*, pp. 599-608. doi.10/1111/j.1365-2036.2006.03228.x.

Koloski, N. A., Talley, N. J., & Boyce, P. M. (2000). The impact of functional gastrointestinal disorders on quality of life. *American Journal of Gastroenterology, 95*, pp. 67-71.

Levi, R. L., Olden, K. W., Naliboff, B. D., Bradley, L. A., Francisconi, C., Drossman, D. A., & Creed, F. (2006). Psychosocial aspects of the functional gastrointestinal disorders. *Gastroenterology, 130*, pp. 1447-1458. doi:10.1053/j.gastro.2005.11.057.

Locke, G. R., Weaver, A. L., Melton, L. J., & Talley, N. J. (2004). Psychosocial factors are linked to functional gastrointestinal disorders: A population based nested case-control study. *American Journal of Gastroenterology, 99*, pp. 350-357. doi:10.1111/j.1572-0241.2004.04043.x

Loyd, R. A., & McClellan, D. A. (2011). Update on the evaluation and management of functional dyspepsia. *American Family Physician, 83*, 547-552.

Lukic, I., Getselter, D., Ziv, O., Oron, O., Reuveni, E., Koren, O., & Elliot, E. (2019). Antidepressants affect gut microbiota and *Ruminococcus flavenfaciens* is able to abolish their effects on depressive-like behavior. *Translational Psychiatry, 9,* pp. 1-16.

Maguen, S., Madden, E., Cohen, B., Bertenthal, D., & Seal, K. (2014). Association of mental health problems with gastrointestinal disorders in Iraq and Afghanistan Veterans. *Depression & Anxiety, 31,* pp. 160-165. doi: 10.1002/da.22072

Martini, F. H., Nath, J. L, & Bartholomew, E. F. (2017). *Fundamentals of Anatomy & Physiology, 11th Ed*. San Francisco, CA: Pearson, pp. 930-984.

National Institute of Diabetes and Digestive and Kidney diseases (NIDDKD). (2019). Definition and facts for GER and GERD. Retrieved from https://www.niddk.nih.gov/health-information/digestive-diseases/acid-reflux-ger-gerd-adults/definition-facts

Peery, A. F., Dellon, E. S., Lund, J., Crockett, S. D., McGowan, C. E., Bulsiewicz, W. J., … Shaheen, N. J. (2013). Burden of gastrointestinal disease in the United States: 2012 update. *Gastroenterology, 143,* pp. 1179-1187. doi:10.1053/j.gastro.2012.08.002.

Pizarro, J., Silver, R. C., & Prause, A. (2006). Physical and mental health costs of traumatic war experiences among Civil War Veterans. *Archives of General Psychiatry, 64,* pp. 193-200.

Quigley, E. M. M. (2013). Gut bacteria in health and disease. *Gastroenterol Hepatol, 9,* pp. 560–569.

Riddle, M. S., Welsh, M., Porter, C. K., Nieh, C., Boyko, E. J., Gackstetter, G., & Hooper, T. (2016). The epidemiology of irritable bowel syndrome in the US military: Findings from the millennium cohort study. *American Journal of Gastroenterology, 111*, pp. 93-104.

Rogers, G. B., Keating, D. J., Young, R. L., Wong, M. L, Licino, J., & Wesselingh, S. (2016). From gut dysbiosis to altered brain function and mental illness: Mechanisms and pathways. *Molecular Psychiatry, 21*, pp. 738-748.

Ross, C. A. (2005). Childhood sexual abuse and psychosomatic symptoms in irritable bowel syndrome. *J. Child Sex Abus, 14,* pp. 27-38.

Rousseaux, C., Thuru, X., & Gelot, A. (2007). Lactobacillus acidophilus modulates intestinal pain and induces opioid and cannabinoid receptors. *Nat Med, 13,* pp. 35-37

Sanchez, M. I., & Bercik, P. (2011). Epidemiology and burden of chronic constipation. *Can Journal of Gastroenterology, 25*, pp. 11B-15B.

Savas, L. S., White, D. L, Wieman, M., Dacis, K., Fitzgerald, S., Smith, S. L., … El-Serag, E.B. (2008). Irritable bowel syndrome and dyspepsia among women Veterans: Prevalence and association with psychological illness. *Alimentary Pharmacology & Therapeutics*, *29*, pp. 115-125. doi:10.1111/j.1365-2036.2008.03847.x.

Stahl, S. M. (2008). *Stahl's Essential Psychopharmacology: Neuroscientific basis and practical applications.* New York, NY: Cambridge University Press.

Tabas, G., Beaves, M., Wang, J., Friday, P., Mardini, H., & Arnold, G. (2004). Paroxetine to treat irritable bowel syndrome not responding to high-fiber diet: A double-blind, placebo-controlled trial. *American Journal of Gastroenterology, 99*, pp. 914-920. doi:10.1111/j.1572-0241.2004.04127x

Tache, Y., Martinez, V., Million, M., & Wang, L. (2001). Stress and the gastrointestinal tract III: Stress-related alterations of gut motor function: role of brain corticotropin-releasing factor receptors. *American Journal of Gastrointestinal & Liver Physiology, 280*, pp. G173-G177.

UNC School of Medicine. (2017). No title. Retrieved Jan. 17, 2017 from https://www.med.unc.edu/ibs/files/educational-gi-handouts/What%20Is%20Functional%20GI.pdf.

U.S. Department of Veterans Affairs. (2018). *About VHA*. Retrieved from https://www.va.gov/health/aboutvha.asp

U.S. Department of Veterans Affairs. (2018). *Health*. Retrieved from www.va.gov/HEALTH

U.S. Department of Veterans Affairs. (2019). *History of PTSD in Veterans: Civil war* DSM-5. Retrieved from https://www.ptsd.va.gov/understand/what/history_ptsd.asp

U.S. Department of Veterans Affairs. (2018). *PTSD*. Retrieved from www.PTSD.VA.gov

Walker, E. A., Gelfand, A., Katon, W. J., Koss, M. P., Von Korff, M., Bernstein, D., & Russo, J. (1999). Adult health status of women with histories of childhood abuse and neglect. *The American Journal of Medicine, 107,* pp. 332-339.

Walker, E. A., Katon, W. J., Roy-Byrne, P. P., Jemelka, R. P., & Russo, J. (1993). Histories of sexual victimization in patients with irritable bowel syndrome and inflammatory bowel disease. *American Journal of Psychiatry, 150*, pp. 1502-1506.

Walker, E. A., Roy-Byrne, P. P., Katon, W. J., Li, L., Amos, D., & Jiranek, G. (2002). Psychiatric illness and irritable bowel syndrome: A comparison with inflammatory bowel disease. *American Journal of Psychiatry, 147,* pp. 1656-1661.

Weinstein, E. A., & Stein, M. H. (1945). Psychogenic disorders of the upper gastrointestinal tract in combat personnel. *War Medicine, 8,* pp. 365-370.

Whitehead, W. E., Palsson, O., & Jones, K. R. (2002). Systematic review of the comorbidity of irritable bowel syndrome with other disorders: What are the causes and implications? *Gastroenterology*, *122*, pp. 1140-1156. doi:10.1053/gast.2002.32392.

Zhang, Y., Chen, H., Long, Z., Cui, Q., & Chen, H. (2016). Altered effective connectivity network of the thalamus in post-traumatic stress disorder: a resting-state FMRI study with granger causality method. *Applied Informatics, 3*, pp. 1-8

Zeng J., Li Y. Q., Zuo X. L., Zhen Y. B., Yang J., Liu C. H. (2008). Clinical trial: Effect of active lactic acid bacteria on mucosal barrier function in patients with

diarrhoea-predominant irritable bowel syndrome. *Aliment Pharmacol Ther*, *28*, pp. 994–1002

Chapter Three: Research Design

Introduction

Chapter Three presents the research design. The Chapter begins by identifying the research question, and the research methodology (i.e. design and rationale) for exploring the aims. It then describes the application of retrospective, correlational, non-experimental principles in the study, including participant population, setting, and sample; and data collection, data analysis, and data management strategies. A discussion of ethical considerations and techniques utilized to protect the rights and confidentiality of study participants is also provided.

Specific Aims, Research Questions, and Hypothesis

Research Question, Specific Aim, and Hypotheses 1

Specific Aim 1.

Specific Aim 1 is: To determine the frequency with which GI Disease and PTSD are diagnosed co-morbidities in Veterans who have served during wartime periods.

Research Question 1.

Research Question 1 is: In Veterans who have served during wartime periods, what is the frequency with which GI Disease and PTSD are diagnosed co-morbidities?

Research Hypothesis 1.

Research Hypothesis 1 is: In Veterans who have served during wartime periods, GI Disease and PTSD are frequently diagnosed co-morbidities.

Research Question, Specific Aim, and Hypothesis 2

Specific Aim 2.

Specific Aim 2 is: To determine the frequency with which a diagnosis of functional or structural GI Disease accompanies a diagnosis of PTSD in Veterans who have served during wartime periods.

Research Question 2.

Research Question 2 is: In Veterans who have served during wartime periods, what is the frequency with which a diagnosis of functional or structural GI Disease accompanies a diagnosis of PTSD?

Research Hypothesis 2.

Research Hypothesis 2 is: In Veterans who have served during wartime periods, a diagnosis of functional or structural GI Disease frequently accompanies a diagnosis of PTSD.

Research Question, Specific Aim, and Hypothesis 3

Specific Aim 3.

Specific Aim 3 is: To determine the frequency with which a diagnosis of PTSD accompanies a diagnosis of functional or structural GI Disease in Veterans who have served during wartime periods.

Research Question 3.

Research Question 3 is: In Veterans who have served during wartime periods, what is the frequency with which a diagnosis of PTSD accompanies a diagnosis of functional or structural GI Disease?

Research Hypothesis 3.

Research Hypothesis 3 is: In Veterans who have served during wartime periods, a diagnosis of PTSD frequently accompanies a diagnosis of functional or structural GI Disease.

Research Methodology: The Design and Rationale

The Design

The goal of the retrospective, correlational methodology is to interpret the data to describe the relationship between GI disease and PTSD.

The following section describes the implementation of Transactional Model of Stress and Coping (TMSC Model) principles in the present study. The TMSC Model allows for the evaluation of coping after a stressful event. In the model, a transaction is conceptually defined as a stressful event between the person and the environment. In the case of PTSD, transactions may encompass not only the initial stressor or trauma, but the daily reminders of the trauma, or triggers, that produce flashbacks and nightmares, causing the individual to relive the initial trauma (Glanz, Rimer, & Viswanath, 2008).

This retrospective, correlational study obtained data from the Department of Veteran's Affairs patient databases, managed by the VA Information Resource Center

(VIRec). The student, who is also an employee of the Department of Veterans Affairs, served as the primary investigator. Additionally, as the primary investigator is acting in the role of student, rather than employee, the Department of Veterans Affairs required that a second employee serve as co-investigator, to be termed secondary investigator going forward. The secondary investigator served as mentor on the project and co-signed required documents for the Department of Veterans Affairs. However, the student/primary investigator performed the entirety of the workload in terms of analyzing data and writing the dissertation to avoid conflict of interest so that the secondary investigator may retain voting privileges within the dissertation committee.

The Rationale for the Design

The rationale for use of the retrospective, correlational design is to make use of existing data for a large population, requiring minimal risk to that population.

Population and Setting

The Population

This population of subjects contains all Veterans that are currently enrolled in the Veterans HealthCare system in the United States. Participants were age 18 or older, include potentially all ethnicities, and males and females.

The Setting

Data is created when a healthcare provider (including, but not limited to, a physician, nurse practitioner, physician assistant, social worker, and clinical pharmacist) enters an ICD9 or ICD10 diagnosis associated with a patient care visit into the

Department of Veteran's Affairs patient charting system, the Computerized Patient Record System (CPRS). Data creation can occur at any inpatient or outpatient encounter within a Department of Veterans Affairs facility anywhere in the United States, but this study utilized outpatient data only. Data is stored not by patient identifier (such as social security number), but by a specific visit that occurred at a specific location and time within the Veterans Healthcare Administration (VHA) system nationally. In order to piece together diagnostic data from a visit with demographic information from the associated patient, the data must be queried from tables in Microsoft SQL Server. SQL, pronounced "sequel," commonly stands for Standard Query Language.

Sampling Method and Access

Participant Inclusion Criteria

Participants/Subjects in the study were Veterans with either or both diagnosis of PTSD and GI Disease. Specific GI Diseases were those that accounted for more than 500,000 ambulatory care visits annually in the United States, which included peptic ulcer disease, gastroesophageal reflux disease, diverticular disease, ulcerative colitis, Crohn's disease, irritable bowel syndrome, and functional dyspepsia, as well as the symptoms of constipation and nausea/vomiting (Everhart & Ruhl, 2009; Kozma, Barghhout, Slaton, Frech, & Reeder, 2002).

Participant Exclusion Criteria

Participants/Subjects were excluded from the study who were not diagnosed with GI Disease nor PTSD. Due to the numerous diagnostic codes that can fall under the term "gastrointestinal disease," specific diseases were only included if they had accumulated

more than 500,000 ambulatory care visits annually in the United States. GI Diseases accumulating less than 500,000 ambulatory care visits were excluded. Diseases with an identifiable, diagnosed non-GI cause were excluded, such as cancer, infection, and acute injury or hernia. Diseases of the liver, gallbladder, and pancreas were also excluded.

The Sampling Method

The data manager at National Data Systems (NDS) assembled a cohort of all patients treated by VHA system with either or both diagnosis of PTSD, GI Disease, and/or GI symptoms since the creation of the database in 1999. Total numbers of patients and Veterans treated by VHA for each year 2000-2019 and total over the course of these years was given to researchers by NDS. This sampling method allowed the researchers to calculate the percentage of those with PTSD who do and do not have GI issues, and the percentage of those with GI issues who do and do not have PTSD.

Demographics of the Veterans.

Expected enrollment table numbers were calculated as follows. According to the Department of Veterans Affairs population estimate models, there are 20.4 million Veterans of the United States Military (2016). The Veteran sample was selected from the patient population treated by the VA, which is reported as nine (9) million Veterans each year (U.S. Department of Veterans Affairs, 2017). As of 2016, the US military gender percentage was 91% male and 9% female. Additionally, military members are 77% White, 12% Black, 7% Hispanic, 2% Asian, and 2% other ethnicities (U.S. Department of Veterans Affairs, 2016).

Demographics of Veterans with PTSD.

The Department of Veterans Affairs estimates 7-8% of the total U.S. population will develop PTSD in their lifetime. Furthermore, rates of diagnosed PTSD vary according to the Veteran's war record, at the following rate:

- 30% of Vietnam Veterans;
- 12% Gulf War Veterans;
- 11-20% of Operation Iraqi Freedom and Operation Enduring Freedom Veterans (U.S. Department of Veterans Affairs, 2017).

In the general adult population, ten percent of women, compared to only four percent of men, will develop PTSD in their lifetime (Department of Veterans Affairs, 2017). Since the military is mainly comprised of men (91%, as cited above), it can be inferred that the study will identify more men than women with PTSD.

A conservative estimate of the potential sample of 630,000 Veterans with PTSD is identified in Table 3.1, *Estimated Sample of Veterans with PTSD.* This table was calculated based upon Veteran demographics cited in the procedures/protocols section.

Table 3.1 Estimated Demographics of Veterans with PTSD

	Total	**Men – 91%**	**Women – 9%**
White – 77%	485,100	441,441	43,659
Black – 12%	75,600	68,796	6,804
Hispanic – 7%	44,100	40,131	3,969
Asian – 2%	12,600	11,466	1,134
Other – 2%	12,600	11,466	1,134
Estimated Total:	**630,000**	573,300	56,700

Demographics of Veterans with GI Disease.

Estimates of the number of GI Disease in the military or Veteran populations were not available. It was assumed that there would be Veterans with a diagnosis of GI disease that would not meet criteria for PTSD. Therefore, the expected total enrollment of Veteran subjects was higher than Table 3.1 projected.

Ethical Considerations

Human Subjects: IRB Approval

Procedures for the study were approved by the Research and Development Committee at the Tennessee Valley Healthcare System (TVHS) branch of the Department of Veterans Affairs (Appendix A). The study was deemed exempt from review by the Institutional Review Board) (IRB) (Appendix B) and the Research Safety Committee (Appendix C) at TVHS. VHA also requires documentation of waiver of consent and HIPAA, which was approved by TVHS (Appendix D). The study was also reviewed and deemed exempt by the University of Texas Medical Branch (UTMB) IRB (Appendix E).

The risks to participants in this study were minimal. Study participants' confidentiality was protected in several ways. HIPAA identifying information was not included with the data set pulled in the SQL query. Data was listed by a code number to replace each participant's name, and any information that could be linked to the participant was removed from the data. The consent process was waived by both IRBs due to minimal risk (Appendices A-E).

Data Transfer to PI.

Once the data manager created a cohort of patients based on given ICD9 and ICD10 codes, it was stored as a table within Microsoft SQL Server. There were separate tables for patient identifiers and patient demographics. In order to collect the data in a usable format, the principle investigator was responsible for querying the data to combine these tables but omit any patient identifying information and extra information that researchers had not requested access to in the IRB and DART applications. In order to identify primary keys to connect the tables, the researcher was given access to CDW confidential metadata reports.

Data Storage.

Data is stored on national servers which are shared by researchers across the country. In order to optimize use of resources for all users, NDS "kills" any query that requires excessive resources. Since this study was quite large, data queries had to be broken up into smaller chunks of time and then combined into one table to create the 20 years of data that was needed.

Data query.

Data was queried one year at a time for each whole year 1999-2018, and partial year Jan 1 – March 31, 2019, as April 1, 2019 was the cut-off date per TVHS IRB application that was submitted. An example of one year of SQL query can be seen in Appendix F. This query was repeated 20 times for years 1999-2019, with only dates changed. These queries combining multiple tables were saved as new permanent tables in SQL Server. Once all twenty-one tables were created, a new SQL query was performed

to combine the tables into one table of all years, combining patients that occurred in multiple years into a single row per unique patient. The twenty-one yearly tables and one combined table were then transferred to SAS 9.4 for analyzation.

Measurement Methods

Guidelines for Querying Data

Data for the study consisted of demographic data and diagnostic codes for PTSD, GI disease, and secondary mental illness. Demographic data included the participant's age in years, gender, ethnicity, and period service.

Table 3.2 Guidelines for Querying Data

A. Any patient with ***any*** of the codes in column A, using diagnosis codes from ICD-9 and ICD-10 to create a cohort	B. *Within those pulled for column A*, **ANY** and **ALL** diagnosis of the following:	C. For ***every*** record pulled, also pull **EACH** of the following:
All Codes for PTSD: F43.10, F43.11, F43.12, 309.81	ICD-10 codes for secondary mental illness: range F01-42, F43.0 and 43.2, F45-99	Age
ICD-9 codes for GI diseases: 530.81, 536.8, 555, 556, 562, 564, and related sub-codes	ICD-9 codes for secondary mental illness: range 290-319	Gender

ICD-10 codes for GI diseases: K21, K27, K30, K50, K51, K57, K58, K59.04 and all related sub-codes		Ethnicity
ICD-9 and ICD-10 codes for GI symptom of nausea/vomiting: R11 and 787.0		Period of Service

The data manager at VHA was responsible for identifying a cohort based on Column A. Then the researcher was responsible for compiling the diagnostic information from the cohort with the data from Columns B and C.

Diagnostic Codes.

ICD-9 or 10 codes were pulled from a visit located anywhere outpatient at VHA. Veteran records would only show in a table if they were treated for the illness in that year. For example, if a Veteran was treated for GERD in 2000, but then resolved and was not treated in 2001, then this Veteran would not be recorded in the 2001-year table (unless treated for one of the other GI diseases or PTSD included in the year 2001). When combining all years, that Veteran would be recorded as positive for a diagnosis of GERD in the "All Years" table.

Veteran Age.

Age was pulled at the time of the last visit. When twenty-one years were combined into one comprehensive table, age was recorded as the most recent age. For example, if a Veteran was aged 40 at last related visit in 2000 and then deceased before 2001, that Veteran would not be recorded in the 2001 table. However, in the "All Years" table that Veteran record would be included, and age would show as 40.

Period of Service.

Period of Service showed as the most recent period of service in which the Veteran served. It is possible that a Veteran served in multiple periods of service. If a Veteran served in both the Vietnam Era and the Persian Gulf War, then CDW stores that Veteran's Period of Service information as "Persian Gulf War," and this is what is shown in both yearly tables and the "All Years" combined tables.

Gender and Ethnicity.

Gender and Ethnicity are collected when a Veteran enters the VHA system after discharge from the military. In most cases this information will not change over time. However, should a Veteran elect to have this information changed in the record, it will change across time. Gender and Ethnicity present in the data record at the time of data collection. In the case of this study, the researcher queried the data between the dates of December 27 and December 31, 2019, so gender and ethnicity in both the yearly tables and the "All Years" table will demonstrate whichever selection was listed in the CDW at those dates.

Secondary Mental Illness.

Secondary mental illnesses were collected by ICD-9 and ICD-10 diagnostic codes and complied into categories based on the DSM-5. Disorders such as major depressive disorder, including all subtypes, and persistent depressive disorder or dysthymia were classified as "depressive disorders." All subtypes of bipolar disorder were combined into a classification as "bipolar disorders." Disorders such as panic disorder, generalized anxiety disorder, obsessive compulsive disorder were classified as "anxiety disorders." Schizophrenia, delusional disorder, and schizoaffective disorder were classified as

"psychotic disorders." Any drug or alcohol disorder was classified as "substance abuse." All types of dementias and Alzheimer's were classified as "dementias." This review is not an exhaustive list of all potential diagnoses included but is a comprehensive list of the classifications of mental illness-classification. For complete range of ICD-9 and ICD-10 codes used under each classification, see SQL code in Appendix F.

Data Collection Process

Definition of Data

Data was created when a provider entered information in the patient record system at the Department of Veterans Affairs. This occurs at any outpatient setting at any VA hospital or clinic throughout the United States. Data is operationally defined as that information collected for this study, i.e. included diagnostic codes and non-identifying demographic information from outpatient visits only. Diagnostic codes were entered by a licensed provider at the time of the patient encounter. Demographic data was formed when the patient is entered into the VA system upon discharge from the United States military. The National Data Systems stores this data into the Corporate Data Warehouse (CDW) for the Department of Veterans Affairs for researchers to collect.

The Veteran Database

The Population.

The specific database used was the CDW, which contains patient diagnostic and demographic information on all patients treated by VHA from 1999 to present.

The Sample.

GI and PTSD Diagnosis.

CDW created a cohort of patients as requested by the researcher according to the specifications described in the sampling methods section. All patients with either or both PTSD and GI disease were pulled into a cohort, as described in the sampling methods section. Researchers are then responsible for querying this data using Microsoft SQL Server.

Secondary Mental Illness.

Additionally, researchers pulled diagnostic information on secondary mental illness within this group. As depression and anxiety have shown to be linked to certain gastrointestinal diseases, pulling secondary mental illness diagnosis allows researchers to discuss their contributions as potential confounding variables.

Patient Outpatient Visits.

Data was queried by patient outpatient visits that occurred within each year time frame, such as January 1, 2015 to December 31, 2015 (See sample query in Addendum F). This created 21 tables for years 1999-2019. Tables for 1999 and for 2019 were partial tables for separate reasons. The year 1999 was the creation of the computerized record database and therefore was a transition year in which not all records were computerized until the end of that calendar year. For this reason, NDS was not able to give the researcher a total number of patients treated within the VHA system in 1999. The year 2019 had to be collected as a partial year because of the start date of project listed on the Department of Veterans Affairs IRB application, which was April 1, 2019. Data collected for 2019 pertained only to visits dated January 1, 2019 to March 31, 2019. For this

reason, numbers of participants from 2019 cannot be accurately compared to total VHA patient counts for 2019.

Data Organization.

Once the data was organized for feasibility into the 21 tables, then those tables were combined with a second SQL query (Addendum G). This second query contained clauses that eliminated patients that repeat in more than one year, so that the patient appears in the All Years table only once. The age recorded in the All Years table is the age of the patient at their last recorded visit that met criteria for study inclusion. Therefore, if the patient's last visit was in 2015 and their age at that visit was 80 years old, then their age would be recorded in the All Years Table as 80 years old, regardless of whether the patient was living or deceased at the time of data collection in December 2019.

The final All Years Table and the 21 yearly tables were saved as permanent files within Microsoft SQL Server. They were transferred to SAS 9.4 analytical software via SAS query language using the "libname" function. This function creates a temporary library of tables, which meant that the tables had to be pulled into SAS at each session. However, since the tables remained permanent in SQL Server, they were not altered with each SAS session.

Limitations and Assumptions

Limitations

This study does not account for Veterans:

- with a GI or PTSD diagnosis who are not being treated by the Department of Veterans Affairs, such as those treated in private or community care:
- who are not being treated at all;
- with a misdiagnosis; or,
- an inaccurate recording of information at the provider level.

Assumptions

This study assumes that:

- The data is accurate,
- The data is accurately recorded and interpreted, and,
- Healthcare providers have accurately diagnosed Veterans with post-traumatic stress disorder and gastrointestinal disease.

Data Analysis Procedures

The goal of data analysis in retrospective, correlational methodology is to interpret the data to describe the relationship between GI Disease and PTSD.

The researcher used SAS 9.4 September 2017 software to transform the data and interpret the statistics.

Descriptive statistics, including means, percentages, histograms and contingency tables were used to describe and explain the data outcomes. Chi-Square with goodness-of-fit tests were used to examine the relationships between the categories and sub-categories of GI Disease and PTSD, as well as differences among categories of demographic data, (e.g. age, gender, ethnicities, period of service, and functional verses structural GI disorders).

Summary of Chapter

Chapter Three presented the research design. It began by identifying the research question, and the research methodology (i.e. design and rationale) for exploring the aims. Then the application of retrospective, correlational, non-experimental principles in the study, including participant population, setting, and sampling methods; and data collection, data analysis, and data management strategies were described. The Chapter also provided a discussion of ethical considerations and techniques utilized to protect the rights and confidentiality of study participants.

Plan for Remaining Chapters

Chapter Four presents the study findings. Chapter Five presents the conclusions, discussion, and recommendations relative to the study findings.

References

Everhart, J. E. & Ruhl, C. E. (2009). Burden of digestive diseases in the United States part I: Overall and upper gastrointestinal diseases. *Gastroenterology. 136,* pp. 376-386.

Glanz, K., Rimer, B. K., &Viswanath, K. (2008). *Health Behavior and Health Education*. San Francisco, CA: Jossey-Bass.

Kozma, C. M., Barghhout, V., Slaton, T., Frech, F., & Reeder, C.E. (2002). Office-based physician visits: A comparison of irritable bowel syndrome with other gastrointestinal disorders using national ambulatory medical care survey data. *Practical Gastroenterology. XXVL,* pp. 58-68.

U.S. Department of Veterans Affairs. (2018). *Health*. Retrieved from www.va.gov/HEALTH .

U.S. Department of Veterans Affairs. (2017). How common is PTSD? Retrieved from https://www.ptsd.va.gov/public/ptsd-overview/basics/how-common-is-ptsd.asp

U.S. Department of Veterans Affairs. (2016). National center for veterans analysis and statistics. Retrieved from https://www.va.gov/vetdata/veteran_population.asp

U.S. Department of Veterans Affairs. (2018). *PTSD*. Retrieved from www.PTSD.VA.gov .

Chapter Four: Findings

Introduction

Chapter Four presents the findings of this study, which were explored via the following three (3) Specific Aims:

- Specific Aim 1 is: "To determine the frequency with which GI Disease and PTSD are diagnosed co-morbidities in Veterans who have served in wartime periods."
- Specific Aim 2 is: "To determine the frequency with which a diagnosis of functional or structural GI Disease accompanies diagnosis of PTSD in Veterans who have served in wartime periods."
- Specific Aim 3 is: "To determine the frequency with which a diagnosis of PTSD accompanies a diagnosis of functional or structural GI Disease in Veterans who have served in wartime periods"

The Chapter begins with a presentation of sample characteristics and a psychometric estimate for the sample. In addition, major findings and conclusions are introduced, with a summary of findings.

Sample Characteristics

There were 6,352,586 participants in the study. Over the course of 2000-2019, the Veterans Health Administration (VHA) treated 13,669,058 Veterans and 15,842,376 total patients. Table 4.1 lists the participants by year compared to the total number of Veterans seen outpatient at VHA and the total number of patients seen outpatient at VHA.

Table 4.1 Number of Participants Vs Number Treated by VHA

Year	Participants	Total Veterans at VA	Total patients at VA
1999	266,462	Unavailable	Unavailable
2000	695,185	4,137,010	4,431,239
2001	839,735	4,518,292	4,807,319
2002	989,659	4,887,748	5,167,846
2003	1,117,463	5,087,136	5,362,023
2004	1,233,347	5,412,239	5,686,579
2005	1,298,007	5,409,677	5,683,618
2006	1,360,045	5,462,608	5,736,797
2007	1,420,272	5,542,431	5,823,942
2008	1,485,388	5,651,143	5,948,585
2009	1,574,482	5,843,242	6,137,507
2010	1,649,775	6,037,369	6,322,244
2011	1,710,642	6,131,588	6,417,966
2012	1,761,223	6,237,423	6,532,244
2013	1,812,052	6,293,772	6,758,436
2014	1,896,691	6,401,604	6,684,799
2015	1,910,396	6,463,211	6,760,186
2016	1,694,932	6,503,450	6,807,985
2017	1,774,055	6,512,798	6,822,857
2018	1,862,059	6,529,365	6,836,679
2019	930,878	6,743,872	6,777,000

Data Transitions and Authorization

Total number of Veterans and patients treated by VHA was unavailable for 1999 as it was the year of transition from paper charts to computerized records. In this study the 2019 data was pulled for the first quarter only, January 1 thru March 31, due to April 1, 2019 data authorization request on IRB application. Therefore 1999 and 2019 data cannot be analyzed by year as full data is not available.

Rate of Disease Among the Veteran Population

Rates of GI disease among Veterans did not exist in the literature prior to this study. Therefore, as a result this study has identified overall rates of GI disease within Veterans treated at VHA as recorded in Table 4.2.

Table 4.2 Rate of Disease among Veterans Treated Outpatient at VHA

Condition	Rate of Disease
PTSD	14.64%
Gastroesophageal Reflux Disease	25.52%
Peptic Ulcer Disease	1.82%
Functional Dyspepsia	20.99%
Crohn's Disease	2.82%
Ulcerative Colitis	.75%
Diverticular Disease	10.22%
Irritable Bowel Syndrome	2.11%
Constipation	6.37%
Nausea/Vomiting	15.80%

Veteran Age by Decade

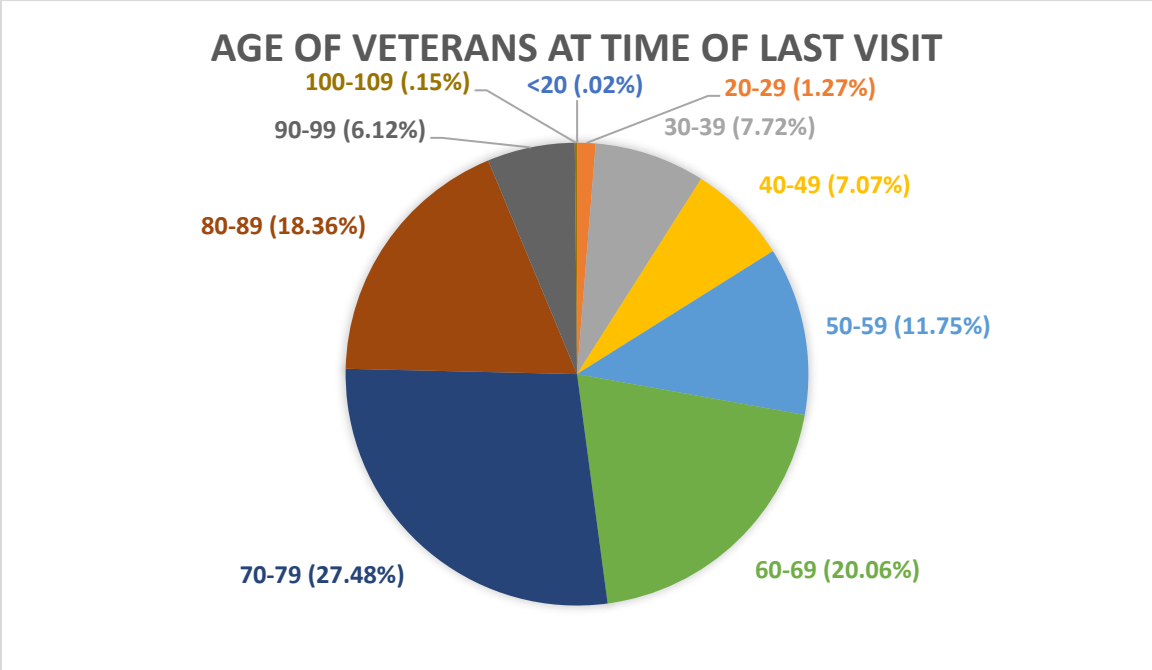
In this study ages ranged from 18 to 140, therefore is assumed that some ages are inaccurate in the patient record. Table 4.3 shows breakdown of participants age at the time of their last visit that met inclusion criteria. When analyzing data, any participant age 110 or above was removed from analysis.

Table 4.3 Veterans' Age by Decade

Age	Number of Participants
<20	1,239
20-29	80,677
30-39	490,447
40-49	449,135
50-59	746,103
60-69	1,274,236
70-79	1,745,874
80-89	1,166,161
90-99	388,816

100-109	9,650
110-119	56
120-129	46
130-139	4

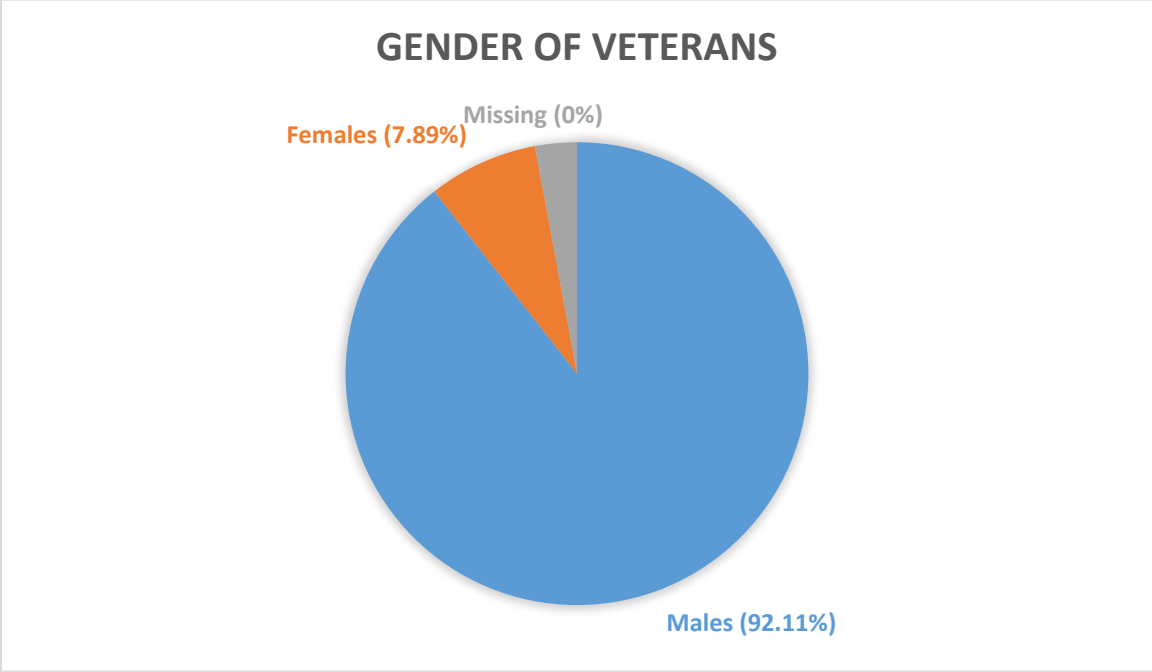
Figure 4.1 Age of Veterans at Time of Last Visit



Gender of Veterans

The participants numbered 500,997 females and 5,851,856 males, with three participants missing gender information. Figure 4.2 shows the percentages of gender within the participants population. The participants with missing gender identification were removed from analysis.

Figure 4.2 Self-Reported Gender of the Veterans



Diagnosis by Gender of Veterans

Frequency counts of Veterans diagnosed with each condition are reported in table 4.4. The expected rate of females was 9%, while the expected rate of males was 91% (U.S. Department of Veterans Affairs, 2016).

Table 4.4 Frequency Counts of Diagnosis by Gender of Veterans

	Female (7.89%)	Male (92.11%)
PTSD only	F = 213125 10.65%	F = 1787994 89.35%
PTSD & GERD	F = 80340 10.19%	F = 708096 89.81%
PTSD & Peptic Ulcer Disease	F = 3817 7.08%	F = 50085 92.92%
PTSD & Functional Dyspepsia	F = 13563 12.34%	F = 96320 87.66%
PTSD & Crohn's Disease	F = 1482 12.65%	F = 10233 87.35%
PTSD & Ulcerative Colitis	F = 2468 11.10%	F = 19757 88.90%
PTSD & Diverticular Disease	F = 16369 5.77%	F = 267276 94.23%

PTSD & Constipation	F = 31421 15.53%	F = 170963 84.47%
PTSD & IBS	F = 27959 25.51%	F = 81641 74.49%
PTSD & Nausea/Vomiting	F = 69667 12.93%	F = 469232 87.07%

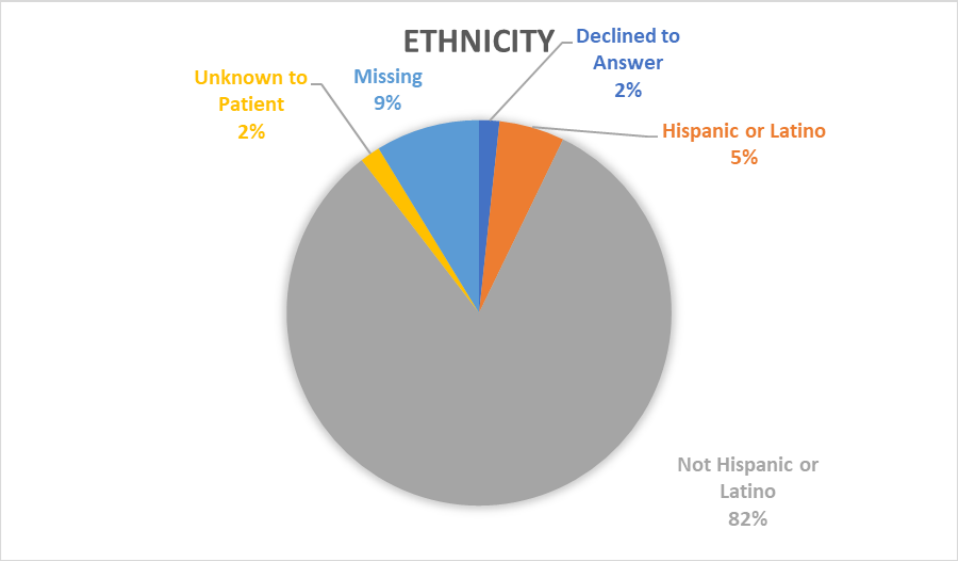
Demographic Data for Self-reported Ethnicities

Demographic data for self-reported ethnicities is as follows:

- 107,264 declined to answer;
- 348,349 as Hispanic or Latino;
- 5,235,078 as Not Hispanic or Latino;
- 106,266 Unknown to Patient; and
- 555,629 participants missing ethnicity data.

Figure 4.3 demonstrates the percentages of ethnicity across the participant population.

Figure 4.3 Self-Reported Ethnicity of the Veterans



Period of Service of Veterans

Period of Service of Veterans was collected, and it was noted that there are some periods of service that participants do not qualify as a Veteran. Table 4.5 demonstrates the exact breakdown of all periods of service within the participant list.

Table 4.5 Period of Service

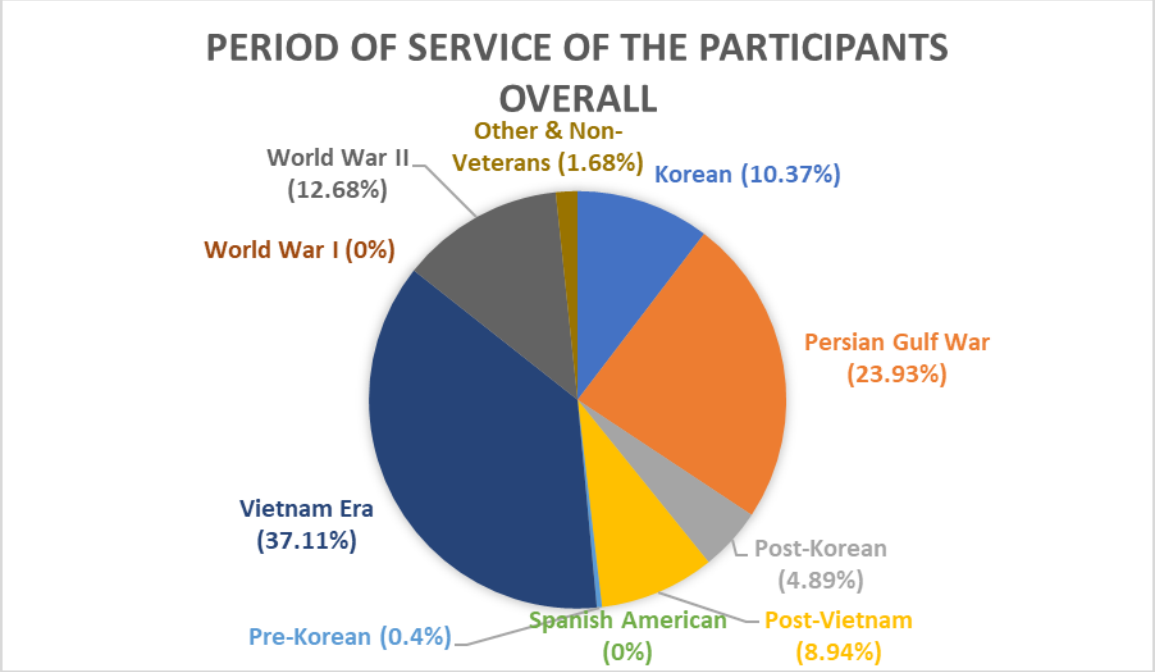
Period of Service	Frequency	% of participants
Missing	1558	0.02
Air Force – Active Duty	789	0.01
Army – Active Duty	1621	0.03
Beneficiaries – Foreign Gov.	22	0
CAV/NPS	197	0
ChampVA – Spouse, Child	22690	0.36
Coast Guard – Active Duty	133	0
Czechoslovakia / Poland SVC	3	0
Donors (non-vet)	4	0
Humanitarian (non-vet)	4354	0.07
Job Corps/ Peace Corps	12	0
Korean	658625	10.37
Medical Remedial enlist	9	0
Merchant Marine	478	0.01
Merchant Marines	1	0
Navy, Marine Active Duty	826	0.01
Observation/Examination	5	0
Office of Workers Comp	19	0
Operation Desert Shield	6	0
Other Federal – Dependents	29	0
Other non-Veteran	45358	0.71
Other – none	15806	0.25
Other – Remimbs. (non-vet)	45	0
Other – USPHS beneficiaries	74	0
Persian Gulf War	1519880	23.93
Post-Korean	310829	4.89
Post-Vietnam	568000	8.94
Pre-Korean	25237	0.40
Railroad Retirement	2	0
Retired, Uniform Services	63	0
Spanish American	125	0
Special Studies	3	0
Special Studies (non-vet)	779	0.01
Tricare	11260	0.18

Vietnam Era	2357688	37.11
WWI	281	0
WWII	805774	12.68

Percentage of Veterans in Each Wartime Period

Figure 4.4 shows the percentages of Veterans who served during wartime periods with other non-Veteran groups combined into a category marked "other." Since many of these "other" category participants were not Veterans, this group was removed from analysis. Together the service periods identified as Korean, Persian Gulf War, Post-Korean, Post-Vietnam, Pre-Korean, Vietnam Era, Spanish American, World War I, and World War II accounted for more than 98% of the sample.

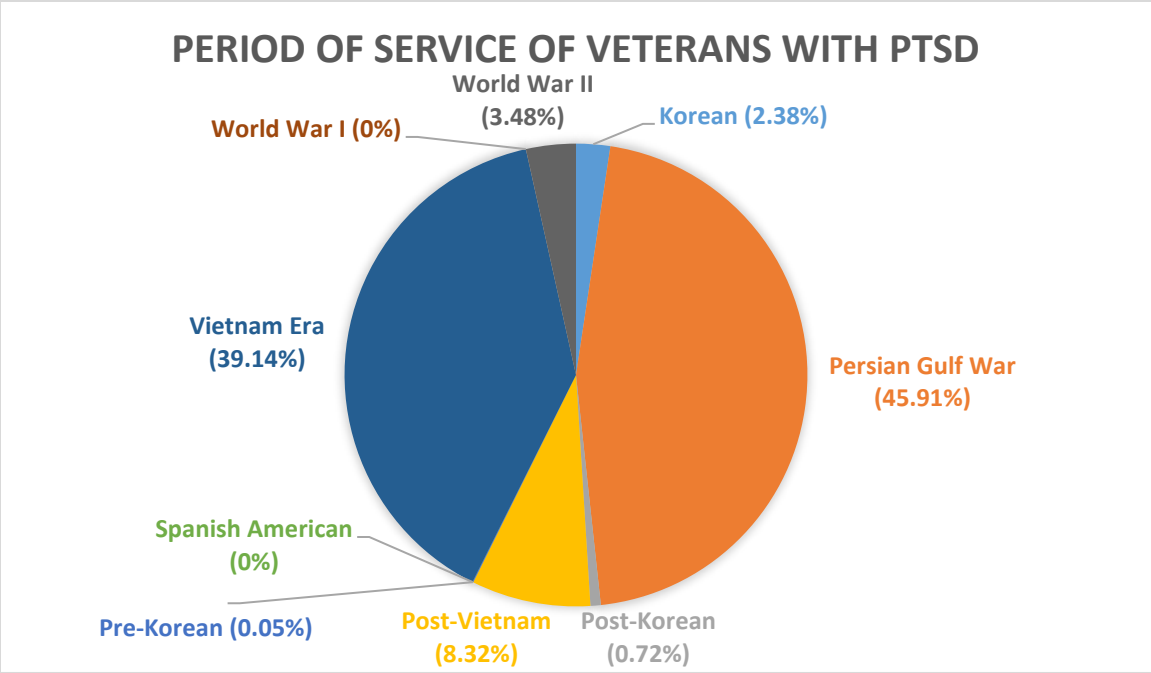
Figure 4.4 Percentage in Each Wartime Period



Period of Service for Veterans with PTSD

The division of period of service among Veterans with PTSD was observed to be different than that of all participants, with the highest rates of PTSD occurring in the Vietnam Era and Persian Gulf War, shown in Figure 4.5.

Figure 4.5 Period of Service of Veterans with PTSD



Period of Service for All Veterans Treated at VHA

Additionally, Vinci data services provided the researcher with population data for the period of service of all Veterans treated by VHA, shown in table 4.6. Of note, some Veterans may have served in two periods of service and therefore may occur more than once in this data. However, in this study, period of service for each Veteran only shows once, listed as the most recent period of service at the time of discharge from the military.

Table 4.6 Period of Service Frequency for All Veterans Treated at VHA

Period of Service	Number of Veterans (2000-2019)
Korean	1,438,639
Persian Gulf War	3,605,995
Post-Korean	691,885
Post-Vietnam	1,259,470
Pre-Korean	66,250
Spanish American	492
Vietnam Era	4,495,928
World War I	4,098
World War II	2,020,736

Psychometric Estimates for the Veteran Sample

Total Observed Counts of Disease

After removal of missing gender, age over 110, and non-Veteran status in Period of Service, the observed frequency counts of the studied conditions were as follows within the participants:

Table 4.7 Total Observed Counts of Disease After Removing Outliers

PTSD	2001180
GERD	3488344
PepUD	248132
FunDys	415307
Crohns	55758
UlcCol	103076
DivtDis	1396359
Const	871109
IBS	288368
N/V	2159137

Disease Rates Over Time

Frequency counts of each disease over time can be viewed in Appendix H. Figures 4.6- 4.10 present the disease rates over time as a percentage of all Veterans treated at VHA.

Figure 4.6 PTSD Only Rates Over Time in Veterans

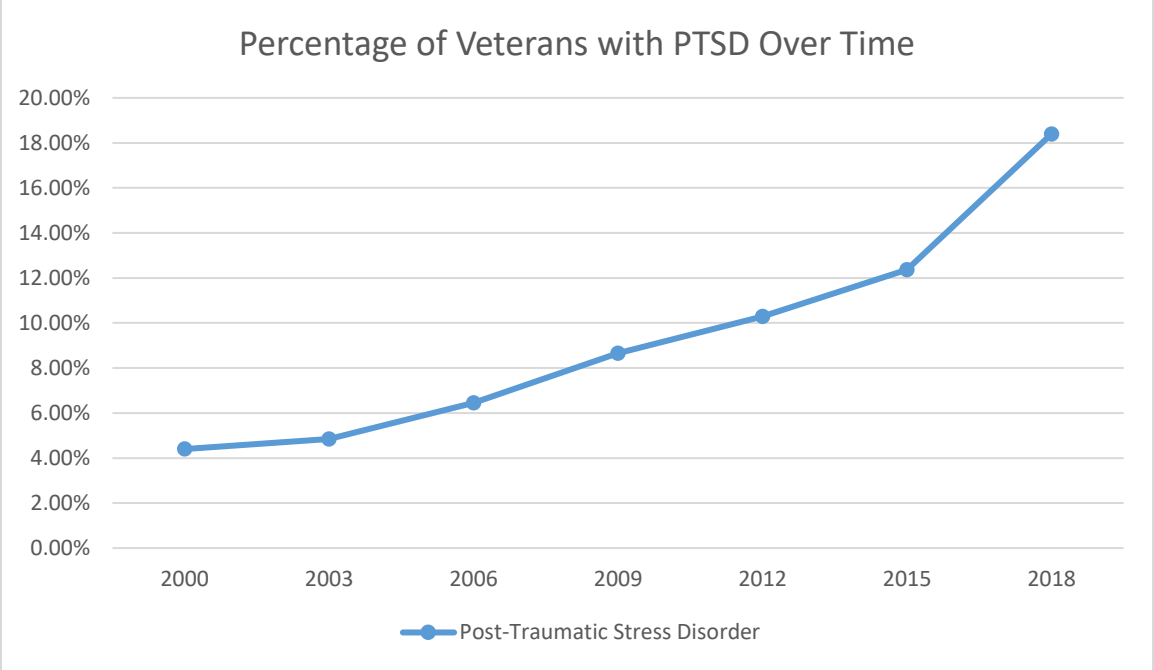


Figure 4.7 Gastroesophageal Reflux Disease Only Rates over Time in Veterans

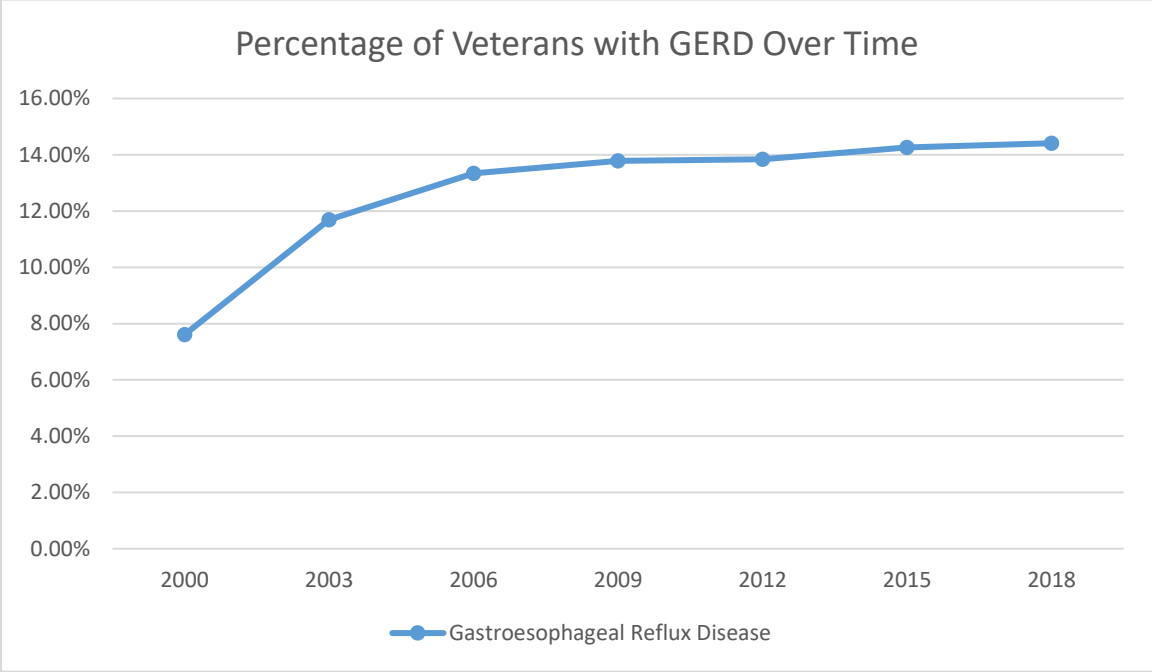


Figure 4.8 Peptic Ulcer Disease, Functional Dyspepsia, IBS, and Diverticular Disease Rates Over Time in Veterans

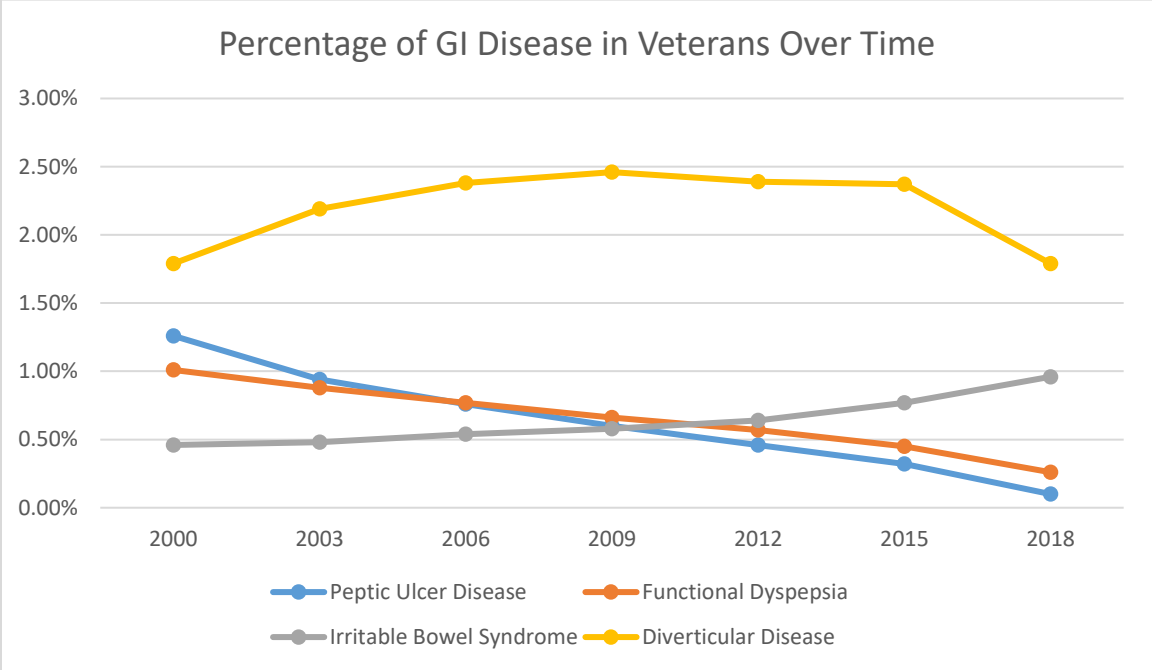


Figure 4.9 Crohn's Disease and Ulcerative Colitis Rates Over Time in Veterans

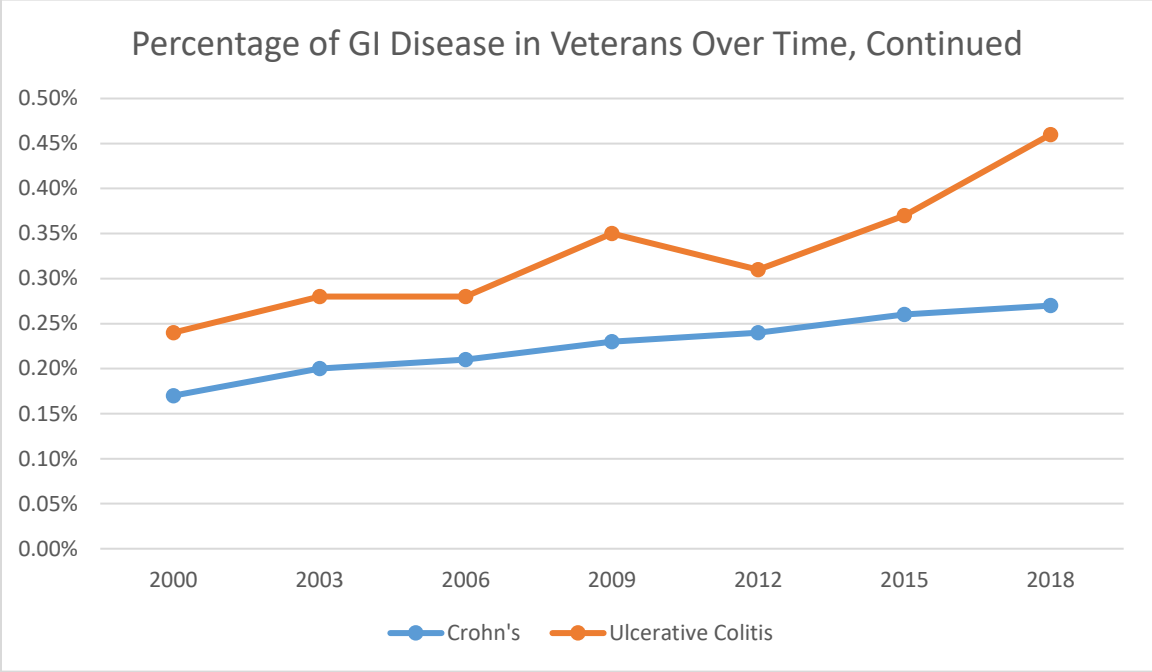
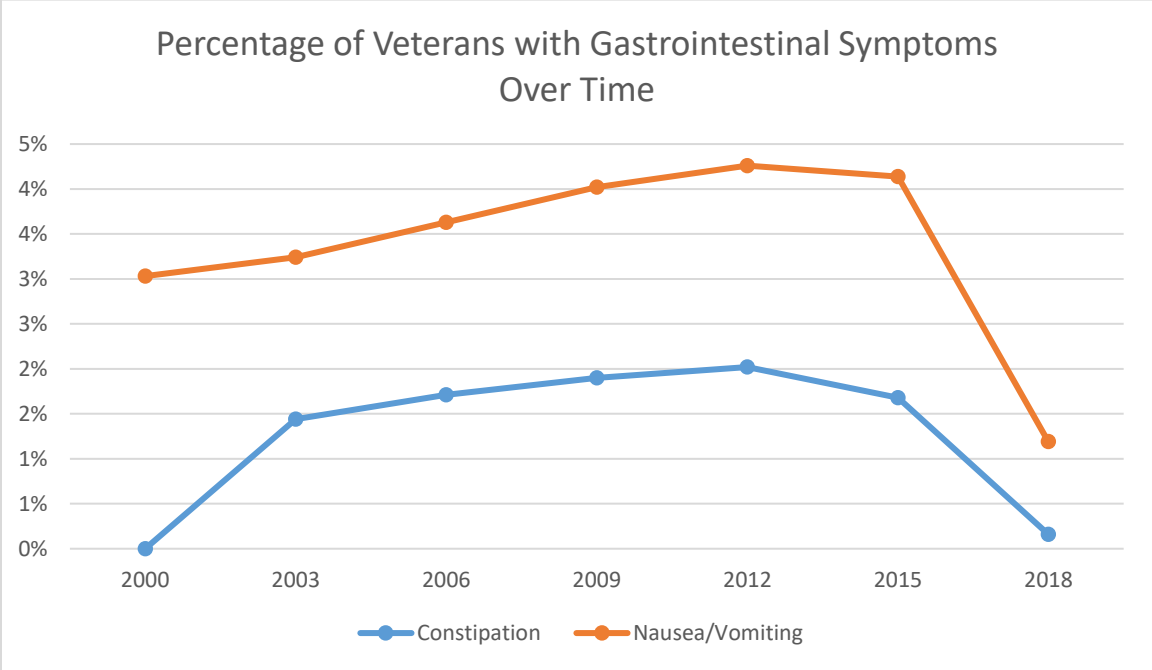


Figure 4.10 Symptoms of Constipation and Nausea/Vomiting Rates Over Time in Veterans



Summary of Disease Rates Over Time in Veterans

It was observed that rates of:

- PTSD within the Veteran population have increased over time since 2000;
- GERD have increased since 2000 but have remained relatively stable from 2009-2018;
- Peptic ulcer disease and functional dyspepsia continue to decrease over time;
- IBS and Crohn's disease have increased over time;
- Ulcerative colitis has fluctuated over time with an upward trend;
- Diverticular disease has fluctuated with a downward trend;
- Constipation and nausea/vomiting steadily increased over time until 2015, when a dramatic decrease was observed.

These changes in rates may be due to a change in coding procedures within VHA in the year 2015, and which warrants further discussion in the limitation section of this paper.

Introduction to Major Findings and Conclusions

The goal of the present study was to explore the relationship between GI disease and PTSD. Research questions are listed below, and findings are be broken down by each GI disease in relation to PTSD.

Specific Aim 1

Specific Aim 1 is: "To determine the frequency with which GI Disease (GERD, Peptic Ulcer Disease/PUD) and PTSD are diagnosed co-morbidities in Veterans who have served in wartime periods."

Research Question 1 is: In Veterans who have served during wartime periods, what is the frequency with which GI Disease and PTSD are diagnosed co-morbidities?

Research Hypothesis 1 is: In Veterans who have served in wartime period, GI Disease and PTSD are frequently diagnosed as co-morbidities.

Research Hypothesis 1 was: Confirmed.

Post-traumatic Stress Disorder and Gastroesophageal Reflux Disease.

Rates of GERD were calculated by the variable of period of service, shown in table 4.8 in chronological order of conflict. Since population data reflects multiple periods of service for Veterans who served in multiple periods whereas this study only reflects the most recent period of service in which the Veteran served, these rates are the minimum seen within the period. Rates of disease per period of service could potentially be higher if multiple periods of service were taken into consideration.

Table 4.8 Rates of GERD by Period of Service

Period of Service	Number of Veterans	Rate of GERD
Spanish American	492	12.60%
World War I	4098	3.22%
World War II	2020736	22.34%
Pre-Korean	66250	23.38%
Korean	1438639	27.93%
Post-Korean	691885	28.29%
Vietnam Era	4495928	30.10%
Post-Vietnam	1259470	26.10%
Persian Gulf War	3605995	19.40%

The frequency of co-occurring PTSD and GERD is reported in Table 4.9.

Table 4.9 Frequency of Co-Occurring PTSD and GERD

Total frequency with both PTSD and GERD	Percent of all Veterans Treated at VHA
784314	5.74%

Post-traumatic Stress Disorder and Peptic Ulcer Disease.

Rates of PUD were calculated by the variable of period of service, shown in table 4.10 in chronological order of conflict. As explained previously, these rates are the minimum seen within the period. Rates of disease per period of service could potentially be higher if multiple periods of service were taken into consideration.

Table 4.10 Rates of Peptic Ulcer Disease by Period of Service

Period of Service	Number of Veterans	Rate of PUD
Spanish American	492	1.02%
World War I	4098	.61%
World War II	2020736	3.25%
Pre-Korean	66250	2.69%
Korean	1438639	3.35%
Post-Korean	691885	2.76%
Vietnam Era	4495928	2.34%
Post-Vietnam	1259470	1.53%
Persian Gulf War	3605995	.62%

The frequency of co-occurring PTSD and PUD is reported in Table 4.11.

Table 4.11 Frequency of Co-Occurring PTSD and PUD

Total frequency with both PTSD and PUD	Percent of all Veterans Treated at VHA
53668	.39%

Post-traumatic Stress Disorder and Functional Dyspepsia.

Rates of functional dyspepsia were calculated by the variable of period of service, shown in table 4.12 in chronological order of conflict. As stated previously, these rates are the minimum seen within the period. Rates of disease per period of service could potentially be higher if multiple periods of service were taken into consideration.

Table 4.12 Rates of Functional Dyspepsia by Period of Service

Period of Service	**Number of Veterans (last 20 years)**	**Rate of Functional Dyspepsia**
Spanish American	492	1.63%
World War I	4098	.39%
World War II	2020736	2.55%
Pre-Korean	66250	2.27%
Korean	1438639	3.30%
Post-Korean	691885	3.29%
Vietnam Era	4495928	3.65%
Post-Vietnam	1259470	3.49%
Persian Gulf War	3605995	2.13%

The frequency of co-occurring PTSD and functional dyspepsia is reported in Table 4.13.

Table 4.13 Frequency of Co-Occurring PTSD and Functional Dyspepsia

Total frequency with both PTSD and functional dyspepsia	Percent of all Veterans Treated at VHA
109210	.80%

Post-traumatic Stress Disorder and Crohn's Disease.

Rates of Crohn's disease were calculated by the variable of period of service, shown in table 4.14 in chronological order of conflict. As with other diseases studied, these rates are the minimum seen within the period. Rates of disease per period of service could potentially be higher if multiple periods of service were taken into consideration.

Table 4.14 Rates of Crohn's Disease by Period of Service

Period of Service	Number of Veterans	Rate of Crohn's Disease
Spanish American	492	.20%
World War I	4098	0%
World War II	2020736	.24%
Pre-Korean	66250	.32%
Korean	1438639	.37%
Post-Korean	691885	.43%
Vietnam Era	4495928	.48%
Post-Vietnam	1259470	.50%
Persian Gulf War	3605995	.36%

The frequency of co-occurring PTSD and Crohn's disease is reported in Table 4.15.

Table 4.15 Frequency of Co-Occurring PTSD and Crohn's Disease

Total frequency with both PTSD and Crohn's disease	Percent of all Veterans Treated at VHA
11633	.09%

Post-traumatic Stress Disorder and Ulcerative Colitis.

Rates of ulcerative colitis were calculated by the variable of period of service, shown in table 4.16 in chronological order of conflict. As previously stated, these rates are the minimum seen within the period. Rates of disease per period of service could potentially be higher if multiple periods of service were taken into consideration.

Table 4.16 Rates of Ulcerative Colitis by Period of Service

Period of Service	**Number of Veterans**	**Rate of Ulcerative Colitis**
Spanish American	492	.20%
World War I	4098	.07%
World War II	2020736	.51%
Pre-Korean	66250	.65%
Korean	1438639	.76%
Post-Korean	691885	.83%
Vietnam Era	4495928	.92%
Post-Vietnam	1259470	.83%
Persian Gulf War	3605995	.61%

The frequency of co-occurring PTSD and ulcerative colitis is reported in Table 4.17.

Table 4.17 Frequency of Co-Occurring PTSD and Ulcerative Colitis

Total frequency with both PTSD and ulcerative colitis	Percent of all Veterans Treated at VHA
22125	.16%

Post-traumatic Stress Disorder and Diverticular Disease.

Rates of diverticular disease were calculated by the variable of period of service, shown in table 4.18 in chronological order of conflict. As stated previously, these rates are the minimum seen within the period. Rates of disease per period of service could potentially be higher if multiple periods of service were taken into consideration.

Table 4.18 Rates of Diverticular Disease by Period of Service

Period of Service	**Number of Veterans**	**Rate of Diverticular Disease**
Spanish American	492	2.85%
World War I	4098	.98%
World War II	2020736	7.83%
Pre-Korean	66250	8.39%
Korean	1438639	12.07%
Post-Korean	691885	13.33%
Vietnam Era	4495928	15.58%
Post-Vietnam	1259470	10.02%
Persian Gulf War	3605995	3.52%

The frequency of co-occurring PTSD and diverticular disease is reported in Table 4.19.

Table 4.19 Frequency of Co-Occurring PTSD and Diverticular Disease

Total frequency with both PTSD and diverticular disease	Percent of all Veterans Treated at VHA
282538	2.07%

Post-traumatic Stress Disorder and Irritable Bowel Syndrome.

Rates of IBS were calculated by the variable of period of service, shown in table 4.20 in chronological order of conflict. Again, these rates are the minimum seen within the period. Rates of disease per period of service could potentially be higher if multiple periods of service were taken into consideration.

Table 4.20 Rates of IBS by Period of Service

Period of Service	**Number of Veterans**	**Rate of IBS**
Spanish American	492	2.24%
World War I	4098	.12%
World War II	2020736	.95%
Pre-Korean	66250	.83%
Korean	1438639	1.21%
Post-Korean	691885	1.33%
Vietnam Era	4495928	1.78%
Post-Vietnam	1259470	2.50%
Persian Gulf War	3605995	3.46%

The frequency of co-occurring PTSD and IBS is reported in Table 4.21.

Table 4.21 Frequency of Co-Occurring PTSD and IBS

Total frequency with both PTSD and IBS	Percent of all Veterans Treated at VHA
108818	.80%

Post-traumatic Stress Disorder and the Symptom of Constipation.

Rates of constipation were calculated by the variable of period of service, shown in table 4.22 in chronological order of conflict. These rates are the minimum seen within the period. Rates of disease per period of service could potentially be higher if multiple periods of service were taken into consideration.

Table 4.22 Rates of Constipation by Period of Service

Period of Service	**Number of Veterans**	**Rate of Constipation**
Spanish American	492	1.42%
World War I	4098	.98%
World War II	2020736	8.57%
Pre-Korean	66250	7.21%
Korean	1438639	8.96%
Post-Korean	691885	7.26%
Vietnam Era	4495928	7.03%
Post-Vietnam	1259470	5.87%
Persian Gulf War	3605995	2.98%

The frequency of co-occurring PTSD and Constipation is reported in Table 4.23.

Table 4.23 Frequency of Co-Occurring PTSD and Constipation

Total frequency with both PTSD and constipation	Percent of all Veterans Treated at VHA
110379	.81%

Post-traumatic Stress Disorder and the Symptoms of Nausea & Vomiting.

Rates of nausea/vomiting were calculated by the variable of period of service, shown in Table 4.24 in chronological order of conflict. These rates are the minimum seen within the period. Rates of disease per period of service could potentially be higher if multiple periods of service were taken into consideration.

Table 4.24 Rates of Nausea/Vomiting by Period of Service

Period of Service	**Number of Veterans**	**Rate of Nausea/Vomiting**
Spanish American	492	7.11%
World War I	4098	2.24%
World War II	2020736	15.42%
Pre-Korean	66250	12.95%
Korean	1438639	17.38%
Post-Korean	691885	15.99%
Vietnam Era	4495928	18.52%
Post-Vietnam	1259470	16.78%
Persian Gulf War	3605995	10.72%

The frequency of co-occurring PTSD and nausea/vomiting is reported in Table 4.25.

Table 4.25 Frequency of Co-Occurring PTSD and Nausea/Vomiting

Total frequency with both PTSD and nausea/vomiting	Percent of all Veterans Treated at VHA
535791	3.92%

Specific Aim 2

Specific Aim 2 is: "To determine the frequency with which a diagnosis of functional or structural GI Disease accompanies a diagnosis of PTSD in Veterans who have served during wartime periods."

Research Question 2 is: In Veterans who have served during wartime periods, what is the frequency with which a diagnosis of functional or structural GI Disease accompanies a diagnosis of PTSD?

Research Hypothesis 2 is: In Veterans who have served during wartime periods, a diagnosis of functional or structural GI Disease frequently accompanies a diagnosis of PTSD.

Research Hypothesis 2 was: Confirmed.

Post-traumatic Stress Disorder and Gastroesophageal Reflux Disease.

Rates of PTSD and GERD were tracked over time and reported below every three years from 2000-2018. The rate of GERD among Veterans with PTSD was compared to the rate of GERD in all Veterans treated at VHA and is shown in Table 4.26. Chi squares were calculated for each year shown and reported in the table. Chi square tests can be affected by the large sample size, so goodness-of-fit tests were performed to validate the chi squares.

Table 4.26 Diagnosis of GERD Over Time Among Veterans with PTSD

Year	Rate of GERD Among Veterans with PTSD	Rate of GERD Among all Veterans	Ratio	P value of chi square	Goodness-of-fit tests: Critical Value 3.84
2000	13.33%	7.61%	1.75	<.0001	8486.39
2003	17.89%	11.69%	1.53	<.0001	9185.64
2006	19.61%	13.34%	1.47	<.0001	12009.15
2009	20.00%	13.78%	1.45	<.0001	16510.45
2012	23.26%	13.84%	1.68	<.0001	41804.24
2015	20.15%	14.26%	1.41	<.0001	22658.22
2018	19.71%	14.41%	1.37	<.0001	20518.95

Based on these results, a diagnosis of GERD is positively correlated with a diagnosis of PTSD in Veterans. Rates of both GERD and PTSD are increasing in the general population of Veterans treated at VHA. The rate of GERD among Veterans with PTSD is increasing over time, continuously surpassing the rate of GERD in the general population. On average Veterans with PTSD were 1.5 times more likely to have GERD than other Veterans.

Post-traumatic Stress Disorder and Peptic Ulcer Disease.

Rates of PTSD and peptic ulcer disease were tracked over time and reported below every three years from 2000-2018. The rate of PUD among Veterans with PTSD was compared to the rate of PUD in all Veterans treated at VHA and is shown in Table

4.27. Chi squares were calculated for each year shown and reported in the table. Goodness-of-fit tests were performed to validate the chi squares.

Table 4.27 Rate of Peptic Ulcer Disease Over Time Among Veterans with PTSD

Year	Rate of PUD Among Veterans with PTSD	Rate of PUD Among All Veterans	Ratio	P value of chi square	Goodness-of-fit tests: Critical Value 3.84
2000	1.89%	1.26%	1.5	<.0001	639.89
2003	1.31%	.94%	1.39	<.0001	367.44
2006	1.04%	.76%	1.37	<.0001	374.76
2009	0.77%	.60%	1.28	<.0001	257.32
2012	0.69%	.46%	1.5	<.0001	655.42
2015	0.40%	.32%	1.25	<.0001	147.39
2018	0.12%	.10%	1.2	<.0001	35.56

Based on these results, a diagnosis of peptic ulcer disease is positively correlated with a diagnosis of PTSD in Veterans. The rate of PUD is falling both in the general population of Veterans and in Veterans with PTSD, while the rate of PTSD is climbing, both in the general population of Veterans and in Veterans with PUD. The rate of PUD in Veterans with PTSD surpasses the rate of PUD in the general population of Veterans in all years except 2018, although the rate continues to increase over time. On average, Veterans with PTSD are 1.36 times more likely to have PUD than the general population of Veterans.

Post-traumatic Stress Disorder and Functional Dyspepsia.

Rates of PTSD and functional dyspepsia were tracked over time and reported below every three years from 2000-2018. The rate of functional dyspepsia among Veterans with PTSD was compared to the rate of functional dyspepsia in all Veterans treated at VHA and is shown in Table 4.28. Chi squares were calculated for each year shown and reported in the table. Goodness-of-fit tests were performed to validate the chi squares.

Table 4.28 Rate of Functional Dyspepsia Over Time Among Veterans with PTSD

Year	Rate of Functional Dyspepsia Among Veterans with PTSD	Rate of Functional Dyspepsia Among All Veterans	Ratio	P value of chi square	Goodness-of-fit tests: Critical Value 3.84
2000	1.94%	1.01%	1.92	<.0001	1567.17
2003	1.66%	.88%	1.87	<.0001	1724.83
2006	1.33%	.77%	1.73	<.0001	1431.38
2009	1.17%	.66%	1.73	<.0001	2028.28
2012	1.13%	.57%	1.98	<.0001	3086.51
2015	0.76%	.45%	1.69	<.0001	1696.18
2018	0.44%	.26%	1.69	<.0001	1086.29

Based on these results, PTSD and functional dyspepsia are bi-directionally correlated. Rates of functional dyspepsia are falling over time, but in Veterans with PTSD the rates of functional dyspepsia continuously surpass those in the general

population of Veterans. Rates of PTSD are climbing over time in both groups. On average, Veterans with PTSD are 1.8 times more likely to have functional dyspepsia than Veterans without PTSD, and although the rate has fluctuated over time, there is a downward trend.

Post-traumatic Stress Disorder and Crohn's Disease.

Rates of PTSD and Crohn's Disease were tracked over time and reported below every three years from 2000-2018. The rate of Crohn's Disease among Veterans with PTSD was compared to the rate of Crohn's Disease in all Veterans treated at VHA and is shown in Table 4.29. Chi squares were calculated for each year shown and reported in the table. Goodness-of-fit tests were performed to validate the chi squares.

Table 4.29 Rates of Crohn's Disease Over Time Among Veterans with PTSD

Year	Rate of Crohn's Among Veterans with PTSD	Rate of Crohn's Among All Veterans	Ratio	P value of chi square	Goodness-of-fit tests: Critical Value 3.84
2000	0.22%	.17%	1.29	<.0001	21.94
2003	0.22%	.20%	1.1	.006379	7.44
2006	0.23%	.21%	1.1	.002867	8.89
2009	0.25%	.23%	1.09	.000625	11.70
2012	0.32%	.24%	1.33	<.0001	136.23
2015	0.28%	.26%	1.08	.001032	10.77
2018	0.29%	.27%	1.07	.000441	12.35

Based on these results, a diagnosis of Crohn's disease is positively correlated with a diagnosis of PTSD in Veterans, although not as drastically as other GI diseases. Rates of Crohn's disease are climbing in both the general population of Veterans and in Veterans with PTSD. The rate of Crohn's disease in Veterans with PTSD continuously surpasses the rate of Crohn's disease in the general population of Veterans. On average, a Veteran with PTSD is 1.15 times more likely to have Crohn's disease as a Veteran in the general population. This rate has fluctuated over time with no general trend.

Post-traumatic Stress Disorder and Ulcerative Colitis.

Rates of PTSD and ulcerative colitis were tracked over time and reported below every three years from 2000-2018. The rate of ulcerative colitis among Veterans with PTSD was compared to the rate of ulcerative colitis in all Veterans treated at VHA and is shown in Table 4.30. Chi squares were calculated for both on each year shown and reported in the table. Goodness-of-fit tests were performed to validate the chi squares.

Table 4.30 Rates of Ulcerative Colitis Over Time Among Veterans with PTSD

Year	Rate of Ulcerative Colitis Among Veterans with PTSD	Rate of Ulcerative Colitis Among All Veterans	Ratio	P value of chi square	Goodness-of-fit tests: Critical Value 3.84
2000	0.27%	.24%	1.13	.024912	5.03
2003	0.28%	.28%	1.0	.75183	0.10
2006	0.28%	.28%	1.0	.977719	0.00078
2009	0.29%	.35%	0.83	<.0001	55.10
2012	0.35%	.31%	1.13	<.0001	25.81

2015	0.38%	.37%	1.03	.1117	2.53
2018	0.51%	.46%	1.11	<.0001	55.77

Based on these observations, a diagnosis of ulcerative colitis is not correlated with a diagnosis of PTSD in Veterans. Rates of ulcerative colitis are climbing in both the general population of Veterans and in Veterans with PTSD. The rate of ulcerative colitis in Veterans with PTSD surpasses the rate of ulcerative colitis in the general population only some of the time. On average, Veterans with PTSD are 1.03 times more likely to have ulcerative colitis than the general population of Veterans. Although chi square and p value show a correlation, goodness-of-fit tests do not in most years. Chi square results are likely due to large sample size.

Post-traumatic Stress Disorder and Diverticular Disease.

Rates of PTSD and diverticular disease were tracked over time and reported below every three years from 2000-2018. The rate of diverticular disease among Veterans with PTSD was compared to the rate of diverticular disease in all Veterans treated at VHA and is shown in Table 4.31. Chi squares were calculated for each year shown and reported in the table. Goodness-of-fit tests were performed to validate the chi squares.

Table 4.31 Rates of Diverticular Disease Over Time Among Veterans with PTSD

Year	Rate of Diverticular Disease Among Veterans with PTSD	Rate of Diverticular Disease Among All Veterans	Ratio	P value of chi square	Goodness-of-fit tests: Critical Value 3.84

2000	2.30%	1.79%	1.28	<.0001	268.16
2003	2.94%	2.19%	1.34	<.0001	641.81
2006	3.18%	2.38%	1.34	<.0001	977.77
2009	3.20%	2.46%	1.30	<.0001	1151.47
2012	3.13%	2.39%	1.31	<.0001	1315.94
2015	2.84%	2.37%	1.20	<.0001	753.94
2018	2.41%	1.79%	1.35	<.0001	1973.20

Based on these observations, a diagnosis of diverticular disease is positively correlated with a diagnosis of PTSD in Veterans. Rates of diverticular disease in the general population climbed until 2009, when they peaked and then began to fall. Rates of diverticular disease in Veterans with PTSD followed the same pattern, but in each year continuously surpassed the rates of diverticular disease in the general population of Veterans. On average, Veterans with PTSD are 1.30 times more likely to have diverticular disease than the general population of Veterans. This rate has fluctuated over time.

Post-traumatic Stress Disorder and Irritable Bowel Syndrome.

Rates of PTSD and irritable bowel syndrome were tracked over time and reported below every three years from 2000-2018. The rate of IBS among Veterans with PTSD was compared to the rate of IBS in all Veterans treated at VHA and is shown in Table 4.32. Chi squares were calculated for each year shown and reported in the table. Goodness-of-fit tests were performed to validate the chi squares.

Table 4.32 Rates of IBS Over Time Among Veterans with PTSD

Year	Rate of IBS Among Veterans with PTSD	Rate of IBS Among All Veterans	Ratio	P value of chi square	Goodness-of-fit tests: Critical Value 3.84
2000	1.39%	.46%	3.02	<.0001	3473.95
2003	1.36%	.48%	2.83	<.0001	4027.52
2006	1.42%	.54%	2.63	<.0001	5083.98
2009	1.49%	.58%	2.57	<.0001	7244.25
2012	1.93%	.64%	3.02	<.0001	14768.56
2015	1.98%	.77%	2.57	<.0001	15211.03
2018	2.38%	.96%	2.48	<.0001	19093.10

Based on these observations, a diagnosis of IBS is positively correlated with a diagnosis of PTSD in Veterans, more so than any other GI disease studied. Rates of IBS have increased over time in both the general population of Veterans and in Veterans with PTSD. The rate of IBS in Veterans with PTSD continuously surpasses the rate of IBS in the general population of Veterans. On average, Veterans with PTSD are 2.73 times more likely to have IBS than the general population of Veterans. This rate has fluctuated over time with no defined trend.

Post-traumatic Stress Disorder and Constipation.

Rates of PTSD and constipation were tracked over time and reported below every three years from 2000-2018. The rate of constipation among Veterans with PTSD was compared to the rate of constipation in all Veterans treated at VHA and is shown in Table

4.33. Chi squares were calculated for each year shown and reported in the table. Goodness-of-fit tests were performed to validate the chi squares.

Table 4.33 Rates of Constipation Over Time Among Veterans with PTSD

Year	Rate of Constipation Among Veterans with PTSD	Rate of Constipation Among All Veterans	Ratio	P value of chi square	Goodness-of-fit tests: Critical Value 3.84
2000	0.00%	0.00%	1.0	N/A	N/A
2003	2.29%	1.44%	1.59	<.0001	1260.79
2006	2.58%	1.71%	1.51	<.0001	1573.78
2009	2.85%	1.90%	1.50	<.0001	2429.53
2012	3.49%	2.02%	1.73	<.0001	6099.88
2015	2.44%	1.68%	1.45	<.0001	2796.38
2018	0.27%	0.16%	1.69	<.0001	641.97

Based on these observations, the symptom of constipation is positively correlated with a diagnosis of PTSD in Veterans. Rates of constipation in the general population of Veterans increased over time until peaking in 2012, then began to fall. Rates of constipation in Veterans with PTSD followed the same pattern, but continuously surpassed the rates of constipation in the general population of Veterans. On average, Veterans with PTSD are 1.50 times as likely to have constipation as the general population of Veterans. This rate has fluctuated over time with a general increasing trend.

Post-traumatic Stress Disorder and Nausea/Vomiting.

Rates of PTSD and nausea and/or vomiting were tracked over time and reported below every three years from 2000-2018. The rate of nausea/vomiting among Veterans with PTSD was compared to the rate of nausea/vomiting in all Veterans treated at VHA and is shown in Table 4.34. Chi squares were calculated for each year shown and reported in the table. Goodness-of-fit tests were performed to validate the chi squares.

Table 4.34 Rates of Nausea/Vomiting Over Time Among Veterans with PTSD

Year	Rate of Nausea/Vomiting Among Veterans with PTSD	Rate of Nausea/Vomiting Among All Veterans	Ratio	P Value of chi square	Goodness-of-fit tests: Critical Value 3.84
2000	8.38%	3.03%	2.77	<.0001	17737.76
2003	9.37%	3.24%	2.89	<.0001	29552.79
2006	9.92%	3.63%	2.73	<.0001	39916.48
2009	10.75%	4.02%	2.67	<.0001	59488.29
2012	12.47%	4.26%	2.93	<.0001	92859.36
2015	9.92%	4.14%	2.40	<.0001	67380.93
2018	2.90%	1.19%	2.44	<.0001	22506.60

Based on these observations, the symptoms of nausea/vomiting are positively correlated with a diagnosis of PTSD in Veterans. The rate of nausea/vomiting increased over time in both the general population of Veterans and Veterans with PTSD, until it decreased dramatically in 2018. This may be due to the change in coding procedures in 2015/2016 years, where VHA began to focus more on coding diagnosis rather than

symptoms. Regardless, the rate of nausea/vomiting in Veterans with PTSD continuously surpassed the rate of nausea/vomiting in the general population of Veterans, even in 2018. On average, Veterans with PTSD are 2.69 times more likely to experience nausea/vomiting than the general population of Veterans. This rate increased over time until 2015, which again may be explained by changes in VHA coding policy.

Specific Aim 3

Specific Aim 3 is: "To determine the frequency with which a diagnosis of PTSD accompanies a diagnosis of functional or structural GI Disease in Veterans who have served during wartime periods."

Research Question 3 is: In Veterans who have served during wartime periods, what is the frequency with which a diagnosis of PTSD accompanies a diagnosis of functional or structural GI Disease?

Research Hypothesis 3 is: In Veterans who have served during wartime periods, a diagnosis of PTSD frequently accompanies a diagnosis of functional or structural GI Disease.

Research Hypothesis 3 was: Confirmed.

Post-traumatic Stress Disorder and Gastroesophageal Reflux Disease.

The rate of PTSD among Veterans with GERD was compared to the rate of PTSD in all Veterans treated at VHA and is shown in Table 4.35. Chi squares were calculated for each year shown and reported in the table. Goodness-of-fit tests were performed to validate the chi squares.

Table 4.35 Diagnosis of PTSD Over Time Among Veterans with GERD

Year	Rate of PTSD Among Veterans with GERD	Rate of PTSD Among all Veterans	Ratio	P value of chi square	Goodness-of-fit tests: Critical Value 3.84
2000	7.71%	4.40%	1.75	<.0001	8219.42
2003	7.42%	4.85%	1.53	<.0001	8532.47
2006	9.50%	6.46%	1.47	<.0001	11110.81
2009	12.58%	8.66%	1.45	<.0001	15621.97
2012	15.14%	10.29%	1.47	<.0001	21999.18
2015	17.47%	12.36%	1.41	<.0001	22249.86
2018	18.87%	18.39%	1.02	<.0001	146.37

Based on these results, a diagnosis of PTSD is positively correlated with a diagnosis of GERD in Veterans. Rates of both GERD and PTSD are increasing in the general population of Veterans treated at VHA. The rate of PTSD among Veterans with GERD is increasing over time, continuously surpassing the rate of PTSD in the general population except in the year 2018, when this seems to have leveled off with the rate of PTSD similar in those with GERD and the general population. On average Veterans with GERD were 1.44 times more likely to have PTSD than other Veterans.

Post-traumatic Stress Disorder and Peptic Ulcer Disease.

The rate of PTSD among Veterans with PUD was compared to the rate of PTSD in all Veterans treated at VHA and is shown in Table 4.36. Chi squares were calculated

for each year shown and reported in the table. Goodness-of-fit tests were performed to validate the chi squares.

Table 4.36 Rate of PTSD Over Time Among Veterans with Peptic Ulcer Disease

Year	Rate of PTSD Among Veterans with PUD	Rate of PTSD Among all Veterans	Ratio	P value of chi square	Goodness-of-fit tests: Critical Value 3.84
2000	6.60%	4.40%	1.5	<.0001	600.48
2003	6.76%	4.85%	1.39	<.0001	377.72
2006	8.87%	6.46%	1.37	<.0001	397.56
2009	11.18%	8.66%	1.29	<.0001	280.58
2012	13.49%	10.29%	1.31	<.0001	319.11
2015	15.49%	12.36%	1.25	<.0001	185.31
2018	16.34%	18.39%	.89	<.0001	18.53

Based on these results, a diagnosis of PTSD is positively correlated with a diagnosis of peptic ulcer disease in Veterans. The rate of PUD is falling both in the general population of Veterans and in Veterans with PTSD, while the rate of PTSD is climbing, both in the general population of Veterans and in Veterans with PUD. On average, Veterans with PUD are 1.29 times more likely to have PTSD than the general population of Veterans, however this rate appears to be decreasing over time.

Post-traumatic Stress Disorder and Functional Dyspepsia.

The rate of PTSD among Veterans with functional dyspepsia was compared to the rate of PTSD in all Veterans treated at VHA and is shown in Table 4.21. Chi squares

were calculated for each year shown and reported in the table. Goodness-of-fit tests were performed to validate the chi squares.

Table 4.37 Rate of PTSD Over Time Among Veterans with Functional Dyspepsia

Year	Rate of PTSD Among Veterans with Functional Dyspepsia	Rate of PTSD Among all Veterans	Ratio	P value of chi square	Goodness-of-fit tests: Critical Value 3.84
2000	8.42%	4.40%	1.91	<.0001	1612.55
2003	9.14%	4.85%	1.88	<.0001	1719.20
2006	11.06%	6.46%	1.71	<.0001	1482.70
2009	15.31%	8.66%	1.77	<.0001	2168.84
2012	17.81%	10.29%	1.73	<.0001	2179.80
2015	20.62%	12.36%	1.67	<.0001	1852.31
2018	23.28%	18.39%	1.27	<.0001	269.27

Based on these results, a diagnosis of PTSD is positively correlated with a diagnosis of functional dyspepsia in Veterans. Rates of functional dyspepsia are falling over time, while rates of PTSD are climbing over time. In Veterans with functional dyspepsia, rates of PTSD continuously surpass rates of PTSD in the general population of Veterans. On average, Veterans with functional dyspepsia are 1.71 times more likely to have PTSD than Veterans without functional dyspepsia. This rate has also fluctuated over time but has a downward trend.

Post-traumatic Stress Disorder and Crohn's Disease.

The rate of PTSD among Veterans with Crohn's Disease was compared to the rate of PTSD in all Veterans treated at VHA and is shown in Table 4.27. Chi squares were calculated for each year shown, reported in the tables. Goodness-of-fit tests were performed to validate the chi squares.

Table 4.38 Rates of PTSD Over Time Among Veterans with Crohn's Disease

Year	Rate of PTSD Among Veterans with Crohn's	Rate of PTSD Among all Veterans	Ratio	P value of chi square	Goodness-of-fit tests: Critical Value 3.84
2000	5.65%	4.40%	1.28	<.0001	25.83
2003	5.49%	4.85%	1.13	.001653	9.09
2006	7.04%	6.46%	1.09	.010371	6.57
2009	9.62%	8.66%	1.11	<.0001	28.54
2012	11.74%	10.29%	1.14	<.0001	34.35
2015	13.32%	12.36%	1.08	.000153	14.34
2018	15.03%	18.39%	0.82	<.0001	130.68

Based on these results, a diagnosis of PTSD is positively correlated with a diagnosis of Crohn's disease in Veterans, although not as strongly as in other GI diseases. The rate of PTSD in Veterans with Crohn's disease surpasses the rate of PTSD in the general population of Veterans in all years except 2018. On average a Veteran with Crohn's disease is 1.09 times more likely to have PTSD than the general population. Although the rate has fluctuated over time, it appears to be trending downward.

Post-traumatic Stress Disorder and Ulcerative Colitis.

The rate of PTSD among Veterans with ulcerative colitis was compared to the rate of PTSD in all Veterans treated at VHA and is shown in Table 4.39. Chi squares were calculated for each year shown and reported in the table. Goodness-of-fit tests were performed to validate the chi squares.

Table 4.39 Rates of PTSD Over Time Among Veterans with Ulcerative Colitis

Year	Rate of PTSD Among Veterans with Ulcerative Colitis	Rate of PTSD Among all Veterans	Ratio	P value of chi square	Goodness-of-fit tests: Critical Value 3.84
2000	4.84%	4.40%	1.1	.032919	4.55
2003	4.97%	4.85%	1.02	<.0001	94.19
2006	6.42%	6.46%	0.99	.841481	0.04
2009	8.52%	8.66%	0.98	.52197	0.41
2012	10.22%	10.29%	0.99	.75183	0.10
2015	12.81%	12.36%	1.04	.037009	4.35
2018	15.43%	18.39%	0.84	<.0001	175.25

Based on these observations, a diagnosis of PTSD is not correlated with a diagnosis of ulcerative colitis. Rates of PTSD are climbing in both the general population of Veterans and in Veterans with ulcerative colitis. The rate of PTSD in Veterans with ulcerative colitis is roughly the same as the rate of PTSD in the general population of Veterans. On average, Veterans with ulcerative colitis are 0.99 times as likely to have PTSD as the general population of Veterans. Although chi square and p value show a correlation, goodness-of-fit tests do not in most years. Chi square results are likely due to large sample size.

Post-traumatic Stress Disorder and Diverticular Disease.

The rate of PTSD among Veterans with diverticular disease was compared to the rate of PTSD in all Veterans treated at VHA and is shown in Table 4.40. Chi squares were calculated for each year shown and reported in the Ttable. Goodness-of-fit tests were performed to validate the chi squares.

Table 4.40 Rates of PTSD Over Time Among Veterans with Diverticular Disease

Year	Rate of PTSD Among Veterans with Diverticular Disease	Rate of PTSD Among all Veterans	Ratio	P value of chi square	Goodness-of-fit tests: Critical Value 3.84
2000	5.67%	4.40%	1.29	<.0001	282.41
2003	6.48%	4.85%	1.34	<.0001	644.21
2006	9.96%	6.46%	1.54	<.0001	2280.00
2009	11.28%	8.66%	1.30	<.0001	1246.05
2012	11.78%	10.29%	1.45	<.0001	360.17

2015	14.83%	12.36%	1.20	<.0001	855.55
2018	15.98%	18.39%	0.89	<.0001	524.41

Based on these observations, a diagnosis of PTSD is positively correlated with a diagnosis of diverticular disease in Veterans. Rates of PTSD have continuously climbed in both the general population of Veterans and in Veterans with diverticular disease. The rate of PTSD in Veterans with diverticular disease continuously surpassed the rate of PTSD in the general population of Veterans except for the year 2018. On average, Veterans with diverticular disease are 1.29 times more likely to have PTSD as Veterans in the general population. This rate has also fluctuated over time.

Post-traumatic Stress Disorder and Irritable Bowel Syndrome.

The rate of PTSD among Veterans with IBS was compared to the rate of PTSD in all Veterans treated at VHA and is shown in Table 4.41. Chi squares were calculated for each year shown and reported in the table. Goodness-of-fit tests were performed to validate the chi squares.

Table 4.41 Rates of PTSD Over Time Among Veterans with IBS

Year	Rate of PTSD Among Veterans with IBS	Rate of PTSD Among all Veterans	Ratio	P value of chi square	Goodness-of-fit tests: Critical Value 3.84
2000	13.61%	4.40%	3.09	<.0001	3762.94
2003	13.82%	4.85%	2.85	<.0001	4242.55
2006	17.10%	6.46%	2.65	<.0001	5485.60
2009	22.31%	8.66%	2.58	<.0001	7952.93

2012	27.14%	10.29%	2.64	<.0001	12313.76
2015	31.72%	12.36%	2.57	<.0001	17226.02
2018	34.39%	18.39%	1.87	<.0001	10631.85

Based on these observations, a diagnosis of PTSD is positively correlated with a diagnosis of IBS in Veterans, more so than any other GI disease studied. Rates of PTSD have increased over time in both the general population of Veterans and in Veterans with IBS. The rate of PTSD in Veterans with IBS continuously surpasses the rate of PTSD in the general population of Veterans. Veterans with IBS are 2.61 times more likely to have PTSD than the general population of Veterans. This rate is falling over time.

Post-traumatic Stress Disorder and Constipation.

The rate of PTSD among Veterans with constipation was compared to the rate of PTSD in all Veterans treated at VHA and is shown in Table 4.51. Chi squares were calculated for each year shown and reported in the table. Goodness-of-fit tests were performed to validate the chi squares.

Table 4.42 Rates of PTSD Over Time Among Veterans with Constipation

Year	Rate of PTSD Among Veterans with Constipation	Rate of PTSD Among all Veterans	Ratio	P value of chi square	Goodness-of-fit tests: Critical Value 3.84
2000	5.48%	4.40%	1.25	.527089	0.40
2003	7.72%	4.85%	1.59	<.0001	1309.52
2006	9.71%	6.46%	1.50	<.0001	1635.86

2009	12.96%	8.66%	1.50	<.0001	2595.37
2012	15.56%	10.29%	1.51	<.0001	3787.93
2015	17.93%	12.36%	1.45	<.0001	95337.52
2018	23.59%	18.39%	1.28	<.0001	183.61

Based on these observations, a diagnosis of PTSD is positively correlated with the symptom of constipation in Veterans. Rates of PTSD have continuously increased over time in both the general population of Veterans and in Veterans with constipation. The rate of PTSD in Veterans with constipation has continuously surpassed the rate of PTSD in the general population of Veterans. On average, Veterans with constipation are 1.44 times more likely to have PTSD than Veterans in the general population. This rate has fluctuated over time with no consistent trend.

Post-traumatic Stress Disorder and Nausea/Vomiting.

The rate of PTSD among Veterans with nausea/vomiting was compared to the rate of PTSD in all Veterans treated at VHA and is shown in Table 4.57. Chi squares were calculated for each year shown and reported in the table. Goodness-of-fit tests were performed to validate the chi squares.

Table 4.43 Rates of PTSD Over Time Among Veterans with Nausea/Vomiting

Year	Rate of PTSD Among Veterans with Nausea/Vomiting	Rate of PTSD Among all Veterans	Ratio	P Value of chi square	Goodness-of-fit tests: Critical Value 3.84
2000	12.19%	4.40%	2.77	<.0001	18058.88
2003	14.01%	4.85%	2.89	<.0001	30013.28

2006	17.63%	6.46%	2.73	<.0001	40997.65
2009	23.20%	8.66%	2.68	<.0001	57238.51
2012	26.39%	10.29%	2.56	<.0001	74555.60
2015	29.67%	12.36%	2.40	<.0001	73964.59
2018	36.36%	18.39%	1.98	<.0001	15486.70

Based on these observations, a diagnosis of PTSD is positively correlated with the symptoms of nausea/vomiting in Veterans. Rates of PTSD are increasing over time in both the general population of Veterans and in Veterans who experience nausea/vomiting. The rate of PTSD in Veterans with nausea/vomiting continuously surpasses the rate of PTSD in the general population of Veterans. On average, Veterans who experience nausea/vomiting are 2.57 times more likely to have PTSD than the general population of Veterans. This rate has a general downward trend over time.

Secondary Mental Illness: Potential Confounding Variables

As discussed in Chapters 1 and 2, previous research has indicated a potential link between GI disease and depression and anxiety (Ford, Miller, Eastwood, & Eastwood, 1987, and Locke, Weaver, Melton, & Talley, 2004). Therefore, *rates of secondary mental illness in participants with PTSD and GERD were observed to assess asmay be potential confounding variables*. Gould and others found in their study that Veterans do not have increased rates of depression and anxiety over non-veterans. They Researchers identified the rate of depression in Veterans as 11% and the rate of anxiety in Veterans as 9.9% (Gould, Rideaux, Spira, & Beaudreau, 2015).

Gastroesophageal Reflux Disease.

In this study it was observed that of the Veterans who were diagnosed with both PTSD and GERD, 78.54% have also been diagnosed with a depressive disorder, while 61.94% have been diagnosed with an anxiety disorder. In order to determine whether these higher rates are correlated with the PTSD diagnosis, the GERD diagnosis, or both, rates have been broken down into tables. Depression and anxiety rates among those with GERD are shown in Table 4.44.

Table 4.44 Depression and Anxiety Among Veterans with GERD

	Depression	Anxiety
Rate of depression/anxiety among Veterans with GERD	F = 1293183 37.07%	F = 996241 28.56%
Rate of GERD among those with both PTSD and depression or anxiety:	F = 615894 **PP = 17.66%**	F = 485561 **PP = 13.92%**
Rate of GERD among those with PTSD and without depression or anxiety:	F = 168414 **PP = 4.83%**	F = 298753 **PP = 8.56%**
Rate of GERD among those without PTSD and with depression or anxiety:	F = 677283 **PP = 19.42%**	F = 510680 **PP = 14.64%**
Rate of GERD among those without PTSD or depression or anxiety:	F = 1984784 **PP = 56.90%**	F = 2151339 **PP = 61.67%**

Depression and Anxiety Among Veterans with GERD.

The rate of depression in Veterans with PTSD is 69.25%, and the rate of anxiety disorders in Veterans with PTSD is 52.18%. Whereas the rates of depression in Veterans with GERD is 37.07% and the rate of anxiety disorders is 28.56%. Each of these rates is higher than the expected rates of 11% depression and 9.9% anxiety reported by Gould, et al., (2015). It appears that depression and anxiety are correlated with both GERD and PTSD.

For those with PTSD, Depressive disorders are recorded in table 4.45, anxiety disorders are recorded in table 4.46. Since rate of PTSD is known to vary by period of service, rates are also broken down by the largest periods of service in the study.

Table 4.45 Rates of PTSD in Veteran by GERD and Depression Diagnoses

	F = total frequency **PP = % of all Veterans with PTSD**	**Overall**	**Korean**	**Persian Gulf War**	**Post-Korean**	**Post-Vietnam**	**Vietnam**	**World War II**
PTSD & GERD	Rate of PTSD among those with both GERD and depression	F = 615898 **PP = 31.12%**	F = 11523 PP = .58%	F = 227003 PP = 11.47%	F = 5143 PP = .26%	F = 64531 PP = 3.26%	F = 286582 PP = 14.48%	F = 16848 PP = .85%
	Rate of PTSD among those with GERD and	F = 168414 **PP = 8.51%**	F = 6832 PP = .35%	F = 62126 PP = 3.14%	F = 1619 PP = .08%	F = 9480 PP = 0.48%	F = 77395 PP = 3.91%	F = 10824 PP = .55%

	without depression							
	Rate of PTSD among those without GERD and with depression	F = 769864 **PP = 38.90%**	F = 12728 PP = .64%	F = 401616 PP = 20.29%	F = 4266 PP = .22%	F = 67064 PP = 3.39%	F = 265862 PP = 13.43%	F = 18042 PP = .91%
	Rate of PTSD among those without GERD or depression	F = 424732 **PP = 21.46%**	F = 11975 PP = .61%	F = 217734 PP = 11.0%	F = 3190 PP = .16%	F = 23606 PP = 1.19%	F = 144805 PP = 7.32%	F = 23083 PP = 1.17%

Table 4.46 Rates of PTSD in Veterans by GERD and Anxiety Diagnoses

	F = total frequency PP = % of all Veterans with PTSD	**Overall**	**Korean**	**Persian Gulf War**	**Post-Korean**	**Post-Vietnam**	**Vietnam**	**World War II**
PTSD & GERD	Rate of PTSD among those with both GERD and anxiety:	F = 485561 **PP = 24.54%**	F = 12233 PP = .62%	F = 188087 PP = 9.50%	F = 4187 PP = .21%	F = 52975 PP = 2.68%	F = 214132 PP = 10.82%	F = 13755 PP = .70%
	Rate of PTSD among those with GERD and without anxiety:	F = 298753 **PP = 15.10%**	F = 10122 PP = .51%	F = 101042 PP = 5.11%	F = 2577 PP = .13%	F = 21036 PP = 1.06%	F = 149845 PP = 7.57%	F = 13917 PP = .70%
	Rate of PTSD among those	F = 558634 **PP = 28.23%**	F = 9091 PP = .46%	F = 308421 PP = 15.89%	F = 2951 PP = .15%	F = 48206 PP = 2.44%	F = 176002 PP = 8.89%	F = 13787 PP = .70%

	without GERD and with anxiety:							
	Rate of PTSD among those without GERD or anxiety:	F = 885962 **PP = 44.77%**	F = 15612 PP = .79%	F = 310929 PP = 15.71%	F = 4505 PP = .23%	F = 42464 PP = 2.15%	F = 234665 PP = 11.86%	F = 277338 PP = 14.01%

High Rates of Depression More Strongly Associated with PTSD.

When examining the tables, we can analyze this data further. If there was no association between either PTSD and GERD or PTSD and Depression, then the expectation would be for the rate of PTSD to be similar for all four categories in table 4.45. The same results would be expected for anxiety in table 4.46. However, the researcher observed the rate of PTSD is highest in the categories of PTSD with both GERD and depression and without GERD but with depression. These rates are similar, at 31.12% and 38.90%, respectively. This result indicates that the high rates of depression are more strongly associated with PTSD than with GERD, which is supported by the rates of depression and anxiety this study found in each of the conditions reported above. Future research will be needed to support these preliminary findings.

Anxiety Rates More Closely Associated with PTSD.

When anxiety disorders are similarly studied in table 4.46, the rate of PTSD is similar in the categories of those with both GERD and anxiety and those without GERD but with anxiety, at 24.54% and 28.23%, respectively. These similar rates in both groups again point to anxiety symptoms being more strongly associated with PTSD rather than with GERD.

Peptic Ulcer Disease.

It was observed that of the Veterans who were diagnosed with both PTSD and PUD, 79.81% have also been diagnosed with a depressive disorder, while 63.69% have been diagnosed with an anxiety disorder. Rates of depression and anxiety in Veterans with PUD are shown in table 4.47.

Table 4.47 Rates of Depression and Anxiety in Veterans with PUD

	Depression	Anxiety
Rate of depression/anxiety among Veterans with PUD	F = 102188 41.18%	F = 77890 31.39%
Rate of PUD among those with both PTSD and depression or anxiety:	F = 42816 **PP = 17.26%**	F = 34156 **PP = 13.77%**
Rate of PUD among those with PTSD and without depression or anxiety:	F = 10698 **PP = 4.31%**	F = 19512 **PP = 7.86%**
Rate of PUD among those without PTSD and with depression or anxiety:	F = 59372 **PP = 23.93%**	F = 43734 **PP = 17.63%**
Rate of PUD among those without PTSD or depression or anxiety:	F = 123974 **PP = 49.96%**	F = 184339 **PP = 74.29**

Depression and Anxiety Among Veterans with Peptic Ulcer Disease.

As mentioned previously, the rate of depression in Veterans with PTSD is 69.25%, and the rate of anxiety disorders in Veterans with PTSD is 52.18%. Whereas the rates of depression in Veterans with PUD is 41.18% and the rate of anxiety disorders is 31.39%. Each of these rates is higher than the expected rates of 11% depression and 9.9% anxiety reported by Gould, et al., (2015). It appears that depression and anxiety are correlated with both PUD and PTSD.

In order to determine whether these higher rates are correlated with the PTSD diagnosis, the PUD diagnosis, or both, rates have been broken down into tables. Depressive disorders are recorded in table 4.48, anxiety disorders are recorded in table 4.49. Since rate of PTSD is known to vary by period of service, rates are also broken down by the largest periods of service in the study.

Table 4.48 Rates of PTSD in Veterans by PUD and Depression Diagnoses

	F = total frequency **PP = % of all Veterans with PTSD**	**Overall**	**Korean**	**Persian Gulf War**	**Post-Korean**	**Post-Vietnam**	**Vietnam**	**World War II**
PTSD & Peptic Ulcer Disease	Rate of PTSD among those with both PUD and depression	F = 42816 **PP = 2.16%**	F = 2170 PP = .11%	F = 7968 PP = .40%	F =606 PP = .03%	F = 4351 PP = .22%	F = 25112 PP = 1.27%	F = 2578 PP = .13%
	Rate of PTSD among those with PUD and without depression	F = 10852 **PP = .55%**	F = 912 PP = .05%	F = 1454 PP = .07%	F = 170 PP = .01%	F = 557 PP = .03%	F = 5919 PP = .30%	F = 1817 PP = .09%
	Rate of PTSD among those without PUD and with depression	F = 1342948 **PP = 67.86%**	F = 26081 PP = 1.32%	F = 620651 PP = 31.36%	F = 8805 PP = 0.44%	F = 127244 PP = 6.43%	F = 527332 PP = 26.65%	F = 32312 P = .12%
	Rate of PTSD among those without PUD or depression	F = 582294 **PP = 29.42%**	F = 17895 PP = .90%	F = 278406 PP = 14.07%	F = 4639 PP = .23%	F = 32529 PP = 1.64%	F = 216281 PP = 10.93%	F = 32090 PP = 1.62%

Table 4.49 Rates of PTSD in Veterans by PUD and Anxiety Diagnoses

	F = total frequency PP = % of all Veterans with PTSD	**Overall**	**Korean**	**Persian Gulf War**	**Post-Korean**	**Post-Vietnam**	**Vietnam**	**World War II**
PTSD & Peptic Ulcer Disease	Rate of PTSD among those with both PUD and anxiety:	F = 34156 **PP = 1.73%**	F = 1800 PP = .09%	F = 6790 PP = .34%	F = 489 PP = .02%	F = 3645 PP = .18%	F = 19193 PP = .97%	F = 2217 PP = .11%
	Rate of PTSD among those with PUD and without anxiety:	F = 19512 **PP = .99%**	F = 1282 PP = .06%	F = 2632 PP = .13%	F = 287 PP = .01%	F = 1263 PP = .06%	F = 11838 PP = .60%	F = 2178 PP = .11%
	Rate of PTSD among those without PUD and with anxiety:	F = 1010039 **PP = 51.04%**	F = 19524 PP = .99%	F = 489718 PP = 24.75%	F = 6649 PP = .34%	F = 97536 PP = 4.93%	F = 370941 PP = 18.74%	F = 25325 PP = 1.28%
	Rate of PTSD among those without PUD or anxiety:	F = 915203 **PP = 46.25%**	F = 24452 PP = 1.24$	F = 409339 PP = 20.69%	F = 6795 PP = .34%	F = 62237 PP = 3.15%	F = 372672 PP = 18.83%	F = 39077 PP = 1.97%

Depression and Anxiety More Closely Associated with PTSD.

The results revealed the rate of PTSD is highest in the category of PTSD without PUD and with depression, at 67.86%. This indicates that the high rates of depression are more strongly associated with PTSD than with PUD, which is supported by the rates of depression and anxiety this study found in each of the conditions reported above. When anxiety disorders are similarly studied in table 4.19, there is a similar result, with the highest rate of PTSD occurring in the category of Veterans with depression but not with PUD. This also points to anxiety symptoms being more strongly associated with PTSD rather than with PUD.

Functional Dyspepsia.

The results revealed that of the Veterans who were diagnosed with both PTSD and functional dyspepsia, 92.78% have also been diagnosed with a depressive disorder, while 67.76% have been diagnosed with an anxiety disorder. Rates of depression and anxiety in Veterans with functional dyspepsia are shown in table 4.50.

Table 4.50 Rates of Depression and Anxiety Among Veterans with Functional Dyspepsia

	Depression	Anxiety
Rate of depression/anxiety among Veterans with Functional Dyspepsia	F = 182615 43.97%	F = 148032 35.64%
Rate of Functional Dyspepsia among those with both PTSD and depression or anxiety:	F = 90379 **PP = 21.76%**	F = 73927 **PP = 17.80%**
Rate of Functional Dyspepsia among those with PTSD and without depression or anxiety:	F = 18831 **PP = 4.53%**	F = 35283 **PP = 8.50%**
Rate of Functional Dyspepsia among those without PTSD and with depression or anxiety:	F = 92236 **PP = 22.21%**	F = 74105 **PP = 17.84**
Rate of Functional Dyspepsia among those without PTSD or depression or anxiety:	F = 206756 **PP = 49.78%**	F = 224887 **PP = 54.15%**

***Depression and Anxiety Among Veterans with Functional Dyspepsia*.**

The rates of depression in Veterans with functional dyspepsia was found to be 43.97% and the rate of anxiety disorders is 35.64%. Both these rates for functional dyspepsia and the rates reported previously for PTSD are higher than the expected rates of 11% depression and 9.9% anxiety reported by Gould, et al., (2015). It appears that depression and anxiety are correlated with both functional dyspepsia and PTSD.

In order to determine whether these higher rates are correlated with the PTSD diagnosis, the functional dyspepsia diagnosis, or both, rates have been broken down into tables. Depressive disorders are recorded in table 4.51, anxiety disorders are recorded in table 4.52. Since rate of PTSD is known to vary by period of service, rates are also broken down by the largest periods of service in the study.

Table 4.51 Rates of PTSD in Veterans by Functional Dyspepsia and Depression Diagnoses

	F = total frequency **PP = % of all Veterans with PTSD**	**Overall**	**Korean**	**Persian Gulf War**	**Post-Korean**	**Post-Vietnam**	**Vietnam**	**World War II**
PTSD & Functional Dyspepsia	Rate of PTSD among those with both FD and depression:	F = 90379 **PP = 4.57%**	F = 2698 PP = .14%	F = 28902 PP = 1.46%	F = 894 PP = .05%	F = 10646 PP = .54%	F = 44396 PP = 2.24%	F = 2802 PP = .14%
	Rate of PTSD among those with FD and without depression:	F = 18831 **PP = .95%**	F = 947 PP = .05%	F = 5667 PP = .29%	F = 185 PP = .01%	F = 1226 PP = .06%	F = 9383 PP = .47%	F = 1399 PP = .07%
	Rate of PTSD among those without FD and with depression:	F = 1295385 **PP = 65.46%**	F = 25553 PP = 1.29%	F = 599717 PP = 30.31 %	F = 8517 P = .43%	F = 120449 PP = 6.09%	F = 508048 PP = 25.67%	F = 32088 PP = 1.62%

	Rate of PTSD among those without FD or depression:	F = 574315 **PP = 29.02%**	F = 17860 PP = .90%	F = 274193 PP = 13.86 %	F = 4624 PP = .23%	F = 31860 PP = 1.61%	F = 212817 PP = 10.75%	F = 32508 PP = 1.64%

Table 4.52 Rates of PTSD in Veterans by Functional Dyspepsia and Anxiety Diagnoses

	F = total frequency **PP = % of all Veterans with PTSD**	**Overall**	**Korean**	**Persian Gulf War**	**Post-Korean**	**Post-Vietnam**	**Vietnam**	**World War II**
PTSD & Functional Dyspepsia	Rate of PTSD among those with both FD and anxiety:	F = 73927 **PP = 3.74%**	F = 2231 PP = .11%	F = 24847 PP = 1.26%	F = 725 PP = .04%	F = 9004 PP = .45%	F = 34709 PP = 1.75%	F = 2376 PP = .12%
	Rate of PTSD among those with FD and without anxiety:	F = 35277 **PP = 1.78%**	F = 1414 PP = .07%	F = 9722 PP = .49%	F = 354 PP = .02%	F = 2868 PP = .14%	F = 19070 PP = .96%	F = 1825 PP = .09%
	Rate of PTSD among those without FD and with anxiety:	F = 970268 **PP = 49.03 %**	F = 19093 PP = .96%	F = 471661 PP = 23.83%	F = 6413 PP = .32%	F = 92177 PP = 4.66%	F = 355425 PP = 17.96%	F = 25166 PP = 1.27%
	Rate of PTSD among those without	F = 899432 **PP = 45.45 %**	F = 24320 PP = 1.23%	F = 402249 PP = 20.33%	F = 6728 PP = .34%	F = 60632 PP = 3.06%	F = 365440 PP = 18.47%	F = 39430 PP = 1.99%

	FD or anxiety:							

Depression and Anxiety More Closely Associated with PTSD.

The results revealed the rate of PTSD is highest in the category of PTSD without functional dyspepsia and with depression, at 65.46%. When anxiety disorders are similarly studied in table 4.25, the highest rates of PTSD occurred in the category of Veterans with anxiety but not with functional dyspepsia at 49.03% and in the category with neither anxiety nor functional dyspepsia at 45.45%. This data indicates that the high rates of depression and anxiety are more strongly associated with PTSD than with functional dyspepsia, which is supported by the rates of depression and anxiety this study found in each of the conditions reported above.

Crohn's Disease.

The results revealed that of the Veterans who were diagnosed with both PTSD and Crohn's disease, 81.43% have also been diagnosed with a depressive disorder, while 65.69% have been diagnosed with an anxiety disorder. Rates of depression and anxiety in Veterans with Crohn's Disease is shown in Ttable 4.53.

Table 4.53 Rates of Depression and Anxiety in Veterans with Crohn's Disease

	Depression	Anxiety
Rate of depression or anxiety among Veterans with Crohn's Disease	F = 22082 39.60%	F = 17205 30.86%
Rate of Crohn's Disease among those with both PTSD and depression or anxiety:	F = 9473 **PP = 16.99%**	F = 7647 **PP = 13.71%**
Rate of Crohn's Disease among those with PTSD and without depression or anxiety:	F = 2160 **PP = 3.87%**	F = 3986 **PP = 7.15%**
Rate of Crohn's Disease among those without PTSD and with depression or anxiety:	F = 12609 **PP = 22.61%**	F = 9558 **PP = 17.15%**
Rate of Crohn's Disease among those without PTSD or depression or anxiety:	F = 24644 **PP = 44.20%**	F = 33524 **PP = 60.12%**

Depression and Anxiety in Veterans with Crohn's Disease.

The rates of depression in Veterans with Crohn's Disease was found to be 39.60% and the rate of anxiety disorders is 30.86%. Both these rates for Crohn's Disease and the rates reported previously for PTSD are higher than the expected rates of 11% depression and 9.9% anxiety reported by Gould, et al., (2015). It appears that depression and anxiety are correlated with both Crohn's Disease and PTSD.

In order to determine whether these higher rates are correlated with the PTSD diagnosis, the Crohn's diagnosis, or both, rates have been broken down into tables. Depressive disorders are recorded in Table 4.54, anxiety disorders are recorded in Table 4.55. Since rate of PTSD is known to vary by period of service, rates are also broken down by the largest periods of service in the study.

Table 4.54 Rates of PTSD in Veterans by Crohn's Disease and Depression Diagnoses

	F = total frequency **PP = % of all Veterans with PTSD**	**Overall**	**Korean**	**Persian Gulf War**	**Post-Korean**	**Post-Vietnam**	**Vietnam**	**World War II**
PTSD & Crohn's	Rate of PTSD among those with both Crohn's and depression	F = 9573 **PP = .48%**	F = 210 PP = .01%	F = 3665 PP = .19%	F = 84 PP = 0%	F = 1091 PP = .06%	F = 4312 PP = .22%	F = 204 PP = .01%
	Rate of PTSD among those with Crohn's and without depression	F = 2160 **PP = .11%**	F = 85 PP = 0%	F = 798 PP = .04%	F = 19 PP = 0%	F = 147 PP = .01%	F = 1019 PP = .05%	F = 92 PP = 0%
	Rate of PTSD among those without Crohn's and with depression	F = 1376291 **PP = 69.55%**	F = 28041 PP = 1.42%	F = 625054 PP = 31.59%	F = 9327 PP = .47%	F = 130504 PP = 6.59%	F = 548132 PP = 27.70%	F = 34686 PP = 1.75%

	Rate of PTSD among those without Crohn's or depression	F = 590986 **PP = 29.86%**	F = 18722 PP = .95%	F = 279062 PP = 14.10%	F = 4790 PP = .24%	F = 32939 PP = 1.66%	F = 221181 PP = 11.18%	F = 33815 PP = 1.71%

Table 4.55 Rates of PTSD in Veterans by Crohn's Disease and Anxiety Diagnoses

	F = total frequency **PP = % of all Veterans with PTSD**	**Overall**	**Korean**	**Persian Gulf War**	**Post-Korean**	**Post-Vietnam**	**Vietnam**	**World War II**
PTSD & Crohn's Disease	Rate of PTSD among those with both Crohn's and anxiety:	F = 7647 **PP = .39%**	F = 161 PP = .01%	F = 3045 PP = .15%	F = 72 PP = 0%	F = 933 PP = .05%	F = 3285 PP = .17%	F = 146 PP = .01%
	Rate of PTSD among those with Crohn's and without anxiety:	F = 3986 **PP = .20%**	F = 134 PP = .01%	F = 1318 PP = .07%	F = 31 PP = 0 %	F = 305 PP = .02%	F = 2046 PP = .10%	F = 150 PP = .01%
	Rate of PTSD among those without Crohn's and with anxiety:	F = 1036548 **PP = 52.38%**	F = 21163 PP = 1.07%	F = 493463 PP = 24.94%	F = 7066 PP = .36%	F = 100248 PP = 5.07%	F = 386849 19.55%	F = 27396 PP = 1.38%
	Rate of PTSD among those without	F = 930729 **PP = 47.03%**	F = 25600 PP = 1.29%	F = 410653 PP = 20.75%	F = 7051 PP = .37%	F = 63195 PP = 3.19%	F = 382464 PP = 19.33%	F = 41105 PP = 2.08%

	Crohn's or anxiety:							

Depression and Anxiety More Closely Associated with PTSD>

The results revealed the rate of PTSD to be highest in the category of PTSD without Crohn's disease and with depression, at 69.55%. When anxiety disorders are similarly studied in table 4.31, the highest rates of PTSD occurred in the category of Veterans with anxiety but not with Crohn's Disease at 52.38%. This data indicates that the high rates of depression and anxiety are more strongly associated with PTSD than with Crohn's Disease, which is supported by the rates of depression and anxiety this study found in each of the conditions reported above.

Ulcerative Colitis.

The results revealed that of the Veterans who were diagnosed with both PTSD and ulcerative colitis, 79.71% have also been diagnosed with a depressive disorder, while 65.69% have been diagnosed with an anxiety disorder. Rates of depression and anxiety in Veterans with ulcerative colitis are shown in Ttable 4.35.

Table 4.56 Rates of Depression and Anxiety in Veterans with Ulcerative Colitis

	Depression	Anxiety
Rate of depression or anxiety among Veterans with Ulcerative Colitis	F = 38654 37.50%	F = 30195 29.29%
Rate of Ulcerative Colitis among those with both PTSD and depression or anxiety:	F = 17635 **PP = 17.11%**	F = 14143 **PP = 13.72%**
Rate of Ulcerative Colitis among those with PTSD and without depression or anxiety:	F = 4490 **PP = 4.36%**	F = 7982 **PP = 7.74%**
Rate of Ulcerative Colitis among those without PTSD and with depression or anxiety:	F = 21019 **PP = 20.39%**	F = 16052 **PP = 15.57%**
Rate of Ulcerative Colitis among those without PTSD or depression or anxiety:	F = 58687 **PP = 56.94%**	F = 63654 **PP = 61.75%**

***Depression and Anxiety in Veterans with Ulcerative Colitis*.**

The rates of depression in Veterans with ulcerative colitis was found to be 37.50% and the rate of anxiety disorders is 29.29%. Both these rates for ulcerative colitis and the rates reported previously for PTSD are higher than the expected rates of 11% depression and 9.9% anxiety reported by Gould, et al., (2015). It appears that depression and anxiety are correlated with both ulcerative colitis and PTSD, although PTSD and ulcerative colitis are not correlated with each other.

In order to determine whether these higher rates are correlated with the PTSD diagnosis, the ulcerative colitis diagnosis, or both, rates have been broken down into tables. Depressive disorders are recorded in Table 4.57, anxiety disorders are recorded in table 4.58. Since rate of PTSD is known to vary by period of service, rates are also broken down by the largest periods of service in the study.

Table 4.57 Rates of PTSD in Veterans by Ulcerative Colitis and Depression Diagnoses

	F = total frequency **PP = % of all Veterans with PTSD**	**Overall**	**Korean**	**Persian Gulf War**	**Post-Korean**	**Post-Vietnam**	**Vietnam**	**World War II**
PTSD & Ulcerative Colitis	Rate of PTSD among those with both UC and depression	F = 13635 **PP = .69%**	F = 420 PP = .02%	F = 6447 PP = .33%	F = 151 PP = .01	F = 1969 PP = .10%	F = 4266 PP = .22%	F = 372 PP = .02%
	Rate of PTSD among those with UC and without depression	F = 4490 **PP = .23%**	F = 186 PP = .01%	F = 1645 PP = .08%	F = 35 PP = 0%	F = 266 PP = .01%	F = 2110 PP = .11%	F = 243 PP = .01%
	Rate of PTSD among those without UC and with	F = 1368129 **PP = 69.14%**	F = 27831 PP = 1.41%	F = 622172 PP = 31.44 %	F = 9260 PP = .47%	F = 129626 PP = 6.55%	F = 544178 PP = 27.50%	F = 34518 PP = 1.74%

	depression							
	Rate of PTSD among those without UC or depression	F = 558356 **PP = 28.22%**	F = 18621 PP = .94%	F = 278215 PP = 14.06 %	F = 4774 PP = .24%	F = 32820 PP = 1.66%	F = 220090 PP = 11.12%	F = 33664 PP = 1.70%

Table 4.58 Rates of PTSD in Veterans by Ulcerative Colitis and Anxiety Diagnoses

	F = total frequency **PP = % of all Veterans with PTSD**	**Overall**	**Korean**	**Persian Gulf War**	**Post-Korean**	**Post-Vietnam**	**Vietnam**	**World War II**
PTSD & Ulcerative Colitis	Rate of PTSD among those with both UC and anxiety:	F = 14143 **PP = .71%**	F = 351 PP = .02%	F = 5488 PP = .28%.	F = 116 PP = .01%	F = 1667 PP = .08%	F = 6211 PP = .31%	F = 304 PP = .02%
	Rate of PTSD among those with UC and without anxiety:	F = 7982 **PP = .40%**	F = 255 PP = .01%	F = 2604 PP = .13%	F = 70 PP = 0%	F = 568 PP = .03%	F = 4165 PP = .21%	F = 311 PP = .02%
	Rate of PTSD among those without UC and with anxiety:	F = 1030052 **PP = 52.05%**	F = 20973 PP = 1.06%	F = 491020 PP = 24.81%	F = 7022 P = .35%	F = 99514 PP = 5.03%	F = 383923 PP = 19.40%	F = 27238 PP = 1.38%
	Rate of PTSD among those without	F = 926733 **PP = 46.83%**	F = 25479 PP = 1.29%	F = 409367 PP = 20.69%	F = 7012 PP = .35%	F = 62932 PP = .318%	F = 380345 PP = 19.22%	F = 40944 PP = 2.07%

	UC or anxiety:							

Depression and Anxiety More Closely Associated with PTSD.

The results revealed the rate of PTSD is highest in the category of PTSD without ulcerative colitis and with depression, at 69.14%. When anxiety disorders are similarly studied in table 4.37, the highest rates of PTSD occurred in the category of Veterans with anxiety but not with ulcerative colitis at the rate of 52.05%. This data indicates that the high rates of depression and anxiety are more strongly associated with PTSD than with ulcerative colitis, which is supported by the rates of depression and anxiety this study found in each of the conditions reported above.

Diverticular Disease.

The results revealed that of the Veterans who were diagnosed with both PTSD and diverticular disease, 77.92% have also been diagnosed with a depressive disorder, while 59.38% have been diagnosed with an anxiety disorder. Rates of depression and anxiety in Veterans with diverticular disease are shown in table 4.59.

Table 4.59 Rates of Depression and Anxiety in Veterans with Diverticular Disease

	Depression	Anxiety
Rate of depression or anxiety among Veterans with Diverticular Disease	F = 462778 33.14%	F = 345636 24.75%
Rate of Diverticular Disease among those with both PTSD and depression or anxiety:	F = 220127 **PP = 15.76%**	F = 167676 **PP = 12.01%**
Rate of Diverticular Disease among those with PTSD and without depression or anxiety:	F = 62481 **PP = 4.47%**	F = 144931 **PP = 10.38%**
Rate of Diverticular Disease among those without PTSD and with depression or anxiety:	F = 242651 **PP = 17.38%**	F = 177959 **PP = 12.74%**
Rate of Diverticular Disease among those without PTSD or depression or anxiety:	F = 858168 **PP = 61.48%**	F = 922860 **PP = 66.09%**

***Depression and Anxiety in Veterans with Diverticular Disease*.**

The rates of depression in Veterans with diverticular disease was found to be 33.14% and the rate of anxiety disorders is 24.75%. Both these rates for functional dyspepsia and the rates reported previously for PTSD are higher than the expected rates of 11% depression and 9.9% anxiety reported by Gould, et al., (2015). It appears that depression and anxiety are correlated with both diverticular disease and PTSD.

In order to determine whether these higher rates are correlated with the PTSD diagnosis, the diverticular disease diagnosis, or both, rates have been broken down into tables. Depressive disorders are recorded in table 4.60, anxiety disorders are recorded in Table 4.61. Since rate of PTSD is known to vary by period of service, rates are also broken down by the largest periods of service in the study.

Table 4.60 Rates of PTSD in Veterans by Diverticular Disease and Depression Diagnoses

	F = total frequency **PP = % of all Veterans with PTSD**	**Overall**	**Korean**	**Persian Gulf War**	**Post-Korean**	**Post-Vietnam**	**Vietnam**	**World War II**
PTSD & Diverticular Disease	Rate of PTSD among those with both DD and depression:	F = 220127 **PP = 11.12 %**	F = 7773 PP = .39%	F = 36131 PP = 1.83%	F = 2679 PP = .14	F = 20918 PP = 1.06%	F = 145116 PP = 7.33%	F = 7400 PP = .37%
	Rate of PTSD among those with DD and without depression:	F = 62481 **PP = 3.16%**	F = 3381 PP = .17%	F = 8240 PP = .42%	F = 869 PP = .04%	F = 3381 PP = .17%	F = 41818 PP = 2.11%	F = 4730 PP = .24%
	Rate of PTSD among those without DD and with depression:	F = 1165637 **PP = 58.9%**	F = 20478 PP = 1.03%	F = 592488 PP =29.94 %	F = 6732 PP = .34%	F = 110677 PP = 5.59%	F = 407328 PP = 20.58%	F = 27490 PP = 1.39 %
	Rate of PTSD among those without DD or depression:	F = 530665 **PP = 26.82 %**	F = 15426 PP = .78%	F = 271620 PP = 13.73%	F = 3940 PP = .20%	F = 29705 PP = 1.50%	F = 180382 PP = 9.12%	F = 29177 PP = 1.47 %

Table 4.61 Rates of PTSD in Veterans by Diverticular Disease and Anxiety Diagnoses

	F = total frequency **PP = % of all Veterans with PTSD**	**Overall**	**Korean**	**Persian Gulf War**	**Post-Korean**	**Post-Vietnam**	**Vietnam**	**World War II**
PTSD & Diverticular Disease	Rate of PTSD among those with both DD and anxiety	F = 167677 **PP = 8.47%**	F = 6193 PP = .31%	F = 29280 PP = 1.48%	F = 2149 PP = .11%	F = 16988 PP = .86%	F = 106835 PP = 5.40%	F = 6150 PP = .31%
	Rate of PTSD among those with DD and without anxiety:	F = 114931 **PP = 5.81%**	F = 4961 PP = .25%	F = 15091 PP = .76%	F = 1399 PP = .07%	F = 7311 PP = .37%	F = 8009 PP = .40%	F = 5980 PP = .30%
	Rate of PTSD among those without DD and with anxiety:	F = 876518 PP = **44.29 %**	F = 15131 PP = .76%	F = 467228 PP = 23.61 %	F = 4989 PP = .25%	F = 84913 PP = 4.29%	F = 283299 PP = 14.32%	F = 21392 PP = 1.08%
	Rate of PTSD among those without DD or anxiety:	F = 819784 PP = **41.43 %**	F = 20773 PP = 1.05%	F = 396880 PP = 20.06 %	F = 5683 PP = .29%	F = 56189 PP = 2.84%	F = 30441 PP = 1.54%	F = 35275 PP = 1.78%

Depression and Anxiety More Closely Associated with PTSD.

The results revealed the rate of PTSD is highest in the categories of PTSD without diverticular disease and with depression, at 58.90%. When anxiety disorders are similarly studied in Table 4.61, the highest rates of PTSD occurred in the category of Veterans with anxiety but not with diverticular disease at 44.29% and in the category with neither anxiety nor diverticular disease at 41.43%. This data indicates that the high rates of depression and anxiety are more strongly associated with PTSD than with diverticular disease, which is supported by the rates of depression and anxiety this study found in each of the conditions reported above.

Irritable Bowel Syndrome.

The results revealed that of the Veterans who were diagnosed with both PTSD and IBS, 82.68% have also been diagnosed with a depressive disorder, while 71.64% have been diagnosed with an anxiety disorder. Rates of depression and anxiety in Veterans with IBS are reported in table 4.62.

Table 4.62 Rates of Depression and Anxiety in Veterans with IBS

	Depression	Anxiety
Rate of depression or anxiety among Veterans with IBS	F = 155215 53.83%	F = 137761 47.77%
Rate of IBS among those with both PTSD and depression or anxiety:	F = 89934 **PP = 31.19%**	F = 77927 **PP = 27.02%**
Rate of IBS among those with PTSD and without depression or anxiety:	F = 18874 **PP = 6.55%**	F = 30881 **PP = 10.71%**
Rate of IBS among those without PTSD and with depression or anxiety:	F = 65281 **PP = 22.64%**	F = 59834 **PP = 20.75%**
Rate of IBS among those without PTSD or depression or anxiety:	F = 108529 **PP = 37.64%**	F = 113976 **PP = 39.52%**

***Depression and Anxiety in Veterans with IBS*.**

The rates of depression in Veterans with IBS was found to be 53.83% and the rate of anxiety disorders is 47.77%. Both these rates for IBS and the rates reported previously for PTSD are higher than the expected rates of 11% depression and 9.9% anxiety reported by Gould, et al., (2015). It appears that depression and anxiety are correlated with both IBS and PTSD.

In order to determine whether these higher rates are correlated with the PTSD diagnosis, the IBS diagnosis, or both, rates have been broken down into tables. Depressive disorders are recorded in Table 4.63, anxiety disorders are recorded in Table 4.64. Since rate of PTSD is known to vary by period of service, rates are also broken down by the largest periods of service in the study.

Table 4.63 Rates of PTSD in Veterans by IBS and Depression Diagnoses

	F = total frequency **PP = % of all Veterans with PTSD**	**Overall**	**Korean**	**Persian Gulf War**	**Post-Korean**	**Post-Vietnam**	**Vietnam**	**World War II**
PTSD & IBS	Rate of PTSD among those with both IBS and depression:	F= 89943 **PP = 4.54%**	F = 1164 PP = .06%	F = 53147 PP = 2.69	F = 472 PP = 0.02	F = 9537 PP = .48%	F = 24093 PP = 1.22%	F = 1497 PP = .08%
	Rate of PTSD among those with IBS and without depression	F = 18874 **PP = .95%**	F = 386 PP = .02%	F = 11915 PP = .60%	F = 97 PP = 0%	F = 1019 PP = .05%	F = 4506 PP = .23%	F = 947 PP = .05%
	Rate of PTSD among those without IBS and with depression	F = 1295830 **PP = 65.48%**	F = 27087 PP = 1.37%	F = 575472 PP = 29.08%	F = 8939 PP = .45%	F = 122058 PP = 6.17%	F = 528351 PP = 26.70%	F = 33393 PP = 1.69%
	Rate of PTSD among those without	F = 574272 **PP = 29.02%**	F = 18421 PP = .93%	F = 267945 PP = 13.54%	F = 4712 PP = .24%	F = 32067 PP = 1.62%	F = 217694 PP = 11.00%	F = 32960 PP = 1.67%

	IBS or depression							

Table 4.64 Rates of PTSD in Veterans by IBS and Anxiety Diagnoses

	F = total frequency **PP = % of all Veterans with PTSD**	**Overall**	**Korean**	**Persian Gulf War**	**Post-Korean**	**Post-Vietnam**	**Vietnam**	**World War II**
PTSD & IBS	Rate of PTSD among those with both IBS and anxiety	F = 77925 **PP = 3.94%**	F = 1068 PP = .05%	F = 46430 PP = 2.35%	F = 427 PP = .02%	F = 8519 PP = .43%	F = 20103 PP = 1.02%	F = 1362 PP = .07%
	Rate of PTSD among those with IBS and without anxiety	F = 30881 **PP = 1.56%**	F = 482 PP = .02%	F = 18632 PP = .94%	F = 142 PP = .01%	F = 2037 PP = .10%	F = 8496 PP = .43%	F = 1082 PP = .05%
	Rate of PTSD among those without IBS and with anxiety	F = 966268 **PP = 48.83%**	F = 20256 PP= 1.02%	F = 450078 PP = 22.74%	F = 6711 PP = .34%	F = 92662 PP = 4.68%	F = 370031 PP = 18.70%	F = 26180 PP = 1.32%
	Rate of PTSD among those without IBS or anxiety:	F = 903834 **PP = 45.67%**	F = 25252 PP = 1.28%	F = 393339 PP = 19.88%	F = 6940 PP = .35%	F = 61463 PP = 3.11%	F = 376014 PP = 19.00%	F = 40173 PP = 2.03%

Depression and Anxiety More Closely Associated with PTSD.

The results revealed the rate of PTSD is highest in the category of PTSD without IBS and with depression, at 65.48%. When anxiety disorders are similarly studied in table 4.49, the highest rates of PTSD occurred in the category of Veterans with anxiety but not with IBS at 48.83% and in the category with neither anxiety nor IBS at 45.67%. This data indicates that the high rates of depression and anxiety are more strongly associated with PTSD than with IBS, which is supported by the rates of depression and anxiety this study found in each of the conditions reported above.

Constipation.

The results revealed that of the Veterans who were diagnosed with both PTSD and constipation, 83.20% have also been diagnosed with a depressive disorder, while 66.83% have been diagnosed with an anxiety disorder. Rates of depression and anxiety in Veterans with constipation are shown in table 4.53.

Table 4.65 Rates of Depression and Anxiety in Veterans with Constipation

	Depression	Anxiety
Rate of depression or anxiety among Veterans with constipation	F = 370649 42.55%	F = 281465 32.31%
Rate of constipation among those with both PTSD and depression or anxiety:	F = 167240 **PP = 19.20%**	F = 134203 **PP = 15.41%**
Rate of constipation among those with PTSD and without depression or anxiety:	F = 33839 **PP = 3.88%%**	F = 66876 **PP = 7.68%**
Rate of constipation among those without PTSD and with depression or anxiety:	F = 203409 **PP = 23.35%**	F = 147262 **PP = 16.91%**
Rate of constipation among those without PTSD or depression or anxiety:	F = 454940 **PP = 52.23%**	F = 511087 **PP = 58.67%**

Depression and Anxiety in Veterans with Constipation.

The rates of depression in Veterans with constipation was found to be 42.55% and the rate of anxiety disorders is 32.31%. Both these rates for constipation and the rates reported previously for PTSD are higher than the expected rates of 11% depression and 9.9% anxiety reported by Gould, et al., (2015). It appears that depression and anxiety are correlated with both constipation and PTSD.

In order to determine whether these higher rates are correlated with the PTSD diagnosis, the constipation diagnosis, or both, rates have been broken down into tables. Depressive disorders are recorded in table 4.66, anxiety disorders are recorded in table 4.67. Since rate of PTSD is known to vary by period of service, rates are also broken down by the largest periods of service in the study.

Table 4.66 Rates of PTSD in Veterans by Constipation and Depression Diagnoses

	F = total frequency **PP = % of all Veterans with PTSD**	**Overall**	**Korean**	**Persian Gulf War**	**Post-Korean**	**Post-Vietnam**	**Vietnam**	**World War II**
PTSD & Constipation	Rate of PTSD among those with both Constipation and depression:	F = 167240 **PP = 8.45%**	F = 7402 PP = .37%	F = 44756 PP = 2.26%	F = 2079 PP = .11%	F = 19797 PP = 1.00%	F = 83794 PP = 4.23%	F = 9300 PP = .47%
	Rate of PTSD among those with Constipation and without depression:	F = 33842 **PP = 1.71%**	F = 2689 PP = .14%	F = 6300 PP = .32%	F = 561 PP = 0.3%	F = 2136 PP = .11%	F = 16977 PP = .86%	F = 5118 PP = .26%
	Rate of PTSD among those without Constipation and with depression:	F = 1218524 **PP = 61.58 %**	F = 20849 PP = 1.05%	F = 583863 PP = 29.50 %	F = 7332 PP = .37%	F = 111798 PP = 5.65%	F = 468650 PP = 23.68%	F = 25590 PP = 1.29 %
	Rate of PTSD among those	F = 559307	F = 16121 PP = .81%	F = 273560	F = 4248 PP = .21%	F = 30950 PP = 1.56%	F = 205223 PP = 10.37%	F = 28789

	without Constipation or depression:	**PP = 28.26 %**		PP = 13.82 %				PP = 1.45 %

Table 4.67 Rates of PTSD in Veterans by Constipation and Anxiety Diagnoses

	F = total frequency **PP = % of all Veterans with PTSD**	Overall	Korean	Persian Gulf War	Post-Korean	Post-Vietnam	Vietnam	World War II
PTSD & Constipation	Rate of PTSD among those with both Constipation and anxiety	F = 134203 **PP = 6.78%**	F = 5888 PP = .28%	F = 37968 PP = 1.92%	F = 1722 PP = .09%	F = 16618 PP = .84%	F = 64356 PP = 3.25%	F = 7562 PP = .38%
	Rate of PTSD among those with Constipation and without anxiety	F = 66879 **PP = 3.38%**	F = 4200 PP = .12%	F = 13088 PP = .66%	F = 918 PP = .05%	F = 5315 PP = 2.67%	F = 36415 PP = 1.84%	F = 6856 PP = .35%
	Rate of PTSD among those without Constipation and with anxiety	F = 909992 **PP = 45.98 %**	F = 15436 PP = .78%	F = 458540 PP = 23.17 %	F = 5416 PP = .27%	F = 84563 PP = 4.27%	F = 325778 PP = 16.46%	F = 19980 PP = 1.01 %
	Rate of PTSD among those without Constipation or anxiety	F = 867839 **PP = 43.85 %**	F = 21534 PP = 1.09%	F = 398883 PP = 20.17 %	F = 6164 PP = .31%	F = 58185 PP = 2.94%	F = 348095 PP = 17.59%	F = 34399 PP = 1.74 %

Depression and Anxiety More Closely Associated with PTSD.

The results revealed the rate of PTSD is highest in the category of PTSD without constipation and with depression, at 61.58%. When anxiety disorders are similarly studied in table 4.55, the highest rates of PTSD occurred in the category of Veterans with anxiety but not with constipation at 45.98% and in the category with neither anxiety nor constipation at 43.85%. This data indicates that the high rates of depression and anxiety are more strongly associated with PTSD than with constipation, which is supported by the rates of depression and anxiety this study found in each of the conditions reported above.

Nausea/Vomiting.

The results revealed that of the Veterans who were diagnosed with both PTSD and nausea/vomiting, 81.56% have also been diagnosed with a depressive disorder, while 65.00% have been diagnosed with an anxiety disorder. Rates of depression and anxiety in Veterans with nausea/vomiting are shown in table 4.68.

Table 4.68 Rates of Depression and Anxiety in Veterans with Nausea/Vomiting

	Depression	Anxiety
Rate of depression or anxiety among Veterans with nausea/vomiting	F = 895234 41.46%	F = 675111 31.28%
Rate of nausea/vomiting among those with both PTSD and depression or anxiety:	F = 436929 **PP = 20.24%**	F = 348020 **PP = 16.12%**
Rate of nausea/vomiting among those with PTSD and without depression or anxiety:	F = 98862 **PP = 4.58%**	F = 187771 **PP = 8.70%**
Rate of nausea/vomiting among those without PTSD and with depression or anxiety:	F = 458299 **PP = 21.23%**	F = 327097 **PP = 15.15%**
Rate of nausea/vomiting among those without PTSD or depression or anxiety:	F = 941136 **PP = 43.59%**	F = 1248594 **PP = 57.83%**

Depression and Anxiety in Veterans with Nausea/Vomiting.

The rates of depression in Veterans with nausea/vomiting was found to be 41.46% and the rate of anxiety disorders is 31.28%. Both these rates for nausea/vomiting and the rates reported previously for PTSD are higher than the expected rates of 11% depression and 9.9% anxiety reported by Gould, et al., (2015). It appears that depression and anxiety are correlated with both nausea/vomiting and PTSD.

In order to determine whether these higher rates are correlated with the PTSD diagnosis, the nausea/vomiting diagnosis, or both, rates have been broken down into tables. Depressive disorders are recorded in table 4.69, anxiety disorders are recorded in Table 4.70. Since rate of PTSD is known to vary by period of service, rates are also broken down by the largest periods of service in the study.

Table 4.69 Rates of PTSD in Veterans by Nausea/Vomiting and Depression Diagnoses

	F = total frequency **PP = % of all Veterans with PTSD**	**Overall**	**Korean**	**Persian Gulf War**	**Post-Korean**	**Post-Vietnam**	**Vietnam**	**World War II**
PTSD & Nausea / Vomiting	Rate of PTSD among those with both N/V and depression:	F = 436929 **PP = 22.08 %**	F = 12915 PP = .65%	F = 150781 PP = 7.62%	F = 4063 PP = .21%	F = 48985 PP = 2.48%	F = 204820 PP = 10.35%	F = 15171 PP = .77%
	Rate of PTSD among those with N/V and without depression:	F = 98862 **PP = 4.99%**	F = 5190 PP = .26%	F = 30919 PP = 1.56%	F = 1158 PP = .06%	F = 6116 PP = .31%	F = 46659 PP = 2.36%	F = 8721 PP = .44%
	Rate of PTSD among those without N/V and with depression:	F = 948835 **PP = 47.95 %**	F = 15336 PP = .77%	F = 477838 PP = 24.15%	F = 5348 PP = .27%	F = 82610 PP = 4.17%	F = 347624 PP = 17.57%	F = 19719 PP = 1.00%

	Rate of PTSD among those without N/V or depression:	F = 494284 **PP = 24.98 %**	F = 13617 PP = .69%	F = 248941 PP = 12.58%	F = 3651 PP = .18%	F = 26970 PP = 1.36%	F = 175541 PP = 8.87%	F = 25186 PP = 1.27%

Table 4.70 Rates of PTSD in Veterans by Nausea/Vomiting and Anxiety Diagnoses

	F = total frequency **PP = % of all Veterans with PTSD**	Overall	Korean	Persian Gulf War	Post-Korean	Post-Vietnam	Vietnam	World War II
PTSD & Nausea/Vomiting	Rate of PTSD among those with both Nausea / Vomiting and anxiety:	F = 348020 **PP = 17.59 %**	F = 10096 PP = .51%	F = 128034 PP = 6.47%	F = 3245 PP = .16%	F = 40932 PP = 2.07%	F = 153472 PP = 7.76%	F = 12101 PP = .61%
	Rate of PTSD among those with Nausea / Vomiting and without anxiety:	F = 187771 **PP = 9.49%**	F = 8009 PP = .40%	F = 53666 PP = 2.71%	F = 1976 PP = .10%	F = 14169 PP = .72%	F = 98007 PP = 4.95%	F = 11791 PP = .60%
	Rate of PTSD among those without Nausea/Vomiting and with anxiety:	F = 696175 **PP = 35.18 %**	F = 11228 PP = .57%	F = 368474 PP = 18.62 %	F = 3893 PP = .20%	F = 60249 PP = 3.04%	F = 236662 PP = 11.96 %	F = 15441 PP = .78%
	Rate of PTSD among those without Nausea/Vomiting or anxiety:	F = 746944 **PP = 37.75 %**	F = 17725 PP = .90%	F = 358305 PP = 18.11 %	F = 5106 PP = .26%	F = 49331 PP = 2.49%	F = 286503 PP = 14.48 %	F = 29464 PP = 1.49 %

Depression and Anxiety More Closely Associated with PTSD.

The results revealed the rate of PTSD is highest in the category of PTSD without nausea/vomiting and with depression, at 47.95%. When anxiety disorders are similarly studied in table 4.70, the highest rates of PTSD occurred in the category of Veterans with anxiety but not with constipation at 35.18% and in the category with neither anxiety nor constipation at 37.75%. This data indicates that the high rates of depression and anxiety are more strongly associated with PTSD than with constipation, which is supported by the rates of depression and anxiety this study found in each of the conditions reported above.

Other Secondary Mental Illness.

Bipolar disorders, psychotic disorders, personality disorders, substance abuse, and dementia were also observed for PTSD and GI Disease and can be found in Appendix M. Findings suggest an association between PTSD and Substance Abuse, which is supported in the literature (Pietrzak, Goldstein, Southwick, & Grant, 2011, & Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995). Findings do not suggest that any of these secondary mental illnesses would be potential confounding variables for the association between PTSD and GI disease.

Summary of Findings and Conclusions

Specific Aim 1

Specific Aim 1 is: "To determine the frequency with which GI Disease (GERD, Peptic Ulcer Disease/PUD) and PTSD are diagnosed co-morbidities in Veterans who have served in wartime periods."

Research Question 1 is: In Veterans who have served during wartime periods, what is the frequency with which GI Disease and PTSD are diagnosed co-morbidities?

Research Hypothesis 1 is: In Veterans who have served in wartime period, GI Disease and PTSD are frequently diagnosed as co-morbidities.

Research Hypothesis 1 was: Confirmed.

Research Hypothesis 1: Findings.

The study identified exact frequencies of which GI diseases and PTSD are diagnosed as co-morbidities within Veterans treated outpatient at VHA nationally. Findings were that:

- PTSD is bi-directionally correlated with the GI Diseases of GERD, peptic ulcer disease, functional dyspepsia, Crohn's disease, diverticular disease, and IBS, and the symptoms of constipation and nausea/vomiting within Veterans who served during wartime periods.
- PTSD is not correlated with ulcerative colitis.

Specific Aim 2

Specific Aim 2 is: "To determine the frequency with which a diagnosis of functional or structural GI Disease accompanies a diagnosis of PTSD in Veterans who have served during wartime periods."

Research Question 2 is: In Veterans who have served during wartime periods, what is the frequency with which a diagnosis of functional or structural GI Disease accompanies a diagnosis of PTSD?

Research Hypothesis 2 is: In Veterans who have served during wartime periods, a diagnosis of functional or structural GI Disease frequently accompanies a diagnosis of PTSD.

Research Hypothesis 2 was: Confirmed.

Research Hypothesis 2 Findings.

The study identified exact frequencies of which GI diseases and PTSD are diagnosed as co-morbidities within Veterans treated outpatient at VHA nationally. Findings were that:

- PTSD is bi-directionally correlated with the GI Diseases of GERD, peptic ulcer disease, functional dyspepsia, Crohn's disease, diverticular disease, and IBS, and the symptoms of constipation and nausea/vomiting within Veterans who served during wartime periods.
- PTSD is not correlated with ulcerative colitis.
- PTSD was most strongly associated with IBS, functional dyspepsia, and the symptoms of nausea/vomiting.
- Probability rates of GI disease among Veterans with PTSD are summarized in Table 4.71.

Table 4.71 Probability of Veterans with PTSD Diagnosed with Co-Occurring GI Disease

	In Veterans with PTSD, likelihood that they will also have the indicated GI Disease
GERD	1.50
Peptic Ulcer Disease	1.36
Functional Dyspepsia	1.80
Crohn's Disease	1.15
Ulcerative Colitis	1.03
Diverticular Disease	1.30
IBS	2.73
Constipation	1.50
Nausea/Vomiting	2.69

Specific Aim 3

Specific Aim 3 is: "To determine the frequency with which a diagnosis of PTSD accompanies a diagnosis of functional or structural GI Disease in Veterans who have served during wartime periods."

Research Question 3 is: In Veterans who have served during wartime periods, what is the frequency with which a diagnosis of PTSD accompanies a diagnosis of functional or structural GI Disease?

Research Hypothesis 3 is: In Veterans who have served during wartime periods, a diagnosis of PTSD frequently accompanies a diagnosis of functional or structural GI Disease.

Research Hypothesis 3 was: Confirmed.

Research Hypothesis 3 Findings.

Findings were that:

- PTSD and GI disease are bi-directionally correlated in both functional and structural GI diseases.
- Functional GI diseases, IBS and Functional Dyspepsia, were more strongly correlated than the structural diseases of GERD, PUD, Crohn's, and diverticular disease.
- PTSD was not correlated with the structural disease of ulcerative colitis.
- Rates of PTSD among Veterans with GI Disease are summarized in Table 4.63

Table 4.72 Probability of Veterans with GI Disease Diagnosed with Co-Occurring PTSD

	In Veterans with GI Disease, likelihood that they will also have PTSD
GERD	1.44
Peptic Ulcer Disease	1.29
Functional Dyspepsia	1.71
Crohn's Disease	1.09
Ulcerative Colitis	.99
Diverticular Disease	1.29
IBS	2.61
Constipation	1.44
Nausea/Vomiting	2.57

Summary of Chapter

Chapter Four presented the findings of this study, which were explored via the following three (3) Specific Aims:

- Specific Aim 1 is: "To determine the frequency with which GI Disease and PTSD are diagnosed co-morbidities in Veterans who have served in wartime periods."
- Specific Aim 2 is: "To determine the frequency with which a diagnosis of functional or structural GI Disease accompanies diagnosis of PTSD in Veterans who have served in wartime periods."
- Specific Aim 3 is: "To determine the frequency with which a diagnosis of PTSD accompanies a diagnosis of functional or structural GI Disease in

Veterans who have served in wartime periods."

The Chapter began with a presentation of sample characteristics and a psychometric estimate for the sample. In addition, major findings and conclusions were introduced, with a summary of findings.

Plan for Remaining Chapter

Chapter Five provide an interpretation of the findings. This interpretation includes conclusions, discussions, and recommendations for future research.

References

Ford, M. J., Miller, P. M., Eastwood, J., & Eastwood, M. A. (1987). Life events, psychiatric illness, and the irritable bowel syndrome. *Gut*, 28, pp. 160-165.

Gould, C. E., Rideaux, T., Spira, A. P., & Beaudreau, S.A. (2015). Depression and anxiety symptoms in male veterans and non-veterans: The health and retirement study. *Int. Journal of Geriatric Psychiatry*, 30, pp. 623-30. doi: 10.1002/gps.4193

Kessler, R. C., Sonnega, A., Bromet, E. J., Hughes, M., & Nelson, C. B. (1995). Posttraumatic stress disorder in the national comorbidity survey. *Archives of General Psychiatry*, 52, pp. 1048-1060. doi:10.1001/archpsyc.1995.03950240066012

Locke, G. R., Weaver, A. L., Melton, L. J., & Talley, N. J. (2004). Psychosocial factors are linked to functional gastrointestinal disorders: A population based nested case-control study. *American Journal of Gastroenterology*, 99, pp. 350-357. doi:10.1111/j.1572-0241.2004.04043.x

Pietrzak, R. H., Goldstein, R. B., Southwick, S. M., & Grant, B. F. (2011). Prevalence and Axis I comorbidity of full and partial posttraumatic stress disorder in the United States: Results from wave 2 of the national epidemiologic survey on alcohol and related condition. *Journal of Anxiety Disorders*, 25, pp. 456-465. doi:10.1016/j.janxdis.2010.11.010

U.S. Department of Veterans Affairs. (2016). National center for Veteran's analysis and statistics. Retrieved from https://www.va.gov/vetdata/veteran_population.asp

Chapter 5:

Conclusions, Discussions, and Recommendations

Introduction

Chapter Five presents a brief summary of this research, beginning with a review of the study's problem and methodology used to answer the research question. The Chapter then presents a comparison of the findings to the extant literature; the implications of the study; the study's strengths, limitations, and assumptions; recommendations for further research; and ends with the conclusions.

Statement of the Problem

GI Disease, such as Irritable Bowel Syndrome (IBS), has been associated with anxiety and depression in numerous studies (Addolorado, et al., 2008; Haug, Mykletun, & Dahl, 2002). Post-traumatic stress disorder (PTSD), which can occur after experiencing or witnessing a traumatic life event (e.g. serving during wartime periods), has also been associated with symptoms of anxiety and depression. In the researcher's clinical experience, GI Disease and PTSD often occur together as co-morbidities. Logically, the *research question* arises regarding whether gastrointestinal disease (i.e., GI Disease) is linked to traumatic life events (i.e., PTSD). The *problem* of this study was to determine the relationship between GI Disease and PTSD in Veterans who have served during wartime periods.

Overview of Methodology

Theoretical Framework

The Transactional Model of Stress and Coping was utilized as the framework to investigate the relationship between PTSD and GI Disease (Lazarus & Folkman, 1984).

According to the TMSC Model, when a person is exposed to a stressor, the risk of harm is assessed, a response termed the primary appraisal; subsequently, capacity to change the situation is determined, a response termed the secondary appraisal. The ability to cope with the stressor leads to several outcomes, which include impacts on emotional well-being, functional status, and health behaviors (Glanz, Rimer, & Viswanath, 2008).

The Sample

Participants/Subjects in the study were Veterans with either or both diagnosis of PTSD and GI Disease. Specific GI Diseases accounted for more than 500,000 ambulatory care visits annually in the United States, which included peptic ulcer disease, gastroesophageal reflux disease, diverticular disease, ulcerative colitis, Crohn's disease, irritable bowel syndrome, and functional dyspepsia, as well as the symptoms of constipation and nausea/vomiting (Everhart & Ruhl, 2009; Kozma, Barghhout, Slaton, Frech, & Reeder, 2002).

Data Management

A data cohort was created by National Data Systems. The researcher then queried the data using standard query language via Microsoft SQL. Data from the cohort was combined with demographic information to form permanent Tables, one for each year 1999-2019. Tables were then combined into one table termed "All Years," where repeated Veterans data was eliminated to form one record per Veteran. Data tables were then exported to SAS 9.4 for analyzation.

Data Analysis

Data was analyzed via SAS 9.4 Analytics Software September 2017 through secure remote access to Veterans Health Administration workspace. Descriptive

statistics, including means, percentages, histograms and contingency tables were used to describe and explain the data outcomes. Chi-Square and goodness-of-fit tests were used to examine the relationships between the categories and sub-categories of GI Disease and PTSD, as well as differences among demographic data.

Interpretation of Major Findings and Conclusions

Specific Aim 1

Specific Aim 1 is: "To determine the frequency with which GI Disease (GERD, Peptic Ulcer Disease/PUD) and PTSD are diagnosed co-morbidities in Veterans who have served in wartime periods."

Research Question 1 is: In Veterans who have served during wartime periods, what is the frequency with which GI Disease and PTSD are diagnosed co-morbidities?

Research Hypothesis 1 is: In Veterans who have served in wartime period, GI Disease and PTSD are frequently diagnosed as co-morbidities.

Research Hypothesis 1 was: Confirmed.

Research Hypothesis 1: Findings.

The study identified exact frequencies of which GI diseases and PTSD are diagnosed as co-morbidities within Veterans treated outpatient at VHA nationally. Findings were that:

- PTSD is bi-directionally correlated with the GI Diseases of GERD, peptic ulcer disease, functional dyspepsia, Crohn's disease, diverticular disease, and IBS, and the symptoms of constipation and nausea/vomiting within Veterans who served

during wartime periods.

- PTSD is not correlated with ulcerative colitis.

Specific Aim 1 Conclusions.

PTSD is bi-directionally correlated with commonly diagnosed GI diseases. In the clinical setting providers can expect to commonly see a triad of GI diagnosis, PTSD, and secondary depression or anxiety. Providers should consider that these diseases are frequently co-occurring when screening and providing treatment.

Specific Aim 2

Specific Aim 2 is: "To determine the frequency with which a diagnosis of functional or structural GI Disease accompanies a diagnosis of PTSD in Veterans who have served during wartime periods."

Research Question 2 is: In Veterans who have served during wartime periods, what is the frequency with which a diagnosis of functional or structural GI Disease accompanies a diagnosis of PTSD?

Research Hypothesis 2 is: In Veterans who have served during wartime periods, a diagnosis of functional or structural GI Disease frequently accompanies a diagnosis of PTSD.

Research Hypothesis 2 was: Confirmed.

Research Hypothesis 2 Findings.

The study identified exact frequencies of which GI diseases and PTSD are diagnosed as co-morbidities within Veterans treated outpatient at VHA nationally. Findings were that:

- PTSD is bi-directionally correlated with the GI Diseases of GERD, peptic ulcer disease, functional dyspepsia, Crohn's disease, diverticular disease, and IBS, and the symptoms of constipation and nausea/vomiting within Veterans who served during wartime periods.
- PTSD is not correlated with ulcerative colitis.
- PTSD was most strongly associated with IBS, functional dyspepsia, and the symptoms of nausea/vomiting.
- Probability rates of GI disease among Veterans with PTSD are summarized in Table 5.1.

Table 5.1 Probability of Veterans with PTSD Diagnosed with Co-Occurring GI Disease

	In Veterans with PTSD, likelihood that they will also have the indicated GI Disease
GERD	1.50
Peptic Ulcer Disease	1.36
Functional Dyspepsia	1.80
Crohn's Disease	1.15
Ulcerative Colitis	1.03
Diverticular Disease	1.30
IBS	2.73
Constipation	1.50
Nausea/Vomiting	2.69

Specific Aim 2 Conclusions.

PTSD is bi-directionally correlated with commonly diagnosed GI diseases. In the clinical setting providers can expect to commonly see a triad of GI diagnosis, PTSD, and secondary depression or anxiety. Providers should consider that these diseases are frequently co-occurring when screening and providing treatment.

Specific Aim 3

Specific Aim 3 is: "To determine the frequency with which a diagnosis of PTSD accompanies a diagnosis of functional or structural GI Disease in Veterans who have served during wartime periods."

Research Question 3 is: In Veterans who have served during wartime periods, what is the frequency with which a diagnosis of PTSD accompanies a diagnosis of functional or structural GI Disease?

Research Hypothesis 3 is: In Veterans who have served during wartime periods, a diagnosis of PTSD frequently accompanies a diagnosis of functional or structural GI Disease.

Research Hypothesis 3 was: Confirmed.

Research Hypothesis 3 Findings.

Findings were that:

- PTSD and GI disease are bi-directionally correlated in both functional and structural GI diseases.
- Functional GI diseases, IBS and Functional Dyspepsia, were more strongly correlated than the structural diseases of GERD, PUD, Crohn's, and diverticular disease.
- PTSD was not correlated with the structural disease of ulcerative colitis.
- Rates of PTSD among Veterans with GI Disease are summarized in Table 5.2

Table 5.2 Probability of Veterans with GI Disease Diagnosed with Co-Occurring PTSD

	In Veterans with GI Disease, likelihood that they will also have PTSD
GERD	1.44
Peptic Ulcer Disease	1.29
Functional Dyspepsia	1.71
Crohn's Disease	1.09
Ulcerative Colitis	.99
Diverticular Disease	1.29
IBS	2.61
Constipation	1.44
Nausea/Vomiting	2.57

Specific Aim 3: Conclusions.

PTSD is Correlated Bi-directionally with Commonly Diagnosed GI Diseases.

PTSD is bi-directionally correlated with commonly diagnosed GI diseases. In the clinical setting providers can expect to commonly see a triad of GI diagnosis, PTSD, and secondary depression or anxiety. Providers should consider that these diseases are frequently co-occurring when screening and providing treatment.

Comparison to Extant Literature

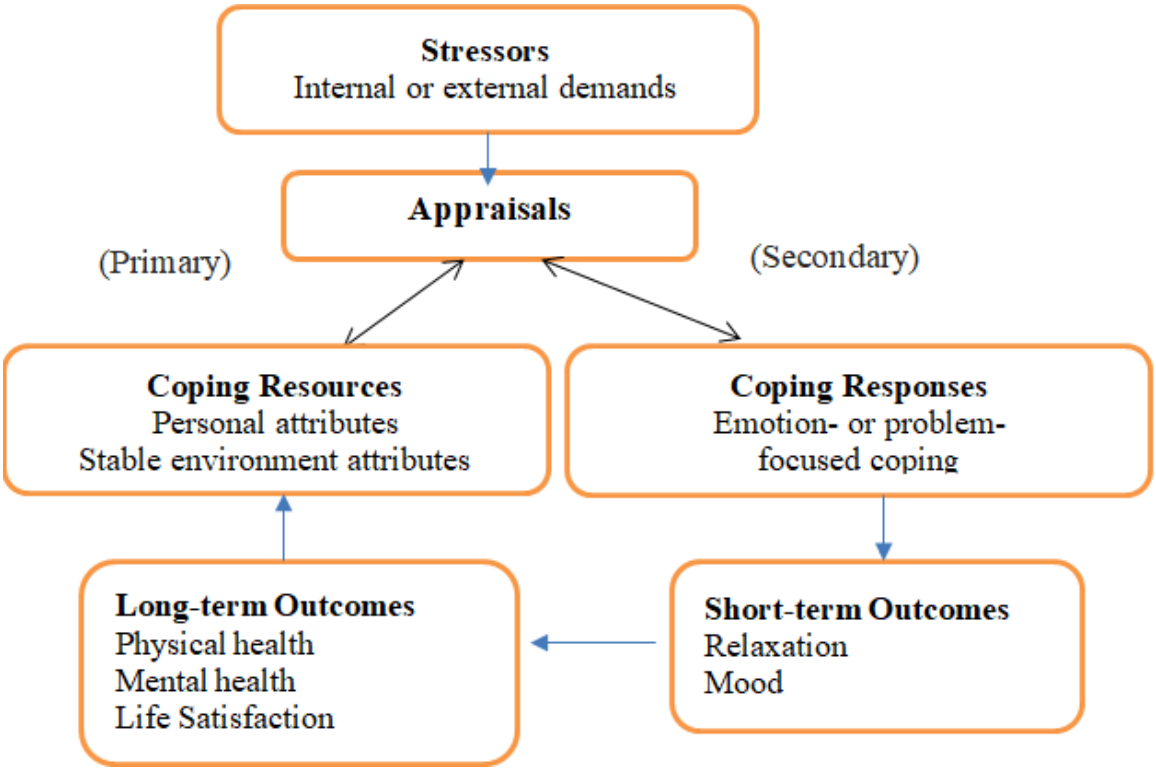
Theoretical Framework

The *theoretical framework* for this study is the Transactional Model of Stress and Coping (TMSC Model), which allows for the evaluation of coping after a stressful event. In the model, a transaction is a stressful event between the person and the environment. In the case of PTSD, transactions could be not only the initial stressor or trauma, but the daily reminders of the trauma, or triggers, that bring on flashbacks and nightmares, causing the individual to relive the initial trauma.

Response to Stressors.

According to the TMSC Model, when a person is exposed to a stressor, the risk of harm is assessed, a response termed the primary appraisal; subsequently, capacity to change the situation is determined, a response termed the secondary appraisal. The ability to cope with the stressor leads to several outcomes, which include impacts on emotional well-being, functional status, and health behaviors (Glanz, Rimer, & Viswanath, 2008,). The model is demonstrated in Figure 5.1 from Lazarus & Folkman (1984).

Figure 5.1 Transactional Model of Stress and Coping



Coping Strategies.

Individuals use coping strategies after the primary and secondary appraisals, and these coping efforts fall into two categories: problem management and emotional regulation. However, some coping strategies that individuals use may not always be beneficial in the long term, such as avoidance and denial, symptoms also associated with PTSD. Glanz et al. (2008, p. 217), suggests a relationship between coping strategies and traumatic events by stating, “When a stressor is perceived as highly threatening and uncontrollable, a person may be more likely to use disengaging coping strategies,” such as distancing, cognitive and behavioral avoidance, and distraction.

Resilience.

Conceptually aligned with the TMSC Model is the concept of *resilience*, which is conceptually defined as "an individual's ability to adapt and recover from stressful situations, trauma, and hardship" (Thompson & Dobbins, 2018, p. 24). Resilience training is now performed in the U.S. military to aide in the prevention of development of PTSD (Thompson & Dobbins, 2018). In a study on resilience and psychological well-being in women with IBS, researchers used the Connor-Davidson Resilience Scale to measure resilience. When compared to healthy women, those with IBS had lower scores of resilience and components of positive relations with others, environmental mastery, purpose in life and acceptance, suggesting that these factors may be involved in the symptoms and exacerbation of IBS (Shahdadi, Balouchi, & Shaykh, 2017). Future research should be performed to assess whether resilience scores are lower than healthy controls in each of the GI diseases in this study, as this data may shed further light on the relationship between GI disease and PTSD.

Literature Review of Research

Specific Aim 1.

Higher Rates of Depression and Anxiety in Veterans with IBS and Functional Dyspepsia.

The current study supports findings related to those of Savas, et al (2008), who found that female Veteran participants with IBS and dyspepsia reported significantly higher levels of anxiety and depression when compared to women without GI diseases. The findings in this study supported higher rates of depression and anxiety in both men and women with IBS and functional dyspepsia than the general population of Veterans.

Strong Association Between PTSD and Peptic Ulcer.

In the Danish population, researchers found that among those with PTSD, risk of any GI disease was 25%, with PTSD having the strongest association with peptic ulcer (Gradus, Farkus, Svensson, Ehrenstein, Lash, & Sorensen, 2017). This study's results were consistent in that a strong association between PTSD and peptic ulcer disease was identified. However, the results were inconsistent in that IBS was the most strongly correlated GI disease with PTSD, rather than PUD. This supports research which found those with IBS were significantly more likely to be diagnosed with PTSD in African Americans (Iorio, Makipour, Palit, & Friedenberg, 2014).

Specific Aim 2.

Rates of Depression and Anxiety Higher in Veterans with GI Disease and/or PTSD.

The study reveals the complexity of Veteran health. Gould and others found in their study that Veterans do not have increased rates of depression and anxiety over non-veterans. They identified the rate of depression in Veterans as 11% and the rate of anxiety in Veterans as 9.9% (Gould, Rideaux, Spira, & Beaudreau, 2015). However, this study found rates of depression and anxiety to be higher, at least in Veterans with GI disease and/or PTSD, summarized in table 5.3. These results highlight the difference in rates of depression and anxiety among Veterans with co-occurring conditions compared to the general population of Veterans.

Table 5.3 Rates of Depression and Anxiety in Veterans with PTSD or GI Disease

Condition	Rate of Depression	Rate of Anxiety
PTSD	69.25%	52.18%
GERD	37.07%	28.56%
Peptic ulcer disease	41.18%	31.39%
Functional dyspepsia	43.97%	35.64%
Crohn's disease	39.60%	30.86%
Ulcerative colitis	37.50%	29.29%
Diverticular disease	33.14%	24.75%
IBS	53.83%	47.77%
Constipation	42.55%	32.31%
Nausea/vomiting	41.46%	31.28%

Additionally, the findings contradict one study that suggested that combat-related trauma was not associated with gastrointestinal disease. Husarewycz, El-Gabalawy, Loysetty, & Sareen (2014), researched the effect of number and type of traumatic life events on physical health symptoms through a national epidemiological survey. They concluded that a trauma where the individual sustained a physical injury was associated with all assessed health conditions, including GI disease, but that combat-related trauma was not associated with any health conditions, including GI disease, (Husarewycz, et al, 2014). Although the study presented in this paper did not assess type of trauma, it is expected that many of the Veterans presenting at VHA with PTSD do have combat-related trauma. Further research in U.S. Veterans with PTSD could assess for type of trauma and determine whether this affects the relationship with GI disease.

Specific Aim 3

Rates of PUD, Functional Dyspepsia, DD, and IBS Lower than General American Population.

The study's findings expand upon the work of previous researchers. Prior to this study, there were estimates on GI disease rates in the general American population, but there was no available data on the rate of GI disease specific to Veterans. A comparison of these rates identified by previous literature and rates identified in Veterans by this study is shown in Table 5.4. Rates of GI Disease in this study were over a twenty-year period of 1999-2019.

Table 5.4 Study Findings of GI Rates in Veterans as Compared to Estimates on GI Rates from the Literature in the American Population

Condition	Rate Among VHA Veteran outpatient population found in this study over 20 years	Rate reported in the Literature for American population
PTSD	14.64%	7-8% (U.S. Dept of Veterans Affairs, 2019)
Gastroesophageal Reflux Disease	25.52%	20% (NIDDKD, 2019)
Peptic Ulcer Disease	1.82%	10% (NIDDKD, 2019)
Functional Dyspepsia	20.99%	40% (Loyd & McClellan, 2011).
Irritable Bowel Disease (Crohn's disease + ulcerative colitis)	3.57%	1.3% (Centers for Disease Control and Prevention, 2019)
Diverticular Disease	10.22%	35-58% (NIDDKD, 2019)
Irritable Bowel Syndrome	2.11%	11% (Canavan, West, & Card, 2014)
Constipation	6.37%	2-27% (Sanchez & Bercik, 2011)
Nausea/Vomiting	15.80%	not reported

Findings show rates of peptic ulcer disease, functional dyspepsia, diverticular disease, and irritable bowel syndrome that are lower than expected in the general American population. It is unclear whether these rates are truly lower in Veterans than in the American population. In each case the literature reports an *estimated* rate of disease, whereas this study recorded an exact count of diagnosis. It is possible that disease is under reported or underdiagnosed in Veterans. It is also important to note that this study does not account for Veterans that were only treated for a disease in an inpatient setting within the VA, which may account for a small amount of the discrepancy in rates. Additionally, rates calculated in this study were over a twenty-year period, while time frame in the literature either varies or is not reported. Therefore, differences in rates identified in this study and those reported in the literature may be due to variations in study design.

Rates of GERD and IBS Higher in Veterans than General Population of Americans.

The rates of GERD and irritable bowel syndrome were higher in Veterans than in the general population of Americans. The rate of PTSD was higher in Veterans than in the general population of Americans, which is supported by previous literature (U.S. Department of Veterans Affairs, 2019).

Study Implications

Specific Aim 1

The implication of findings is that clinical providers can expect to frequently see Veterans with a triad of PTSD, GI disease, and depression or anxiety. Nurses working in primary care settings are the optimally situated to screen for all conditions and refer to specialist care as appropriate.

Specific Aim 2

Clinical providers, including advanced practice nurses, working in the field of mental health can expect a high frequency of co-occurring GI disease in Veterans diagnosed with PTSD with or without depression and anxiety. Mental health providers and nurses should routinely screen for GI symptoms in Veterans who have been diagnosed with these mental health conditions. When positive, providers should consult with primary care or gastroenterology for coordination of care. Since several antidepressants have evidence to support use in GI diseases, mental health prescribers should consider these medications when applicable to treat two conditions with one medication.

Specific Aim 3

Clinical providers working in the field of gastroenterology can expect a high frequency of co-occurring PTSD and anxiety and depression in the Veteran population within those patients diagnosed with commonly occurring GI diseases. Nurses and providers working in gastroenterology should routinely screen for PTSD, depression, and anxiety in patients with GERD, peptic ulcer disease, functional dyspepsia, Crohn's disease, diverticular disease, IBS, and symptoms of constipation and nausea/vomiting. When positive, providers should refer patients to mental health for treatment of co-occurring mental illness.

Study Strengths

Specific Aim 1

The study's participant recruitment strategy was a strength because it gathered the exact counts of PTSD and GI disease within the Veteran population treated in outpatient care across VHA nationally. Frequencies and rates of diseases are not estimated, but exact counts as of March 31, 2018. These findings may provide information that will enhance future research by providing population information on Veterans treated by VHA.

Specific Aim 2

An additional strength of the study was that the researcher was able to observe rates of secondary mental illness among Veterans with PTSD and those with GI disease. Rates of depression and anxiety in GI disease were compared to the national averages for Veterans and found to be higher than expected. In the future clinicians will be able

improve screening processes for depression and anxiety within patients experiencing GI disease and/or PTSD.

Specific Aim 3

Finally, the study results compared structural vs functional GI diseases. Bases on past research it was expected that functional diseases could be correlated with mental health conditions, but the study found that structural GI diseases are also correlated with PTSD and depression and anxiety. This information may prove useful to clinicians who previously only screened patients with IBS for depression and anxiety, as it would now be reasonable to screen Veterans with GI disease for PTSD, depression, and anxiety.

Limitations and Assumptions

Limitations

The study was limited by lack of access to population data for all VHA-treated Veterans. The study did not have access to exact rates of age, ethnicity, and period of service for the entire population treated by VHA. The literature showed estimated rates of depression and anxiety for Veterans, as well as estimated rates of gender, but the specific data was not accessible through VHA. The study could not control for all possible confounding variables together without this data.

Another limitation is that this study did not gather race in addition to ethnicity, therefore the study may not be generalizable across race and ethnicities.

Rates of disease in this study were identified over a twenty-year period and were identified as 14.64% of the population with PTSD, 25.52% with GERD, 1.82% with peptic ulcer disease, 20.99% with functional dyspepsia, 3.57% with irritable bowel disease 10. 22% with diverticular disease, 2.11% with IBS, 6.37% with constipation, and

15.80% with nausea/vomiting. Some of these rates were inconsistent with those in the current literature, which may be due to study design. Due to the changes of disease prevalence over time, future studies should report estimates by time.

Additionally, data gathered included both ICD-9 codes and ICD-10 codes. The United States, including VHA, made the switch from ICD-9 to ICD-10 codes in the year 2015. In years 2016 and forward, this study found rates of disease to be unexpectedly dissimilar from the trend from the previous years. It is likely that the change in ICD coding procedures has influenced the results of the study. In order to confirm this effect, future studies should be repeated with data gathered by month rather than by year to follow the change more precisely as coding changed.

Assumptions

The accepted standard of diagnosis for mental health disorders is the DSM-5, (APA, 2013). PTSD was categorized in prior versions as an anxiety disorder until 2013, when the revised DSM-5 reclassified PTSD under "Trauma- and Stressor-Related Disorders" (APA, p. 271). Since Veteran records for this study were reviewed from as far back as 1999, many Veteran's diagnosis of mental illness may be based on the prior version, the DSM-IV-TR (APA, 2000), and possibly even the DSM-IV (APA, 1994). The DSM-5 expands the criterion set for PTSD, to allow the traumatic event to include learning that a traumatic event occurred to a close relationship and "experiencing repeated or extreme exposure to aversive details of the traumatic events," (APA, 2013, p.271). This updated diagnostic criterion allows for more cases of PTSD diagnosis than under former versions. It is assumed that the healthcare provider used the most up-to-date version of the DSM available at the time of diagnosis and is therefore a potential

limitation of this study. Since the latest version expanded the diagnosis rather than reducing it, it is expected that there are no false diagnoses from this change in the study. However, there is a potential for some "missed" cases, or those individuals who would have later qualified for PTSD if they had lived or been treated under the more modern criteria.

Recommendations for Further Research

Controlling Confounding Variables

Future research studies should attempt to control for confounding variables by gathering population data from the Department of Veterans Affairs. In order to gain access to this information, it should be requested as part of the IRB application and DART data request application. Data on the entire VHA population should be collected for both demographics and secondary mental illness. In future both race and ethnicity should be collected.

Smaller Sample Size

A similar study should be done with a smaller sample size but with data on those with depression and anxiety who do not have PTSD. A multilevel correlation between PTSD, depression, anxiety, and GI disease should be performed, with access to population-level data, in order to control for potential confounding variables in mental health diagnosis. Previous research identifying depression and anxiety as correlating with GI disease should be reviewed and potentially repeated to account for PTSD as a possible confounding variable.

Confirm Research Findings

Further research is also recommended to verify this study's findings of rates of GI disease in Veterans as compared to the general American population. The study should be repeated in the general population to determine if PTSD is related to GI disease in groups outside of U.S. Veterans.

Conclusions

Bi-directional Correlation Between PTSD and GI Disease

This study identified rates of PTSD and co-occurring GI disease and found that PTSD is bi-directionally correlated with the GI diseases of GERD, PUD, functional dyspepsia, Crohn's disease, diverticular disease, and IBS, and the GI symptoms of constipation and nausea/vomiting. The study also identified a high level of correlation between PTSD with each depression and anxiety.

Explore PTSD as a Confounding Variable

Previous research has reported a correlation between depression and anxiety and GI disease. The researcher recommends that this research be reviewed to account for PTSD as a potential confounding variable. However, whether PTSD or depression/anxiety is the confounding variable, clinically the presentation will often look the same as a triad of PTSD, depression/anxiety, and GI disease diagnosis. The researcher recommends improved screening in both directions. Providers in mental health clinics who see a presentation of PTSD should be screening for GI disease, while PCPs and gastroenterologists who see a GI presentation should be screening for trauma and PTSD. Improved diagnosis rates may lead to improved treatment.

Summary of Chapter

Chapter Five presented a brief summary of this research, beginning with a review of the study's problem and methodology used to answer the research question. The Chapter then presented a comparison of the findings to the extant literature; the implications of the study; the study's strengths, limitations, and assumptions; recommendations for further research; and ended with the conclusions

References

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders 5th ed.* Arlington, VA: American Psychiatric Association.

American Psychiatric Association (APA). (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., Text Revision). Arlington, VA: American Psychiatric Association.

Canavan, C., West, J., & Card, T. (2014). The epidemiology of irritable bowel syndrome. *Clinical Epidemiology*, 6, pp. 71-80.

Centers for Disease Control and Prevention. (2019). Inflammatory bowel disease: Data and statistics. Retrieved from https://www.cdc.gov/ibd/data-statistics.htm

Everhart, J. E. & Ruhl, C. E. (2009). Burden of digestive diseases in the United States part I: Overall and upper gastrointestinal diseases. *Gastroenterology*, 136, pp. 376-386.

Glanz, K., Rimer, B. K., &Viswanath, K. (2008). *Health behavior and health education*. San Francisco, CA: Jossey-Bass.

Gould, C. E., Rideaux, T., Spira, A. P., & Beaudreau, S.A. (2015). Depression and anxiety symptoms in male veterans and non-veterans: The health and retirement study. *Int. Journal of Geriatric Psychiatry*, 30, pp. 623-30. doi: 10.1002/gps.4193

Gradus, J. L., Farkas, D. K., Svensson, E., Ehrenstein, V., Lash, T. L., & Sorensen, H. T. (2017). Posttraumatic stress disorder and gastrointestinal disorders in the Danish population. *Epidemiology, 28,* 354-360.

Husarewycz, M. N., El-Gabalawy, R., Loysetty, S., & Sareen, J. (2014). The association between number and type of traumatic life experiences and physical conditions in a nationally representative sample. *Gen Hosp Psychiatry, 36*, pp. 26-32.

Iorio, N., Makipour, K., Palit, A., & Friedenberg, F. K. (2014). Post-traumatic stress disorder is associated with irritable bowel syndrome in African Americans. *Journal of Neurogastroenterology & Motility, 20*, pp. 523-530. doi:10.5056/jnm14040.

Kozma, C. M., Barghhout, V., Slaton, T., Frech, F., & Reeder, C.E. (2002). Office-based physician visits: A comparison of irritable bowel syndrome with other gastrointestinal disorders using national ambulatory medical care survey data. *Practical Gastroenterology,* XXVL, pp. 58-68.

Lazarus, R. S., and Folkman, S. (1984). Stress, appraisal, and coping. New York: Springer Pub

Loyd, R. A., & McClellan, D. A. (2011). Update on the evaluation and management of functional dyspepsia. *American Family Physician, 83*, pp. 547-552.

National Institute of Diabetes and Digestive and Kidney diseases (NIDDKD). (2019). Definition and facts for GER and GERD. Retrieved from https://www.niddk.nih.gov/health-information/digestive-diseases/acid-reflux-ger-gerd-adults/definition-facts

Sanchez, M. I., & Bercik, P. (2011). Epidemiology and burden of chronic constipation. *Can Journal of Gastroenterology*, 25, 11B-15B.

Savas, L. S., White, D. L, Wieman, M., Dacis, K., Fitzgerald, S., Smith, S. L., … El-Serag, E.B. (2008). Irritable bowel syndrome and dyspepsia among women Veterans: Prevalence and association with psychological illness. *Alimentary Pharmacology & Therapeutics*. *29*, pp. 115-125. doi:10.1111/j.1365-2036.2008.03847.x.

Shahdadi, H., Balouchi, A., & Shaykh, A. (2017). Comparison of resilience and psychological wellbeing in women with irritable bowel syndrome and normal women. *Mater Sociomed, 29(2),* pp. 105-108. doi: 10.5455/msm.2017.29.105-108

Thompson, S.R., & Dobbins, S. (2018). The applicability of resilience training to the mitigation of trauma-related mental illness in military personnel. *Journal of the American Psychiatric Nurses Association, 24*, pp. 23-34. doi:10.1177/1078390317739957

U.S. Department of Veterans Affairs. (2019). How common is PTSD in adults? Retrieved from https://www.ptsd.va.gov/understand/common/common_adults.asp

Appendices

Appendix A: Approval Letter Department of Veterans Affairs Research and Development Committee

DEPARTMENT OF VETERANS AFFAIRS
RESEARCH AND DEVELOPMENT COMMITTEE
VA Tennessee Valley Healthcare System (626/151)
1310 24th Avenue South
Nashville, TN 37212-2637

DATE: July 25, 2019
FROM: Associate Chief of Staff/Research and Development (151)

SUBJECT: **Approval of New Project Submission**

TO: Kelsey Kent, PhDc
RE: [1359188-1] The Relationship Between Gastrointestinal Disease and PTSD in United States Military Veterans

1. This is your official **APPROVAL** letter. The above referenced *new project submission* has been fully approved by the R&D Committee and all required subcommittees on the dates indicated above. **You are now authorized to begin work on this project.**
2. Please refer to the subcommittee approval memos for details regarding their approval expiration dates. The maximum duration of approval is one year. If exemption has been given by all subcommittees, annual review by the R&D committee will be required **prior to 7/25/2020.**
3. You are reminded that you are responsible for ensuring that all study personnel remain current with all applicable training and credentialing requirements. Non-compliant employees may not work on any projects. Non-compliance by the principal investigator of the requirements or failure to comply with the PI responsibilities listed in *Attachment A* may result in study termination.
4. **You must acknowledge your VA employment and support on all published materials resulting from this study in accordance with VHA Handbook 1200.19.**

Donald H. Rubin, MD.
ACOS for Research

Attachment 1: PI Responsibilities
Attachment 2: Research Integrity Officer Letter/Notification

This electronically generated document serves as official notice to sponsors and others of approval, disapproval or other R&D decisions. Only those individuals who have been granted authority by the institution to create letters on behalf of the R&D are able to do so. A copy of this document has been retained within TVHS IRBNet records. The IRBNet System is fully compliant with the technology requirements for Electronic Records per CFR 21, Part 11, Section 11.10 – Controls for Closed Systems, and the technology requirements for Electronic Signatures per CFR 21, Part 11 Subpart C – Electronic Signatures

Attachment 1: PI Responsibilites

Principal Investigator Responsibilities for the Conduct Research at VA TVHS

Appendix B: Department of Veterans Affairs IRB Exemption Letter

DEPARTMENT OF VETERANS AFFAIRS
INSTITUTIONAL REVIEW BOARD
Tennessee Valley Healthcare System (626/151)
1310 24th Avenue South
Nashville, TN 37212-2637

DATE:	June 27, 2019
TO:	Kelsey Kent, PhDc, Principal Investigator
FROM:	VA TVHS Institutional Review Board Chair (IRB)
SUBJECT:	**DETERMINATION OF EXEMPT STATUS**
PROTOCOL TITLE:	[1359188-1] The Relationship Between Gastrointestinal Disease and PTSD in United States Military Veterans
SUBMISSION TYPE:	New Project
REVIEW TYPE:	Exempt Review
RISK DETERMINATION:	MINIMAL RISK
EFFECTIVE DATE:	June 27, 2019

This research project **may not be initiated** until you have received written confirmation of final approval from the Associated Chief of Staff (ACOS) for Research Service.

The study meets and follows the post-2018 Common Rule requirement.

The TVHS IRB designated reviewer reviewed your application and determined this protocol meets criteria for **exemption** under 38CFR16.104(d) based on the below indicated exemption category number:

- [ ] Category 1
- [ ] Category 2(i)
- [x] Category 3(i)(a)
- [ ] Category 4
- [ ] Category 5
- [ ] Category 6
- [ ] Category 2(ii)
- [ ] Category 3(i)(b)

The following documents were reviewed:

- Form 011/COI - Callaway-Lane (none)
- Form 011/COI - Kent (None)
- Supp L Waiver or Alt of Consent or HIPAA Auth
- Form 002 Cost Impact
- IRB Application/Part 2
- Form 001/Study Personnel Listing

Appendix C: Department of Veterans Affairs Research Safety Committee Exemption Letter

DEPARTMENT OF VETERANS AFFAIRS
RESEARCH SAFETY SUBCOMMITTEE (RSS)
Tennessee Valley Healthcare System (626/151)
1310 24th Avenue South
Nashville, TN 37013

DATE:	June 21, 2019
FROM:	TVHS Research Safety Subcommittee Chair
SUBJECT:	**EXEMPT**
PROTOCOL TITLE:	[1359188-1] The Relationship Between Gastrointestinal Disease and PTSD in United States Military Veterans
TO:	Kelsey Kent, PhDc

1. The TVHS Research Safety Subcommittee has reviewed the above mentioned study **on June 19, 2019 via the exempt administrative process.**
2. The following documents were reviewed/approved with this review:

- Application Form - *Form 006/Research Safety Initial Application (UPDATED: 04/8/2019)
- Conflict of Interest - Other - *Form 011/COI - Callaway-Lane (none) (UPDATED: 05/17/2019)
- Conflict of Interest - Other - *Form 011/COI - Kent (None) (UPDATED: 04/8/2019)
- Other - *Supp L Waiver or Alt of Consent or HIPAA Auth (UPDATED: 05/20/2019)
- Other - *Form 002 Cost Impact (UPDATED: 04/17/2019)
- Other - *IRB Application/Part 2 (UPDATED: 04/8/2019)
- Other - *Form 001/Study Personnel Listing (UPDATED: 04/8/2019)
- Other - *Supp D - Exemption Request (UPDATED: 04/8/2019)
- Other - *UTMB IRB Approval (UPDATED: 04/8/2019)
- Other - *UTMB-Academic Affiliation (UPDATED: 03/4/2019)
- Protocol - *Protocol (UPDATED: 04/8/2019)
- VA - Privacy and Data Security Plan - *VA - Privacy and Data Security Plan (UPDATED: 03/4/2019)
- VA - R&D Request to Review Research Proposal - *VA - R&D Request to Review Research Proposal (UPDATED: 04/8/2019)
- VA TVHS - IRB Application Part 1 - *VA TVHS - IRB Application Part 1 (UPDATED: 04/8/2019)

3. Based on the finding that the research does not use any of the following: substances defined in Title 42 Code of Federal Regulations (CFR) 72.6 as biological hazards; human or non-human cells, cell lines, tissue samples or biological fluids; animals; hazardous chemicals or toxic compressed gases; controlled substances; or ionizing radiation, the project is exempt from annual biosafety review.

Appendix D: Department of Veterans Affairs Waiver of Consent/HIPAA

VA Tennessee Valley Healthcare System
INSTITUTIONAL REVIEW BOARD
Request for Waiver or Alteration of Consent and/or HIPAA Authorization for Study Participation
Supplement L
(Meets Post 2018 Requirements)

Complete this form if you are requesting a waiver or alteration of consent and/or of HIPAA Authorization. Section V can be used to request a waiver for documentation of consent. Note: Waivers and Alterations of Consent are not permitted for FDA-regulated research other than studies of the safety and/or effectiveness of In Vitro Diagnostic Devices.

Principal Investigator: ***K*** [redacted]
IRBNet ID Number: 1359188-1
Study Title: ***The Relationship Between PTSD and Gastrointestinal Disease in U.S. Military Veterans***

I. SECONDARY USE OF COLLECTED IDENTIFIABLE DATA/SPECIMENS FOR WHICH BROAD CONSENT WAS OBTAINED

If an individual provided broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens, waiver of consent is not necessary as the individual has previously provided consent for the use of their identifiable private information or identifiable biospecimens. However, TVHS IRB must determine that broad consent was given and that the proposed use of identifiable private information or identifiable biospecimens is within the scope of the individual's consent.

Please select one of the criteria below:

[X]	**This research does NOT include the secondary use of stored or maintained identifiable data/specimens for which broad consent was obtained. Skip to Section II.** 38 CFR 46.116(a)(1) through (4), (a)(6), and (d)
[ ]	**This research DOES include the secondary use of stored or maintained identifiable data/specimens for which broad consent was obtained/given Please provide the following:** ☐ **Enter the IRBNet # of the study/project or provide a copy of the IRB Approval Letter:** ☐ **PI's Name:** ☐ **Include copy of the current IRB Approved Broad Consent Form used in the above study** **Skip to Section IV.** 38 CFR 46.116(a)(1) through (4), (a)(6), and (d)

II REQUEST FOR WAIVER OF INFORMED CONSENT

The TVHS IRB may waive or alter the requirement to obtain consent from research subjects when the investigator justifies, and the IRB agrees, that specific criteria have been met. Please explain how your research study meets these criteria by answering each of the following questions.
The elements of consent are described at the end of this form for your reference.

Please select one of the criteria below:

[ ]	**38 CFR 46.116(e)** **To request waiver based on this criteria Both must be true:** ✓ The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii)

	procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; ***Please explain:*** ✓ The research could not practicably be carried out without the waiver or alteration. ***Please explain:***
X	**38 CFR 46.116(f)** **To request waiver based on this criteria all must be true (select boxes below and explain):** ✓ The research involves no more than minimal risk. ***Please explain: No experimentation, using de-identified data ONLY for retrospective, correlational study utilizing big data*** ✓ The research could not be carried out without the waiver or alteration. ***Please explain: Big data, expecting several million participants, with only de-identified data used*** ✓ If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format. ***Please explain: N/A – ONLY de-identified data required*** ✓ The waiver or alteration will not adversely affect the rights and welfare of the subjects. ***Please explain: The P.I. and other staff will not be able to identify the subjects, maintaining their right to privacy.*** ✓ Whenever appropriate, the subjects or legally authorized representative will be provided with additional pertinent information after participation. ***Please explain: N/A, subjects will not be able to be identified***

III. REQUEST FOR ALTERATION OF CONSENT

An IRB may approve a consent procedure that omits some, or alters some or all, of the basic elements of informed consent (listed in table at the end of the form) provided one of the criteria in section II are satisfied. An IRB may not omit or alter any of the general requirements of informed consent (i.e. obtaining legally effective informed consent, seeking consent from subjects under circumstance that provide sufficient opportunity to discuss and consider participation without coercion, providing information in a language understandable to subjects, and or providing information that a reasonable person would want to have to make an informed decision about participation in a study). The General Elements of consent are listed at the end of this form for your reference.

Describe which element(s) of consent you wish to alter or exclude and why?

If applicable, explain:

IV. REQUEST FOR WAIVER OR ALTERATION OF HIPPA

The TVHS IRB may waive or alter the requirement to obtain authorization from research subjects in order to use or disclose their protected health information (PHI), provided that the PHI used or disclosed is the minimum necessary to achieve the research purpose; and the investigator justifies, and the IRB agrees, that specific criteria have been met. Please explain how your research study meets the criteria by

answering each of the following questions. The elements of PHI are described at the end of this form for your reference.

a) If this is a request for an Alteration of HIPAA, describe the proposed alteration and the rationale:

Explain: N/A

b) Describe the PHI needed to conduct the study, the source of the information, and justify why it is the minimum necessary to achieve the research purpose:

Explain: No protected health information required. Requested information includes diagnosis codes (ICD-9 & ICD-10), ethnicity, age (NO date of birth), period of service, and birth sex.

c) Describe how the use or disclosure of PHI involves no more than minimal risk to the privacy of the subjects in this study:

Explain: Minimal risk as data will not include any HIPPA identifiers. Researchers will NOT be able to connect data with any specific participant or patient.

d) Describe your plan to protect PHI from improper use and disclosure:
Note:

Explain: All data will be stored on a password-protected, secure, VA-research drive. Only the PI will have access to this drive. NO HIPPA-identifiers will be included in this study.

e) Describe your plan to destroy the identifiers, include how and when:

Explain: Will NOT collect any identifiers.

f) Describe why it is not practicable to obtain Authorization from the subjects:

Explain: Subjects will not be known to the researcher, so will not be possible to contact them for consent.

g) Describe why the research cannot be done without the PHI:

Explain: No PHI is requested for this study.

YES (Required)	NO	
X		***h)*** *I attest that the requested information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the requested information would be permitted by the Privacy Rule.*

V. REQUEST FOR WAIVER OF DOCUMENTATION OF THE CONSENT PROCESS

This section applies if verbal consent or other types of consent will be obtained from the participant, but the VA Research Consent Form will not use to document the consent process. **Otherwise leave blank.**
NOTE: In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

If applying for waiver of documentation of the consent process, chose criteria below:

☐ The research involves no more than minimal risk; and involves only procedures that do not require written consent outside of research.
Please explain:

☐ The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality.
Please explain:

☐ If the subjects or legally authorized representatives are members of a distinct cultural

	group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained. ***Please explain:***
Explain how, in the absence of signed written consent forms, consent will be documented, e.g. tape recordings, videos, chart notes, etc.	

VA Tennessee Valley Healthcare System
Institutional Review Board
Review and Determination by IRB Chairman or Designee

Waivers:
- [X] Informed Consent Waived[1]
- [X] HIPAA Authorization Waived[2]
- [ ] Documentation of Consent Waived[3] (Note: Waiving documentation of consent does NOT eliminate the requirement for informed consent)

IRB Determination:
- [X] Approved
- [ ] Approved Pending minor modification
- [ ] Deferred
- [ ] Denied – does not meet criteria for waiver

- [X] The use or disclosure of the requested information involves no more than a minimal risk to the privacy of individuals based on, at least, the presence of the following elements: adequate plan to protect identifiers from improper use and disclosure; adequate plan to destroy identifiers at earliest opportunity; and adequate written assurance that identifiers will not be reused or disclosed.
- [X] The research could not practicably be conducted without the waiver or alteration; and
- [X] If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format
- [X] The research could not practicably be conducted without access to and use of the requested information.
- [X] The alteration or waiver will not adversely affect the privacy rights and welfare of the individuals.
- [X] Whenever appropriate, the subjects or legally authorized representative will be provided with additional pertinent information after participation.

Signature of IRB Chairman (or designee)

6/27/2019
Date Waiver Approved

[1] The requested Waiver of Informed Consent/Alteration of the Informed Consent Process has been granted in accordance with the requirements set forth in 38 CFR 16.116(f) and 45 CFR 46.116(f).
[2] The approval of the waiver of Consent/HIPAA authorization satisfies the following criteria based on the regulatory requirements established in 45CFR 164.512(i)(2).
[3] The requested Waiver of Documentation of Informed Consent has been granted in accordance with the requirements set forth in 38 CFR 16.117(c) and 45 CFR 46.117(c).

Appendix E: University of Texas Medical Branch IRB Determination Letter

utmb Health

Working together to work wonders.™

Institutional Review Board
301 University Blvd.
Galveston, TX 77555-0158
Submission Page

26-Mar-2019

MEMORANDUM

TO: Kelsey Kent
Grad School Biomedical Science GSBS9999

FROM: Vicki McNamara
IRB Staff

RE: IRB Staff Review
Not Human Subjects Research Determination

IRB Number: IRB #: 19-0039

TITLE: The Relationship Between Post-Traumatic Stress Disorder and Gastrointestinal Disease in United States Military Veterans

The UTMB Institutional Review Board (IRB) Chairman or designee reviewed the above referenced project on **26-Mar-2019** and determined the procedures involved do not meet the definition of, "research with human subjects" as defined by both the Office of Human Research Protection regulations at 45 CFR 46.102(d)(f) and the FDA regulations at 21 CFR 56.

If the goals and/or activities of the project change, or if new activities are proposed, please contact the IRB office so that we may determine whether or not the revised plan involves research with human subjects and would then require IRB review.

If you haveany questions, please do not hesitate to contact the IRB office via email at IRB@utmb.edu.

Additional Information

PI is receiving de-identified data and will not be able to link the data back to any subject

Appendix F: Microsoft SQL Code to Create Table for One Year of Data

```
use ORD_Kent_201908062D;
go
if object_id('tempdb..#DiagnosticCodes', 'U') is not null drop table #DiagnosticCodes;
if object_id('tempdb..#Staging', 'U') is not null drop table #Staging;
if object_id('tempdb..#MentalIllness', 'U') is not null drop table #MentalIllness;
declare
        @start_date_inclusive datetime2
      , @end_date_exclusive datetime2
;
set @start_date_inclusive = '1/1/2015';
set @end_date_exclusive = '1/1/2016';
create table #DiagnosticCodes(
        ICDSID int not null primary key
      , ICDCode varchar(50) not null
      , ICDDescription varchar(100) null
);
create table #Staging (
        VisitBeginDate date not null
      , VisitEndDate date not null
      , PatientICN varchar(50) not null primary key
      , Age numeric(18,0) null
      , Ethnicity varchar(50) null
      , Gender char(1) null
      , PeriodOfService varchar(50) null
      , VisitCount_PTSD int not null default 0
      , VisitCount_GERD int not null default 0
      , VisitCount_PepticUlcerDisease int not null default 0
      , VisitCount_FunctionalDyspepsia int not null default 0
      , VisitCount_Crohns int not null default 0
      , VisitCount_UlcerativeColitis int not null default 0
      , VisitCount_DiverticularCisease int not null default 0
      , VisitCount_Constipation int not null default 0
      , VisitCount_IrritableBowelSyndrome int not null default 0
```

```
34              , VisitCount_NauseaVomiting int not null default 0
35              , MDD int not null default 0
36              , Bipolar int not null default 0
37              , Anxiety int not null default 0
38              , Psychosis int not null default 0
39              , SA int not null default 0
40              , Dementia int not null default 0
41              , PDs int not null default 0
42  );
43  create table #MentalIllness(
44                PatientICN varchar(50) not null
45              , ICDCode varchar(50) not null
46  );
47  with diagnostic_codes as (
48              select
49                        c.ICD9SID as ICDSID
50                      , c.ICD9Code as ICDCode
51                      , d.ICD9Description as ICDDescription
52              from CDWWork.Dim.ICD9 c
53                      join CDWWork.Dim.ICD9DescriptionVersion d
54                              on c.ICD9SID = d.ICD9SID
55                              and d.CurrentVersionFlag = 'Y'
56              union  --not using union all here to make sure we do not get dups
57              select
58                        c.ICD10SID as ICDSID
59                      , c.ICD10Code as ICDCode
60                      , d.ICD10Description as ICDDescription
61              from CDWWork.Dim.ICD10 c
62                      join CDWWork.Dim.ICD10DescriptionVersion d
63                              on c.ICD10SID = d.ICD10SID
64                              and d.CurrentVersionFlag = 'Y'
65  )
66  insert #DiagnosticCodes(ICDSID, ICDCode, ICDDescription)
```

```
select
        ICDSID
      , ICDCode
      , ICDDescription
from diagnostic_codes icd
where
      icd.ICDCode in ('309.81','F43.10','F43.11','F43.12') --this specific list
      or icd.ICDCode in ('530.81','K21.0','K21.9') --this specific list
      or left(icd.ICDCode,3) = '533' or left(icd.ICDCode,3) = 'K27' --all subcodes of 533 and K27
      or icd.ICDCode in ('536.8') or left(icd.ICDCode,3) = 'K30' --536.8 specifically plus all subcodes of K30
      or left(icd.ICDCode,3) = '555' or left(icd.ICDCode,3) = 'K50' --all subcodes of 555 and K50
      or left(icd.ICDCode,3) = '556' or left(icd.ICDCode,3) = 'K51' --all subcodes of 556 and K51
      or left(icd.ICDCode,3) = '562' or left(icd.ICDCode,3) = 'K57' --all subcodes of 562 and K57
      or icd.ICDCode in ('564.00', '564.01', '564.02', '564.09', 'K59.04') --this specific list
      or icd.ICDCode in ('564.1') or left(icd.ICDCode,3) = 'K58' --564.1 specifically plus all subcodes of K58
      or left(icd.ICDCode,3) = 'R11' or left(icd.ICDCode,3) = '787' --all subcodes of R11 and 787
;
with patient_info as (
      select
            p.PatientICN
          , p.Age
          , p.Gender
          , p.PeriodOfService
          , ethnic.Ethnicity
          , row_number() over (partition by p.PatientICN order by v.VisitDateTime desc) as OrderOfRecency
      from Src.Outpat_VDiagnosis v
            join Src.SPatient_SPatient as p
                  on v.PatientSID = p.PatientSID
            join #DiagnosticCodes icd  --limit the patient scope to only those conditions in scope
                  on (v.ICD9SID = icd.ICDSID or v.ICD10SID = icd.ICDSID)
            left join Src.PatSub_PatientEthnicity ethnic
```

```
101                             on p.PatientSID = ethnic.PatientSID
102             where v.VisitDateTime >= @start_date_inclusive and v.VisitDateTime < @end_date_exclusive
103                     and p.PatientICN is not null
104 )
105 insert #Staging(
106               VisitBeginDate
107             , VisitEndDate
108             , PatientICN
109             , Age
110             , Ethnicity
111             , Gender
112             , PeriodOfService
113 )
114 select
115               cast(@start_date_inclusive as date)
116             , dateadd(day, -1, cast(@end_date_exclusive as date))
117             , PatientICN
118             , Age
119             , Ethnicity
120             , Gender
121             , PeriodOfService
122 from patient_info
123 where OrderOfRecency = 1 --retrieve the most recent Age, Gender, Service data
124 /************************************************************
125 PTSD: F43.10, F43.11, F43.12, or 309.81
126 ************************************************************/
127 update stg
128 set VisitCount_PTSD = x.NbrOfVisits
129 from #Staging stg
130             join (
131                     select
132                             p.PatientICN
133                       , count(*) as NbrOfVisits
```

```
134                     from Src.Outpat_VDiagnosis v
135                             join Src.SPatient_SPatient as p
136                                     on v.PatientSID = p.PatientSID
137                             join #DiagnosticCodes icd
138                                     on (v.ICD9SID = icd.ICDSID or v.ICD10SID = icd.ICDSID)
139                     where v.VisitDateTime >= @start_date_inclusive and v.VisitDateTime <
140 @end_date_exclusive
141                             and icd.ICDCode in ('309.81','F43.10','F43.11','F43.12')
142                     group by p.PatientICN
143             ) x
144                     on stg.PatientICN = x.PatientICN
145 ;
146 /************************************************************
147 GERD - 530.81, K21.0, or K21.9
148 ************************************************************/
149 update stg
150 set VisitCount_GERD = x.NbrOfVisits
151 from #Staging stg
152             join (
153                     select
154                             p.PatientICN
155                      , count(*) as NbrOfVisits
156                     from Src.Outpat_VDiagnosis v
157                             join Src.SPatient_SPatient as p
158                                     on v.PatientSID = p.PatientSID
159                             join #DiagnosticCodes icd
160                                     on (v.ICD9SID = icd.ICDSID or v.ICD10SID = icd.ICDSID)
161                     where v.VisitDateTime >= @start_date_inclusive and v.VisitDateTime <
162 @end_date_exclusive
163                             and icd.ICDCode in ('530.81','K21.0','K21.9')
164                     group by p.PatientICN
165             ) x
166                     on stg.PatientICN = x.PatientICN
167 ;
```

```
/************************************************************
Peptic Ulcer Disease - 533, K27.0 (and all sub-codes of K27)
Peptic Ulcer disease needs subcodes of 533.
************************************************************/
update stg
set VisitCount_PepticUlcerDisease = x.NbrOfVisits
from #Staging stg
	join (
		select
			p.PatientICN
		  , count(*) as NbrOfVisits
		from Src.Outpat_VDiagnosis v
			join Src.SPatient_SPatient as p
				on v.PatientSID = p.PatientSID
			join #DiagnosticCodes icd
				on (v.ICD9SID = icd.ICDSID or v.ICD10SID = icd.ICDSID)
		where v.VisitDateTime >= @start_date_inclusive and v.VisitDateTime <
@end_date_exclusive
			and (left(icd.ICDCode,3) = '533' or left(icd.ICDCode,3) = 'K27')
		group by p.PatientICN
	) x
		on stg.PatientICN = x.PatientICN
;
/************************************************************
Functional Dyspepsia - 536.8 or K30
************************************************************/
update stg
set VisitCount_Dyspepsia = x.NbrOfVisits
from #Staging stg
	join (
		select
			p.PatientICN
		  , count(*) as NbrOfVisits
		from Src.Outpat_VDiagnosis v
```

```
                join Src.SPatient_SPatient as p
                        on v.PatientSID = p.PatientSID
                join #DiagnosticCodes icd
                        on (v.ICD9SID = icd.ICDSID or v.ICD10SID = icd.ICDSID)
        where v.VisitDateTime >= @start_date_inclusive and v.VisitDateTime <
@end_date_exclusive
                and (icd.ICDCode in ('536.8') or left(icd.ICDCode,3) = 'K30')
        group by p.PatientICN
    ) x
        on stg.PatientICN = x.PatientICN
;
/*************************************************************
Crohn's - 555, K50 (and all subcodes of K50)
Crohn’s needs subcodes of 555.
*************************************************************/
update stg
set VisitCount_Crohns = x.NbrOfVisits
from #Staging stg
    join (
        select
            p.PatientICN
          , count(*) as NbrOfVisits
        from Src.Outpat_VDiagnosis v
            join Src.SPatient_SPatient as p
                on v.PatientSID = p.PatientSID
            join #DiagnosticCodes icd
                on (v.ICD9SID = icd.ICDSID or v.ICD10SID = icd.ICDSID)
        where v.VisitDateTime >= @start_date_inclusive and v.VisitDateTime <
@end_date_exclusive
            and (left(icd.ICDCode,3) = '555' or left(icd.ICDCode,3) = 'K50')
        group by p.PatientICN
    ) x
        on stg.PatientICN = x.PatientICN
;
```

```
/*************************************************************
Ulcerative colitis - 556, K51 (and all subcodes of K51)
Ulcerative Colitis of 556
*************************************************************/
update stg
set VisitCount_UlcerativeColitis = x.NbrOfVisits
from #Staging stg
	join (
		select
			p.PatientICN
		  , count(*) as NbrOfVisits
		from Src.Outpat_VDiagnosis v
			join Src.SPatient_SPatient as p
				on v.PatientSID = p.PatientSID
			join #DiagnosticCodes icd
				on (v.ICD9SID = icd.ICDSID or v.ICD10SID = icd.ICDSID)
		where v.VisitDateTime >= @start_date_inclusive and v.VisitDateTime <
@end_date_exclusive
			and (left(icd.ICDCode,3) = '556' or left(icd.ICDCode,3) = 'K51')
		group by p.PatientICN
	) x
		on stg.PatientICN = x.PatientICN
;
/*************************************************************
Diverticular Disease - 562 or K57 (and all subcodes)
Diverticular disease of 562.
*************************************************************/
update stg
set VisitCount_DiverticularCisease = x.NbrOfVisits
from #Staging stg
	join (
		select
			p.PatientICN
		  , count(*) as NbrOfVisits
```

```
270                     from Src.Outpat_VDiagnosis v
271                             join Src.SPatient_SPatient as p
272                                     on v.PatientSID = p.PatientSID
273                             join #DiagnosticCodes icd
274                                     on (v.ICD9SID = icd.ICDSID or v.ICD10SID = icd.ICDSID)
275                     where v.VisitDateTime >= @start_date_inclusive and v.VisitDateTime <
276 @end_date_exclusive
277                             and (left(icd.ICDCode,3) = '562' or left(icd.ICDCode,3) = 'K57')
278                     group by p.PatientICN
279             ) x
280                     on stg.PatientICN = x.PatientICN
281 ;
282 /*************************************************************
283 Constipation - 564.0 or K59.04
284 Constipation needs subcodes of 564.0 (654.00, 564.01, 564.02, & 564.09)
285 *************************************************************/
286 update stg
287 set VisitCount_Constipation = x.NbrOfVisits
288 from #Staging stg
289             join (
290                     select
291                             p.PatientICN
292                       , count(*) as NbrOfVisits
293                     from Src.Outpat_VDiagnosis v
294                             join Src.SPatient_SPatient as p
295                                     on v.PatientSID = p.PatientSID
296                             join #DiagnosticCodes icd
297                                     on (v.ICD9SID = icd.ICDSID or v.ICD10SID = icd.ICDSID)
298                     where v.VisitDateTime >= @start_date_inclusive and v.VisitDateTime <
299 @end_date_exclusive
300                             and icd.ICDCode in ('564.00', '564.01', '564.02', '564.09', 'K59.04')
301                     group by p.PatientICN
302             ) x
303                     on stg.PatientICN = x.PatientICN
```

```
;
/*************************************************************
Irritable Bowel Syndrome - 564.1 or K58 (and all subcodes)
*************************************************************/
update stg
set VisitCount_IrritableBowelSyndrome = x.NbrOfVisits
from #Staging stg
	join (
		select
			p.PatientICN
		  , count(*) as NbrOfVisits
		from Src.Outpat_VDiagnosis v
			join Src.SPatient_SPatient as p
				on v.PatientSID = p.PatientSID
			join #DiagnosticCodes icd
				on (v.ICD9SID = icd.ICDSID or v.ICD10SID = icd.ICDSID)
		where v.VisitDateTime >= @start_date_inclusive and v.VisitDateTime <
@end_date_exclusive
			and (icd.ICDCode in ('564.1') or left(icd.ICDCode,3) = 'K58')
		group by p.PatientICN
	) x
		on stg.PatientICN = x.PatientICN
;
/*************************************************************
Nausea/vomiting - R11
Also added to Nausea Vomiting was the 787.0, and it also needs subcodes.
*************************************************************/
update stg
set VisitCount_NauseaVomiting = x.NbrOfVisits
from #Staging stg
	join (
		select
			p.PatientICN
		  , count(*) as NbrOfVisits
```

```
                from Src.Outpat_VDiagnosis v
                        join Src.SPatient_SPatient as p
                                on v.PatientSID = p.PatientSID
                        join #DiagnosticCodes icd
                                on (v.ICD9SID = icd.ICDSID or v.ICD10SID = icd.ICDSID)
                where v.VisitDateTime >= @start_date_inclusive and v.VisitDateTime <
@end_date_exclusive
                        and (left(icd.ICDCode,3) = 'R11' or left(icd.ICDCode,3) = '787')
                group by p.PatientICN
        ) x
                on stg.PatientICN = x.PatientICN
;
/************************************************************
Secondary mental illness: 290-319, F01-F42, F43.0, F43.2, F45-99
************************************************************/
with patients_with_mental_illness_diag as (
        select distinct
                 p.PatientICN
                , icd.ICDCode
        from Src.Outpat_VDiagnosis v
                join Src.SPatient_SPatient as p
                        on v.PatientSID = p.PatientSID
                join #Staging stg
                        on p.PatientICN = stg.PatientICN
                join (
                        select
                                 c.ICD9SID as ICDSID
                                , c.ICD9Code as ICDCode
                                , d.ICD9Description as ICDDescription
                        from CDWWork.Dim.ICD9 c
                                join CDWWork.Dim.ICD9DescriptionVersion d
                                        on c.ICD9SID = d.ICD9SID
                                        and d.CurrentVersionFlag = 'Y'
                        union  --not using union all here to make sure we do not get dups
```

```
372                                 select
373                                         c.ICD10SID as ICDSID
374                                         , c.ICD10Code as ICDCode
375                                         , d.ICD10Description as ICDDescription
376                                 from CDWWork.Dim.ICD10 c
377                                         join CDWWork.Dim.ICD10DescriptionVersion d
378                                                 on c.ICD10SID = d.ICD10SID
379                                                 and d.CurrentVersionFlag = 'Y'
380                         ) icd
381                                 on (v.ICD9SID = icd.ICDSID or v.ICD10SID = icd.ICDSID)
382             where v.VisitDateTime >= @start_date_inclusive and v.VisitDateTime < @end_date_exclusive
383                         and (
384                                 (left(icd.ICDCode,3) between '290' and '319')
385                                 or (left(icd.ICDCode,1) = 'F' and substring(icd.ICDCode,2,2) between '01' and
386 '42')
387                                 or icd.ICDCode = 'F43.0'
388                                 or icd.ICDCode = 'F43.2'
389                                 or (left(icd.ICDCode,1) = 'F' and substring(icd.ICDCode,2,2) between '45' and
390 '99')
391                         )
392 )
393 insert #MentalIllness(PatientICN, ICDCode)
394 select PatientICN, ICDCode from patients_with_mental_illness_diag;
395 /*************************************************************
396 Depressive Disorders (MDD) 296.2x, 296.3x, 311.x F32-F33.x
397 *************************************************************/
398 update stg
399 set MDD = 1
400 from #Staging stg
401             join #MentalIllness x
402                         on stg.PatientICN = x.PatientICN
403 where left(x.ICDCode,5) = '296.2'
404             or left(x.ICDCode,5) = '296.3'
405             or left(x.ICDCode,3) = '311'
```

```
406             or left(x.ICDCode,3) = 'F32'
407             or left(x.ICDCode,3) = 'F33'
408     ;
409     /************************************************************
410     Bipolar Disorders (Bipolar) 296.0x, 296.1x, 296.4x - 296.8x F30-F31.x
411     ************************************************************/
412     update stg
413     set Bipolar = 1
414     from #Staging stg
415             join #MentalIllness x
416                     on stg.PatientICN = x.PatientICN
417     where left(x.ICDCode,5) = '296.0'
418             or left(x.ICDCode,5) = '296.1'
419             or left(x.ICDCode,5) = '296.4'
420             or left(x.ICDCode,5) = '296.5'
421             or left(x.ICDCode,5) = '296.6'
422             or left(x.ICDCode,5) = '296.7'
423             or left(x.ICDCode,5) = '296.8'
424             or left(x.ICDCode,3) = 'F30'
425             or left(x.ICDCode,3) = 'F31'
426     ;
427     /************************************************************
428     Anxiety disorders (Anxiety) 300.x F40-F45.x
429     ************************************************************/
430     update stg
431     set Anxiety = 1
432     from #Staging stg
433             join #MentalIllness x
434                     on stg.PatientICN = x.PatientICN
435     where left(x.ICDCode,3) = '300'
436             or left(x.ICDCode,3) = 'F40'
437             or left(x.ICDCode,3) = 'F41'
438             or left(x.ICDCode,3) = 'F42'
```

```
439             or left(x.ICDCode,3) = 'F43'
440             or left(x.ICDCode,3) = 'F44'
441             or left(x.ICDCode,3) = 'F45'
442     ;
443     /************************************************************
444     Psychotic disorders (Psychosis) 295.x, 297.x, 298.x F20-F29.x
445     ************************************************************/
446     update stg
447     set Psychosis = 1
448     from #Staging stg
449             join #MentalIllness x
450                     on stg.PatientICN = x.PatientICN
451     where left(x.ICDCode,3) = '295'
452             or left(x.ICDCode,3) = '297'
453             or left(x.ICDCode,3) = '298'
454             or left(x.ICDCode,3) = 'F20'
455             or left(x.ICDCode,3) = 'F21'
456             or left(x.ICDCode,3) = 'F22'
457             or left(x.ICDCode,3) = 'F23'
458             or left(x.ICDCode,3) = 'F24'
459             or left(x.ICDCode,3) = 'F25'
460             or left(x.ICDCode,3) = 'F26'
461             or left(x.ICDCode,3) = 'F27'
462             or left(x.ICDCode,3) = 'F28'
463             or left(x.ICDCode,3) = 'F29'
464     ;
465     /************************************************************
466     Substance Abuse (SA) 303 - 305.x F10-F19.x
467     ************************************************************/
468     update stg
469     set SA = 1
470     from #Staging stg
471             join #MentalIllness x
```

```
472                         on stg.PatientICN = x.PatientICN
473     where left(x.ICDCode,3) = '303'
474             or left(x.ICDCode,3) = '304'
475             or left(x.ICDCode,3) = '305'
476             or left(x.ICDCode,3) = 'F10'
477             or left(x.ICDCode,3) = 'F11'
478             or left(x.ICDCode,3) = 'F12'
479             or left(x.ICDCode,3) = 'F13'
480             or left(x.ICDCode,3) = 'F14'
481             or left(x.ICDCode,3) = 'F15'
482             or left(x.ICDCode,3) = 'F16'
483             or left(x.ICDCode,3) = 'F17'
484             or left(x.ICDCode,3) = 'F18'
485             or left(x.ICDCode,3) = 'F19'
486     ;
487     /************************************************************
488     Dementias (Dementia) 290.x F01-F03.x
489     ************************************************************/
490     update stg
491     set Dementia = 1
492     from #Staging stg
493             join #MentalIllness x
494                     on stg.PatientICN = x.PatientICN
495     where left(x.ICDCode,3) = '290'
496             or left(x.ICDCode,3) = 'F01'
497             or left(x.ICDCode,3) = 'F02'
498             or left(x.ICDCode,3) = 'F03'
499     ;
500     /************************************************************
501     Personality Disorders (PDs) 301.x F60-F69.x
502     ************************************************************/
503     update stg
504     set PDs = 1
```

```
505  from #Staging stg
506          join #MentalIllness x
507              on stg.PatientICN = x.PatientICN
508  where left(x.ICDCode,3) = '301'
509          or left(x.ICDCode,3) = 'F60'
510          or left(x.ICDCode,3) = 'F61'
511          or left(x.ICDCode,3) = 'F62'
512          or left(x.ICDCode,3) = 'F63'
513          or left(x.ICDCode,3) = 'F64'
514          or left(x.ICDCode,3) = 'F65'
515          or left(x.ICDCode,3) = 'F66'
516          or left(x.ICDCode,3) = 'F67'
517          or left(x.ICDCode,3) = 'F68'
518          or left(x.ICDCode,3) = 'F69'
519  ;
520  select *
521  --into Kelsey_2015
522  from #Staging;
523  if object_id('tempdb..#DiagnosticCodes', 'U') is not null drop table #DiagnosticCodes;
524  if object_id('tempdb..#Staging', 'U') is not null drop table #Staging;
525  if object_id('tempdb..#MentalIllness', 'U') is not null drop table #MentalIllness;
526  go
527
```

Appendix G: Microsoft SQL Code to Combine Tables 1999-2019

```
use ORD_Kent_201908062D;
go
create table Kent_AllYears (
        PatientICN varchar(50) not null primary key
      , Age numeric(18,0) null
      , Ethnicity varchar(50) null
      , Gender char(1) null
      , PeriodOfService varchar(50) null
      , PTSD int not null default 0
      , GERD int not null default 0
      , PepticUlcerDisease int not null default 0
      , FunctionalDyspepsia int not null default 0
      , Crohns int not null default 0
      , UlcerativeColitis int not null default 0
      , DiverticularDisease int not null default 0
      , Constipation int not null default 0
      , IrritableBowelSyndrome int not null default 0
      , NauseaVomiting int not null default 0
      , MDD int not null default 0
      , Bipolar int not null default 0
      , Anxiety int not null default 0
      , Psychosis int not null default 0
      , SA int not null default 0
      , Dementia int not null default 0
      , PDs int not null default 0
);
go
insert Kent_AllYears(PatientICN) select PatientICN from Kent_1999;
go
insert Kent_AllYears(PatientICN) select PatientICN from Kent_2000 where PatientICN not in (select
PatientICN from Kent_AllYears);
go
insert Kent_AllYears(PatientICN) select PatientICN from Kent_2001 where PatientICN not in (select
PatientICN from Kent_AllYears);
```

```
go
insert Kent_AllYears(PatientICN) select PatientICN from Kent_2002 where PatientICN not in (select
PatientICN from Kent_AllYears);
go
insert Kent_AllYears(PatientICN) select PatientICN from Kent_2003 where PatientICN not in (select
PatientICN from Kent_AllYears);
go
insert Kent_AllYears(PatientICN) select PatientICN from Kent_2004 where PatientICN not in (select
PatientICN from Kent_AllYears);
go
insert Kent_AllYears(PatientICN) select PatientICN from Kent_2005 where PatientICN not in (select
PatientICN from Kent_AllYears);
go
insert Kent_AllYears(PatientICN) select PatientICN from Kent_2006 where PatientICN not in (select
PatientICN from Kent_AllYears);
go
insert Kent_AllYears(PatientICN) select PatientICN from Kent_2007 where PatientICN not in (select
PatientICN from Kent_AllYears);
go
insert Kent_AllYears(PatientICN) select PatientICN from Kent_2008 where PatientICN not in (select
PatientICN from Kent_AllYears);
go
insert Kent_AllYears(PatientICN) select PatientICN from Kent_2009 where PatientICN not in (select
PatientICN from Kent_AllYears);
go
insert Kent_AllYears(PatientICN) select PatientICN from Kent_2010 where PatientICN not in (select
PatientICN from Kent_AllYears);
go
insert Kent_AllYears(PatientICN) select PatientICN from Kent_2011 where PatientICN not in (select
PatientICN from Kent_AllYears);
go
insert Kent_AllYears(PatientICN) select PatientICN from Kent_2012 where PatientICN not in (select
PatientICN from Kent_AllYears);
go
insert Kent_AllYears(PatientICN) select PatientICN from Kent_2013 where PatientICN not in (select
PatientICN from Kent_AllYears);
go
```

```
insert Kent_AllYears(PatientICN) select PatientICN from Kent_2014 where PatientICN not in (select
PatientICN from Kent_AllYears);

go

insert Kent_AllYears(PatientICN) select PatientICN from Kent_2015 where PatientICN not in (select
PatientICN from Kent_AllYears);

go

insert Kent_AllYears(PatientICN) select PatientICN from Kent_2016 where PatientICN not in (select
PatientICN from Kent_AllYears);

go

insert Kent_AllYears(PatientICN) select PatientICN from Kent_2017 where PatientICN not in (select
PatientICN from Kent_AllYears);

go

insert Kent_AllYears(PatientICN) select PatientICN from Kent_2018 where PatientICN not in (select
PatientICN from Kent_AllYears);

go

insert Kent_AllYears(PatientICN) select PatientICN from Kent_2019 where PatientICN not in (select
PatientICN from Kent_AllYears);

go

update x

set

        Age = y.Age

      , Ethnicity = y.Ethnicity

      , Gender = y.Gender

      , PeriodOfService = y.PeriodOfService

      , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end

      , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end

      , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
x.PepticUlcerDisease end

      , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
x.FunctionalDyspepsia end

      , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end

      , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
end

      , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
x.DiverticularDisease end

      , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end

      , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
x.IrritableBowelSyndrome end
```

```
110             , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
111     end
112             , MDD = case when y.MDD > 0 then 1 else x.MDD end
113             , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
114             , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
115             , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
116             , SA = case when y.SA > 0 then 1 else x.SA end
117             , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
118             , PDs = case when y.PDs > 0 then 1 else x.PDs end
119     from Kent_AllYears x
120             join Kent_1999 y
121                     on x.PatientICN = y.PatientICN
122     ;
123     go
124     update x
125     set
126               Age = y.Age
127             , Ethnicity = y.Ethnicity
128             , Gender = y.Gender
129             , PeriodOfService = y.PeriodOfService
130             , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
131             , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
132             , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
133     x.PepticUlcerDisease end
134             , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
135     x.FunctionalDyspepsia end
136             , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
137             , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
138     end
139             , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
140     x.DiverticularDisease end
141             , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
142             , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
143     x.IrritableBowelSyndrome end
144             , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
145     end
```

```
146             , MDD = case when y.MDD > 0 then 1 else x.MDD end
147             , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
148             , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
149             , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
150             , SA = case when y.SA > 0 then 1 else x.SA end
151             , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
152             , PDs = case when y.PDs > 0 then 1 else x.PDs end
153     from Kent_AllYears x
154             join Kent_2000 y
155                     on x.PatientICN = y.PatientICN
156     ;
157     go
158     update x
159     set
160               Age = y.Age
161             , Ethnicity = y.Ethnicity
162             , Gender = y.Gender
163             , PeriodOfService = y.PeriodOfService
164             , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
165             , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
166             , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
167     x.PepticUlcerDisease end
168             , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
169     x.FunctionalDyspepsia end
170             , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
171             , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
172     end
173             , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
174     x.DiverticularDisease end
175             , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
176             , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
177     x.IrritableBowelSyndrome end
178             , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
179     end
180             , MDD = case when y.MDD > 0 then 1 else x.MDD end
181             , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
```

```
182             , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
183             , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
184             , SA = case when y.SA > 0 then 1 else x.SA end
185             , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
186             , PDs = case when y.PDs > 0 then 1 else x.PDs end
187     from Kent_AllYears x
188             join Kent_2001 y
189                     on x.PatientICN = y.PatientICN
190     ;
191     go
192     update x
193     set
194               Age = y.Age
195             , Ethnicity = y.Ethnicity
196             , Gender = y.Gender
197             , PeriodOfService = y.PeriodOfService
198             , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
199             , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
200             , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
201     x.PepticUlcerDisease end
202             , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
203     x.FunctionalDyspepsia end
204             , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
205             , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
206     end
207             , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
208     x.DiverticularDisease end
209             , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
210             , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
211     x.IrritableBowelSyndrome end
212             , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
213     end
214             , MDD = case when y.MDD > 0 then 1 else x.MDD end
215             , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
216             , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
217             , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
```

```
218             , SA = case when y.SA > 0 then 1 else x.SA end
219             , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
220             , PDs = case when y.PDs > 0 then 1 else x.PDs end
221     from Kent_AllYears x
222             join Kent_2002 y
223                     on x.PatientICN = y.PatientICN
224     ;
225     go
226     update x
227     set
228               Age = y.Age
229             , Ethnicity = y.Ethnicity
230             , Gender = y.Gender
231             , PeriodOfService = y.PeriodOfService
232             , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
233             , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
234             , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
235     x.PepticUlcerDisease end
236             , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
237     x.FunctionalDyspepsia end
238             , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
239             , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
240     end
241             , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
242     x.DiverticularDisease end
243             , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
244             , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
245     x.IrritableBowelSyndrome end
246             , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
247     end
248             , MDD = case when y.MDD > 0 then 1 else x.MDD end
249             , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
250             , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
251             , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
252             , SA = case when y.SA > 0 then 1 else x.SA end
253             , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
```

```
254             , PDs = case when y.PDs > 0 then 1 else x.PDs end
255     from Kent_AllYears x
256             join Kent_2003 y
257                     on x.PatientICN = y.PatientICN
258     ;
259     go
260     update x
261     set
262               Age = y.Age
263             , Ethnicity = y.Ethnicity
264             , Gender = y.Gender
265             , PeriodOfService = y.PeriodOfService
266             , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
267             , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
268             , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
269     x.PepticUlcerDisease end
270             , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
271     x.FunctionalDyspepsia end
272             , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
273             , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
274     end
275             , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
276     x.DiverticularDisease end
277             , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
278             , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
279     x.IrritableBowelSyndrome end
280             , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
281     end
282             , MDD = case when y.MDD > 0 then 1 else x.MDD end
283             , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
284             , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
285             , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
286             , SA = case when y.SA > 0 then 1 else x.SA end
287             , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
288             , PDs = case when y.PDs > 0 then 1 else x.PDs end
289     from Kent_AllYears x
```

```
290             join Kent_2004 y
291                     on x.PatientICN = y.PatientICN
292 ;
293 go
294 update x
295 set
296               Age = y.Age
297             , Ethnicity = y.Ethnicity
298             , Gender = y.Gender
299             , PeriodOfService = y.PeriodOfService
300             , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
301             , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
302             , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
303 x.PepticUlcerDisease end
304             , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
305 x.FunctionalDyspepsia end
306             , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
307             , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
308 end
309             , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
310 x.DiverticularDisease end
311             , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
312             , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
313 x.IrritableBowelSyndrome end
314             , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
315 end
316             , MDD = case when y.MDD > 0 then 1 else x.MDD end
317             , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
318             , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
319             , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
320             , SA = case when y.SA > 0 then 1 else x.SA end
321             , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
322             , PDs = case when y.PDs > 0 then 1 else x.PDs end
323 from Kent_AllYears x
324             join Kent_2005 y
325                     on x.PatientICN = y.PatientICN
```

```
;
go
update x
set
        Age = y.Age
      , Ethnicity = y.Ethnicity
      , Gender = y.Gender
      , PeriodOfService = y.PeriodOfService
      , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
      , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
      , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
x.PepticUlcerDisease end
      , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
x.FunctionalDyspepsia end
      , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
      , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
end
      , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
x.DiverticularDisease end
      , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
      , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
x.IrritableBowelSyndrome end
      , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
end
      , MDD = case when y.MDD > 0 then 1 else x.MDD end
      , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
      , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
      , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
      , SA = case when y.SA > 0 then 1 else x.SA end
      , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
      , PDs = case when y.PDs > 0 then 1 else x.PDs end
from Kent_AllYears x
      join Kent_2006 y
            on x.PatientICN = y.PatientICN
;
go
```

```
update x
set
        Age = y.Age
      , Ethnicity = y.Ethnicity
      , Gender = y.Gender
      , PeriodOfService = y.PeriodOfService
      , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
      , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
      , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
x.PepticUlcerDisease end
      , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
x.FunctionalDyspepsia end
      , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
      , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
end
      , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
x.DiverticularDisease end
      , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
      , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
x.IrritableBowelSyndrome end
      , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
end
      , MDD = case when y.MDD > 0 then 1 else x.MDD end
      , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
      , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
      , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
      , SA = case when y.SA > 0 then 1 else x.SA end
      , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
      , PDs = case when y.PDs > 0 then 1 else x.PDs end
from Kent_AllYears x
      join Kent_2007 y
            on x.PatientICN = y.PatientICN
;
go
update x
set
```

```
398             Age = y.Age
399             , Ethnicity = y.Ethnicity
400             , Gender = y.Gender
401             , PeriodOfService = y.PeriodOfService
402             , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
403             , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
404             , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
405 x.PepticUlcerDisease end
406             , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
407 x.FunctionalDyspepsia end
408             , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
409             , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
410 end
411             , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
412 x.DiverticularDisease end
413             , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
414             , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
415 x.IrritableBowelSyndrome end
416             , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
417 end
418             , MDD = case when y.MDD > 0 then 1 else x.MDD end
419             , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
420             , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
421             , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
422             , SA = case when y.SA > 0 then 1 else x.SA end
423             , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
424             , PDs = case when y.PDs > 0 then 1 else x.PDs end
425 from Kent_AllYears x
426             join Kent_2008 y
427                     on x.PatientICN = y.PatientICN
428 ;
429 go
430 update x
431 set
432             Age = y.Age
433             , Ethnicity = y.Ethnicity
```

```
434             , Gender = y.Gender
435             , PeriodOfService = y.PeriodOfService
436             , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
437             , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
438             , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
439     x.PepticUlcerDisease end
440             , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
441     x.FunctionalDyspepsia end
442             , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
443             , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
444     end
445             , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
446     x.DiverticularDisease end
447             , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
448             , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
449     x.IrritableBowelSyndrome end
450             , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
451     end
452             , MDD = case when y.MDD > 0 then 1 else x.MDD end
453             , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
454             , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
455             , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
456             , SA = case when y.SA > 0 then 1 else x.SA end
457             , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
458             , PDs = case when y.PDs > 0 then 1 else x.PDs end
459     from Kent_AllYears x
460             join Kent_2009 y
461                     on x.PatientICN = y.PatientICN
462     ;
463     go
464     update x
465     set
466               Age = y.Age
467             , Ethnicity = y.Ethnicity
468             , Gender = y.Gender
469             , PeriodOfService = y.PeriodOfService
```

```
470             , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
471             , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
472             , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
473     x.PepticUlcerDisease end
474             , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
475     x.FunctionalDyspepsia end
476             , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
477             , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
478     end
479             , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
480     x.DiverticularDisease end
481             , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
482             , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
483     x.IrritableBowelSyndrome end
484             , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
485     end
486             , MDD = case when y.MDD > 0 then 1 else x.MDD end
487             , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
488             , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
489             , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
490             , SA = case when y.SA > 0 then 1 else x.SA end
491             , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
492             , PDs = case when y.PDs > 0 then 1 else x.PDs end
493     from Kent_AllYears x
494             join Kent_2010 y
495                     on x.PatientICN = y.PatientICN
496     ;
497     go
498     update x
499     set
500               Age = y.Age
501             , Ethnicity = y.Ethnicity
502             , Gender = y.Gender
503             , PeriodOfService = y.PeriodOfService
504             , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
505             , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
```

```
506             , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
507     x.PepticUlcerDisease end
508             , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
509     x.FunctionalDyspepsia end
510             , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
511             , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
512     end
513             , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
514     x.DiverticularDisease end
515             , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
516             , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
517     x.IrritableBowelSyndrome end
518             , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
519     end
520             , MDD = case when y.MDD > 0 then 1 else x.MDD end
521             , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
522             , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
523             , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
524             , SA = case when y.SA > 0 then 1 else x.SA end
525             , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
526             , PDs = case when y.PDs > 0 then 1 else x.PDs end
527     from Kent_AllYears x
528             join Kent_2011 y
529                     on x.PatientICN = y.PatientICN
530     ;
531     go
532     update x
533     set
534               Age = y.Age
535             , Ethnicity = y.Ethnicity
536             , Gender = y.Gender
537             , PeriodOfService = y.PeriodOfService
538             , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
539             , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
540             , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
541     x.PepticUlcerDisease end
```

```
542             , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
543     x.FunctionalDyspepsia end
544             , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
545             , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
546     end
547             , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
548     x.DiverticularDisease end
549             , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
550             , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
551     x.IrritableBowelSyndrome end
552             , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
553     end
554             , MDD = case when y.MDD > 0 then 1 else x.MDD end
555             , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
556             , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
557             , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
558             , SA = case when y.SA > 0 then 1 else x.SA end
559             , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
560             , PDs = case when y.PDs > 0 then 1 else x.PDs end
561     from Kent_AllYears x
562             join Kent_2012 y
563                     on x.PatientICN = y.PatientICN
564     ;
565     go
566     update x
567     set
568               Age = y.Age
569             , Ethnicity = y.Ethnicity
570             , Gender = y.Gender
571             , PeriodOfService = y.PeriodOfService
572             , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
573             , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
574             , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
575     x.PepticUlcerDisease end
576             , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
577     x.FunctionalDyspepsia end
```

```
578             , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
579             , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
580     end
581             , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
582     x.DiverticularDisease end
583             , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
584             , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
585     x.IrritableBowelSyndrome end
586             , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
587     end
588             , MDD = case when y.MDD > 0 then 1 else x.MDD end
589             , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
590             , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
591             , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
592             , SA = case when y.SA > 0 then 1 else x.SA end
593             , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
594             , PDs = case when y.PDs > 0 then 1 else x.PDs end
595     from Kent_AllYears x
596             join Kent_2013 y
597                     on x.PatientICN = y.PatientICN
598     ;
599     go
600     update x
601     set
602               Age = y.Age
603             , Ethnicity = y.Ethnicity
604             , Gender = y.Gender
605             , PeriodOfService = y.PeriodOfService
606             , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
607             , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
608             , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
609     x.PepticUlcerDisease end
610             , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
611     x.FunctionalDyspepsia end
612             , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
```

```
613             , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
614     end
615             , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
616     x.DiverticularDisease end
617             , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
618             , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
619     x.IrritableBowelSyndrome end
620             , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
621     end
622             , MDD = case when y.MDD > 0 then 1 else x.MDD end
623             , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
624             , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
625             , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
626             , SA = case when y.SA > 0 then 1 else x.SA end
627             , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
628             , PDs = case when y.PDs > 0 then 1 else x.PDs end
629     from Kent_AllYears x
630             join Kent_2014 y
631                     on x.PatientICN = y.PatientICN
632     ;
633     go
634     update x
635     set
636               Age = y.Age
637             , Ethnicity = y.Ethnicity
638             , Gender = y.Gender
639             , PeriodOfService = y.PeriodOfService
640             , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
641             , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
642             , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
643     x.PepticUlcerDisease end
644             , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
645     x.FunctionalDyspepsia end
646             , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
647             , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
648     end
```

```
649             , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
650     x.DiverticularDisease end
651             , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
652             , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
653     x.IrritableBowelSyndrome end
654             , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
655     end
656             , MDD = case when y.MDD > 0 then 1 else x.MDD end
657             , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
658             , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
659             , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
660             , SA = case when y.SA > 0 then 1 else x.SA end
661             , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
662             , PDs = case when y.PDs > 0 then 1 else x.PDs end
663     from Kent_AllYears x
664             join Kent_2015 y
665                     on x.PatientICN = y.PatientICN
666     ;
667     go
668     update x
669     set
670               Age = y.Age
671             , Ethnicity = y.Ethnicity
672             , Gender = y.Gender
673             , PeriodOfService = y.PeriodOfService
674             , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
675             , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
676             , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
677     x.PepticUlcerDisease end
678             , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
679     x.FunctionalDyspepsia end
680             , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
681             , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
682     end
683             , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
684     x.DiverticularDisease end
```

```
685             , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
686             , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
687     x.IrritableBowelSyndrome end
688             , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
689     end
690             , MDD = case when y.MDD > 0 then 1 else x.MDD end
691             , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
692             , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
693             , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
694             , SA = case when y.SA > 0 then 1 else x.SA end
695             , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
696             , PDs = case when y.PDs > 0 then 1 else x.PDs end
697     from Kent_AllYears x
698             join Kent_2016 y
699                     on x.PatientICN = y.PatientICN
700     ;
701     go
702     update x
703     set
704               Age = y.Age
705             , Ethnicity = y.Ethnicity
706             , Gender = y.Gender
707             , PeriodOfService = y.PeriodOfService
708             , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
709             , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
710             , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
711     x.PepticUlcerDisease end
712             , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
713     x.FunctionalDyspepsia end
714             , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
715             , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
716     end
717             , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
718     x.DiverticularDisease end
719             , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
```

```
720             , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
721     x.IrritableBowelSyndrome end
722             , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
723     end
724             , MDD = case when y.MDD > 0 then 1 else x.MDD end
725             , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
726             , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
727             , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
728             , SA = case when y.SA > 0 then 1 else x.SA end
729             , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
730             , PDs = case when y.PDs > 0 then 1 else x.PDs end
731     from Kent_AllYears x
732             join Kent_2017 y
733                     on x.PatientICN = y.PatientICN
734     ;
735     go
736     update x
737     set
738               Age = y.Age
739             , Ethnicity = y.Ethnicity
740             , Gender = y.Gender
741             , PeriodOfService = y.PeriodOfService
742             , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
743             , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
744             , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
745     x.PepticUlcerDisease end
746             , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
747     x.FunctionalDyspepsia end
748             , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
749             , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
750     end
751             , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
752     x.DiverticularDisease end
753             , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
754             , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
755     x.IrritableBowelSyndrome end
```

```
        , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
end
        , MDD = case when y.MDD > 0 then 1 else x.MDD end
        , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
        , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
        , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
        , SA = case when y.SA > 0 then 1 else x.SA end
        , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
        , PDs = case when y.PDs > 0 then 1 else x.PDs end
from Kent_AllYears x
        join Kent_2018 y
                on x.PatientICN = y.PatientICN
;
go
update x
set
          Age = y.Age
        , Ethnicity = y.Ethnicity
        , Gender = y.Gender
        , PeriodOfService = y.PeriodOfService
        , PTSD = case when y.VisitCount_PTSD > 0 then 1 else x.PTSD end
        , GERD = case when y.VisitCount_GERD > 0 then 1 else x.GERD end
        , PepticUlcerDisease = case when y.VisitCount_PepticUlcerDisease > 0 then 1 else
x.PepticUlcerDisease end
        , FunctionalDyspepsia = case when y.VisitCount_FunctionalDyspepsia > 0 then 1 else
x.FunctionalDyspepsia end
        , Crohns = case when y.VisitCount_Crohns > 0 then 1 else x.Crohns end
        , UlcerativeColitis = case when y.VisitCount_UlcerativeColitis > 0 then 1 else x.UlcerativeColitis
end
        , DiverticularDisease = case when y.VisitCount_DiverticularCisease > 0 then 1 else
x.DiverticularDisease end
        , Constipation = case when y.VisitCount_Constipation > 0 then 1 else x.Constipation end
        , IrritableBowelSyndrome = case when y.VisitCount_IrritableBowelSyndrome > 0 then 1 else
x.IrritableBowelSyndrome end
        , NauseaVomiting = case when y.VisitCount_NauseaVomiting > 0 then 1 else x.NauseaVomiting
end
```

```
792             , MDD = case when y.MDD > 0 then 1 else x.MDD end
793             , Bipolar = case when y.Bipolar > 0 then 1 else x.Bipolar end
794             , Anxiety = case when y.Anxiety > 0 then 1 else x.Anxiety end
795             , Psychosis = case when y.Psychosis > 0 then 1 else x.Psychosis end
796             , SA = case when y.SA > 0 then 1 else x.SA end
797             , Dementia = case when y.Dementia > 0 then 1 else x.Dementia end
798             , PDs = case when y.PDs > 0 then 1 else x.PDs end
799     from Kent_AllYears x
800             join Kent_2019 y
801                     on x.PatientICN = y.PatientICN
802     ;
803     go
804
```

Appendix H: Frequency of Disease Observed Over Time

Year		PTSD	GERD	PepUD	FuncDys	Crohns	UlcCol	DivtDis	Const.	IBS	N/V
1999	Female	5473	4497	426	544	208	187	590	0	866	2451
	Male	96779	91191	16303	10704	2736	3371	18291	1	4669	31818
	Total	**102252**	**95688**	**16729**	**11248**	**2944**	**3558**	**18881**	**1**	**5535**	**34269**
2000	Female	10874	15455	1483	2467	514	519	2284	3	3259	9420
	Male	172796	302528	51058	40109	6514	9588	72160	144	15847	118288
	Total	**183670**	**317986**	**52541**	**42576**	**7028**	**10107**	**74444**	**147**	**19106**	**127708**
2001	Female	12290	19291	1384	2571	580	562	2715	740	3723	10505
	Male	189439	396603	51079	43780	7548	11091	87177	12116	17128	133221
	Total	**201729**	**415894**	**52463**	**46351**	**8128**	**11653**	**89892**	**12856**	**20851**	**143726**
2002	Female	13724	23277	1345	2655	620	568	2999	4176	4151	11350
	Male	208522	483518	48545	42774	8402	12291	95916	61357	17870	143217
	Total	**222246**	**506795**	**49890**	**45429**	**9022**	**12859**	**98915**	**65533**	**22021**	**154567**
2003	Female	15266	28259	1342	2625	665	643	3479	5108	5040	12569
	Male	232789	571764	46897	42838	9542	13512	109084	69108	19917	155375
	Total	**248055**	**520623**	**48239**	**45463**	**10207**	**14155**	**112563**	**74216**	**24957**	**167944**
2004	Female	18060	33251	1394	2896	742	650	3994	6299	6040	14656
	Male	265587	638035	46007	43463	10077	14136	122429	75860	21522	168667
	Total	**283647**	**671286**	**47401**	**46359**	**10819**	**14786**	**126423**	**82159**	**27562**	**183323**
2005	Female	21164	35926	1366	3067	817	732	4232	6754	6473	15677
	Male	301233	666795	42716	41081	10563	14338	123486	81411	22159	174951
	Total	**322397**	**702721**	**44082**	**44148**	**11380**	**15070**	**127718**	**88165**	**28632**	**190628**
2006	Female	23734	39103	1327	3107	851	782	4555	7878	6929	17284
	Male	330586	696327	40402	39931	10959	14704	126473	86982	23029	185293
	Total	**354320**	**735430**	**41729**	**43038**	**11810**	**15486**	**131028**	**94860**	**29958**	**202577**
2007	Female	28004	41369	1345	3079	875	818	4857	8840	7254	18974
	Male	376372	713594	37739	38455	11249	14989	129587	89611	23729	192744
	Total	**404376**	**754963**	**39084**	**41534**	**12124**	**15807**	**134444**	**98451**	**30983**	**211718**
2008	Female	33116	44870	1356	3105	927	897	5406	9850	7613	20258
	Male	421744	731967	35225	36459	11645	15430	135934	94966	24111	198607
	Total	**454860**	**776837**	**36581**	**39564**	**12572**	**16327**	**141340**	**104816**	**31724**	**218865**
2009	Female	38594	48467	1362	3248	1076	1007	5866	11015	8280	22713

	Male	469635	763779	33902	36058	12358	16239	138864	101553	26148	216314
	Total	**508229**	**812246**	**35264**	**39306**	**13434**	**17246**	**144730**	**112568**	**34428**	**239027**
2010	Female	44278	51437	1362	3337	1153	1090	6275	11795	8826	24205
	Male	517904	787610	31719	34572	12992	16995	141659	105682	27619	226829
	Total	**562182**	**839047**	**33081**	**37909**	**14145**	**18085**	**147934**	**117477**	**36445**	**251034**
2011	Female	50280	54209	1385	3430	1254	1148	6624	12788	9381	25500
	Male	562276	801811	29881	33622	13413	17700	142163	110287	28788	232359
	Total	**612556**	**856020**	**31266**	**37052**	**14667**	**18848**	**148787**	**123075**	**38169**	**257859**
2012	Female	57230	57120	1364	3431	1342	1199	6825	13738	10037	27764
	Male	597239	813046	27597	32636	13943	18038	143656	113526	30583	241839
	Total	**654469**	**870166**	**28961**	**36067**	**15285**	**19237**	**150481**	**127264**	**40620**	**269603**
2013	Female	65448	60392	1307	3415	1404	1283	7346	14533	10745	29896
	Male	631879	823417	25927	31118	14237	18488	144227	113354	31455	252178
	Total	**697327**	**883809**	**27234**	**34533**	**15641**	**19771**	**151573**	**127887**	**42200**	**282074**
2014	Female	75120	64926	1217	3438	1554	1442	7969	15370	11850	33713
	Male	675361	852100	24284	29808	15042	19385	150981	114650	34106	273104
	Total	**750481**	**917026**	**25501**	**33246**	**16596**	**20827**	**158950**	**130020**	**45956**	**306817**
2015	Female	85462	67846	1074	3420	1582	1777	8207	13492	13202	30823
	Male	716250	859440	19490	26331	15267	22150	145814	96300	37143	239913
	Total	**801712**	**927286**	**20564**	**29751**	**16849**	**23927**	**154021**	**109792**	**50345**	**270736**
2016	Female	92420	65973	469	2271	1572	2330	7516	293	13348	13558
	Male	715666	791364	6441	15520	14893	27093	119693	959	37128	58138
	Total	**808086**	**857337**	**6910**	**17791**	**16465**	**29423**	**127209**	**1252**	**50476**	**71696**
2017	Female	103111	71061	506	2319	1664	2336	7718	1569	15062	14614
	Male	751751	829112	6205	15144	15514	27275	120953	5615	41493	60750
	Total	**854862**	**900173**	**6711**	**17463**	**17178**	**29611**	**128671**	**7184**	**56555**	**75364**
2018	Female	116037	77783	545	2410	1774	2445	8529	2340	17120	15830
	Male	789683	869482	6126	14683	15896	27747	128341	7932	45905	64347
	Total	**905720**	**947265**	**6671**	**17093**	**17670**	**30192**	**136870**	**10272**	**63025**	**80177**
2019	Female	76506	30227	168	647	1013	1126	2604	863	6510	4962
	Male	486496	320234	1764	4278	8469	11815	37610	2649	16969	19497
	Total	**563002**	**350461**	**1932**	**4925**	**9482**	**12941**	**40214**	**3512**	**23479**	**24459**

Appendix I : Frequency of Diseases Observed by Period of Service

	Korean	PGW	Post-K	Post-V	Pre-K	Sp.Am.	Vietnam	WWI	WWII	Total	% of All Veterans treated outpatient at VA
PTSD	47058	908479	14220	164681	948	30	774644	53	68797	1978910	14%
GERD	401777	699734	195731	328693	15488	62	1353239	132	451525	3446381	25%
PepUD	48206	22257	19095	19240	1779	5	105378	25	65759	281744	2%
FunDys	47502	76872	22785	43986	1501	8	164091	16	51441	408202	3%
Crohns	5313	13141	2966	6296	214	1	21744	5039	55758	110472	1%
UlcCol	10900	22138	5739	10969	437	1	41368	3	10276	101831	1%
DivtDis	173603	126953	92234	126213	5559	14	700539	40	158272	1383427	10%
Const	128916	107504	50236	73990	4779	7	316161	40	177795	859428	6%
IBS	17426	124690	9195	31454	553	11	80047	5	19237	282618	2%
N/V	249867	386551	110658	211320	8581	35	832719	92	311659	2111482	15%

Appendix J: GI Disease Rates by Period of Service Among Veterans Positive for PTSD

	Korean	PGW	Post-K	Post-V	Pre-K	Sp.Am.	Vietnam	WWI	WWII	Total	% of All Veterans Treated Outpatient at VHA (13669058)	% of All Cases of PTSD in Veterans (1978910)
GERD	22355	289129	6764	74011	381	7	363977	18	27672	784314	5.74%	39.63%
PepUD	3082	9422	776	4908	50	2	31031	2	4395	53668	0.39%	2.71%
FunDys	3645	34569	1079	11872	60	2	53779	3	4201	109210	0.80%	5.52%
Crohns	295	4363	103	1238	7	0	5331	0	296	11633	0.09%	0.59%
UlcCol	606	8092	186	2235	12	0	10376	3	615	22125	0.16%	1.12%
DivtDis	11154	44371	3548	24229	161	2	186934	9	12130	282538	2.07%	14.28%
Const	10088	51056	2640	21933	166	1	10071	6	14418	110379	0.81%	5.58%
IBS	1550	65062	569	10556	24	2	28559	2	2494	108818	0.80%	5.50%
N/V	18105	181700	5221	55101	283	2	251479	8	23892	535791	3.92%	27.08%

Appendix K: Frequency Counts of Diseases Over Time by Period of Service

PTSD	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Korean	9837	10423	11016	11577	12179	12787	13396	13800	13372	13214	13097	12933	11956	11224	10628	9806	8482	7856	7200
Persian Gu	14720	16514	18871	22733	32886	49040	65930	92922	124314	155794	186688	216786	250818	288348	334681	383262	412302	451884	796710
Post-Kore	1860	1967	2041	2068	2168	2290	2513	2673	2637	2714	2826	2915	2809	2813	2841	2883	2728	2754	2794
Post-Vietn	9750	11062	12242	13767	15653	18144	20020	23270	26861	31671	36761	41826	36348	50801	55602	60376	62255	67171	72834
Pre-Korea	124	136	140	159	154	167	198	195	176	201	177	203	195	176	171	170	154	150	129
Spanish A	1	2	1	1	1	1	3	5	4	8	9	5	7	9	8	10	9	9	9
Vietnam E	127542	140929	156673	176211	198919	218390	231015	250950	268449	286610	305750	322426	328755	331992	335831	335737	314071	317055	318008
WWI	7	4	4	5	5	7	8	13	12	17	16	19	16	14	18	18	18	17	17
WWI	18302	19237	19816	20204	20358	20013	19730	18984	17145	16031	14752	13265	11115	9418	8109	6825	5124	4172	3373

GERD	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Korean	60330	81191	98814	113566	122445	124055	124929	121788	117139	113933	110065	105141	99421	92779	88658	82008	68991	65562	61356
Persian Gu	19108	24178	29724	37686	48239	56936	67035	77860	92012	108985	124082	136634	152369	170441	193624	211678	217343	242256	273551
Post-Kore	20966	29812	39525	49014	53966	56393	58065	57950	57089	57150	56681	55652	54409	52948	52556	50693	44948	44961	44335
Post-Vietn	16089	20843	26033	33484	40353	43889	48625	53260	59205	67782	74930	80263	85642	91522	99108	104035	98960	107766	116342
Pre-Korea	2082	3009	3805	4344	4675	4789	4798	4635	4348	4183	3921	3696	3383	3100	2893	2633	2085	1969	1801
Spanish A	5	13	12	14	17	16	17	17	17	13	10	9	13	16	10	9	7	12	10
Vietnam E	108268	139625	173260	213356	248291	269195	289511	308234	327347	350876	370367	386064	396787	405755	421215	425907	385708	403677	420258
WWI	25	29	31	30	30	29	32	28	23	27	23	24	22	25	21	24	16	22	26
WWI	87945	113361	131066	143095	147018	140723	135720	124477	112804	102272	92086	81607	71329	60867	52699	44348	33482	28260	23329

PUD	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Korean	10472	10839	10388	10016	9547	8781	8154	7514	6678	6158	5531	4773	4250	3797	3483	2620	826	779	699
Persian Gu	1983	1811	1779	1783	1934	2017	2109	2269	2416	2681	2836	2849	2940	3053	2990	2636	1140	1148	1312
Post-Kore	3479	3642	3760	3709	3658	3409	3326	3024	2738	2533	2404	2239	2050	1920	1730	1377	460	425	423
Post-Vietn	2212	2120	2021	2070	2228	2157	2186	2252	2382	2501	2435	2565	2572	2492	2489	2118	811	860	862
Pre-Korea	328	369	379	363	350	322	287	279	230	212	186	174	147	134	115	75	26	20	23
Spanish A	0	0	1	0	1	1	1	0	2	2	0	1	0	0	1	0	0	0	0
Vietnam E	16827	16373	15813	15876	16404	15774	15567	15196	14868	14720	14317	14318	13421	12909	12349	10061	3104	3061	3014
WWI	8	7	5	3	2	1	2	3	1	3	4	4	1	1	1	1	0	0	0
WWI	16890	17026	15498	14159	13013	11377	9876	8353	7039	6257	5168	4163	3414	2755	2194	1574	484	348	277

FD	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Korean	7271	7929	7508	7250	7154	6437	6154	5535	4706	4256	3761	3459	3104	2777	2420	2067	921	767	688
Persian Gu	3043	3351	3535	3683	4368	4638	5101	5565	6090	6882	7363	7777	8189	8482	8824	8530	5994	6363	6693
Post-Kore	2847	3232	3319	3403	3458	3197	2895	2732	2414	2187	2055	1834	1746	1587	1479	1225	635	573	528
Post-Vietn	2808	3131	3198	3513	3888	3844	3870	3851	3669	4287	4367	4546	4468	4446	4395	4108	2686	2546	2578
Pre-Korea	243	238	249	258	252	236	185	167	144	150	120	100	102	94	76	57	211	17	19
Spanish A	0	1	0	1	2	1	1	0	0	0	1	1	0	1	0	1	0	1	0
Vietnam E	15678	17190	17352	18014	18651	18217	18113	17937	17381	17353	16692	16311	15959	15046	14318	12371	6920	6649	6148
WWI	4	1	1	1	2	0	1	1	1	1	2	1	0	1	0	0	0	1	1
WWI	10005	1064	9598	8689	7838	6835	5999	5110	4266	3650	2985	2551	2027	1671	1342	1025	425	355	253

Crohn's	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Korean	929	1191	1373	1534	1588	1645	1652	1602	1554	1498	1458	1400	1291	1217	1164	1057	892	821	727
Persian Gu	782	857	892	1016	1168	1372	1529	1762	2030	2397	2713	3041	3530	3885	4460	4812	5093	5516	6075
Post-Kore	432	562	661	799	859	888	890	910	896	896	936	892	886	833	857	809	690	708	700
Post-Vietr	780	852	921	1030	1132	1221	1280	1349	1446	1625	1740	1891	1991	2111	2748	2365	2363	2518	2616
Pre-Korea	37	47	54	60	61	62	76	78	68	63	52	54	51	44	37	35	22	17	19
Spanish A	0	0	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1
Vietnam E	2762	3009	3421	3990	4277	4543	4839	5043	5321	5772	6130	6409	6667	6809	7116	7204	6971	7174	7176
WWI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
WWI	1214	1502	1583	1652	1602	1513	1404	1252	1140	1058	984	832	723	601	579	431	298	277	218

UC	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Korean	1784	2163	2392	2617	2669	2700	2667	2585	2502	2459	2395	2308	2130	1969	1893	1883	1923	1816	1598
Persian Gu	926	996	1064	1254	1407	1545	1758	1991	2323	6252	3044	3377	3762	4188	4864	5995	8130	8573	9281
Post-Kore	669	824	1031	1236	1266	1304	1292	1298	1269	1300	1327	1339	1279	1259	1244	1312	1431	1378	1293
Post-Vietr	791	835	924	990	1062	1124	1169	1291	1382	1556	1729	1846	1996	2097	2230	2772	3668	3714	3825
Pre-Korea	60	98	94	113	105	98	112	103	93	95	83	88	77	69	64	54	55	51	44
Spanish A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Vietnam E	3352	3821	4293	4859	5259	5538	5885	6252	6650	7294	7819	8338	8666	9021	9551	10936	13263	13283	13484
WWI	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	2	1	0
WWI	2423	2809	2972	2986	2913	2644	2494	2180	1996	1775	1567	1420	1206	1043	842	812	786	605	453

DD	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Korean	17216	21378	23031	25130	27104	26412	25754	24860	23769	21036	19011	17134	15349	13488	12149	10330	6549	5798	5471
Persian Gu	1485	1758	2125	2671	3493	4159	4785	5769	7330	8897	10060	11315	12775	14776	17394	19475	19167	21683	25126
Post-Kore	5773	7631	9170	10979	12251	12271	12404	12174	12206	11960	11473	10942	10252	9814	9332	8247	5694	5189	5060
Post-Vietr	1347	1726	2086	2624	3428	3919	4867	5776	7633	9700	11539	13011	14747	16134	18573	19447	18097	19226	2114
Pre-Korea	557	720	818	282	942	904	863	793	739	579	530	475	421	333	292	236	138	167	143
Spanish A	2	1	0	2	2	1	1	1	0	1	1	1	0	0	0	1	0	1	2
Vietnam E	22100	27775	32540	40962	50231	54329	59224	65020	72011	77874	82916	85110	87898	89548	94595	90997	74316	73744	77403
WWI	3	1	4	2	4	3	4	4	3	3	7	4	5	3	3	3	0	3	3
WWI	25386	28204	28457	28541	27990	24564	22074	18975	16485	13511	11167	9567	7808	6269	5359	4151	2281	1878	1538

IBS	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Korean	2467	2668	2706	2810	2947	2949	2922	2704	2573	2420	2344	2233	2113	1886	1809	1681	1359	1313	1313
Persian Gu	3208	3231	3654	4658	5983	6772	7821	8975	10359	12308	13964	15683	17945	19862	23111	26978	29337	34051	39360
Post-Kore	944	1129	1261	1414	1475	1487	1456	1467	1333	1322	1317	1268	1207	1196	1199	1110	960	1035	1056
Post-Vietr	1911	2101	2234	2763	3090	3292	3419	3641	3779	4198	4551	4770	5062	5200	5678	6056	5937	6410	6977
Pre-Korea	68	81	98	90	93	98	91	92	86	79	76	76	65	54	52	48	40	38	33
Spanish A	0	0	0	2	0	1	2	2	0	3	2	3	4	4	0	2	0	1	2
Vietnam E	6625	7240	7710	8771	9625	9922	10352	10624	10533	11249	11570	11703	12103	12137	12437	12973	11570	12451	13124
WWI	0	0	1	1	1	1	1	1	2	3	1	0	1	1	2	0	1	1	0
WWI	3621	3892	3815	3826	3663	3391	3234	2800	2455	2197	1965	1972	1516	1292	1135	929	674	617	516

Appendix L: Rates of Secondary Mental Illness in those with both PTSD and GI Disease

	MDD	Anxiety	Bipolar	Psychosis	PDs	SA	Dementia
PTSD & GERD	619269 (78.54% of those with both PTSD & GERD)	488387 (61.94%)	101780 (12.91%)	98298 (12.47%	87782 (11.13%)	458383 (57.38%)	34805 (4.41%)
PTSD & PepUl	43017 (79.81%)	34328 (63.69%)	7884 (14.63%)	9866 (18.30%)	7034 (13.05%)	34187 (63.42%)	3829 (7.10%)
PTSD & FD	90959 (92.78%)	74459 (67.76%)	17536 (15.96%)	19107 (17.39%)	16022 (14.58%)	68811 (62.62%)	5762 (5.24%)
PTSD & Crohns	9540 (81.43%)	7696 (65.69%)	1753 (14.96%)	1544 (13.18%)	1549 (13.18%)	6960 (59.41%)	487 (4.16%)
PTSD & UC	17715 (79.71%)	14211 (63.94%)	3131 (14.09%)	2884 (12.98%)	2769 (12.46%)	12601 (56.70%)	1085 (4.88%)
PTSD & DD	221010 (77.92%)	168422 (59.38%)	32475 (11.45%)	35284 (12.44%)	27724 (9.77%)	164463 (57.98%)	16269 (5.74%)
PTSD & Const.	168394 (83.20%)	135252 (66.83%)	35166 (17.28%)	41879 (20.69%)	31722 (15.62%)	121804 (60.18%)	15952 (7.88%)
PTSD & IBS	90616 (82.68%)	78515 (71.64%)	18261 (16.66%)	12623 (11.52%)	16951 (15.47%)	59541 (54.93%)	3267 (2.98%)
PTSD & N/V	439539 (81.56%)	350263 (65.00%)	85798 (15.92%)	89270 (16.57%)	75700 (14.05%)	332789 (61.75%)	31983 (5.93%)

Appendix M: PTSD Rates broken down by GI Disease and Secondary Mental Illness

	F = total frequency PP = % of all Veterans with PTSD	Bipolar Disorders	Psychotic Disorders	Personality Disorders	Substance Abuse	Dementias
PTSD & GERD	Rate of PTSD among those with both GERD and indicated mental illness:	F = 82361 PP = 4.16%	F = 97888 PP = 4.95%	F = 87177 PP = 4.41%	F = 450358 PP = 22.78	F = 34767 PP = 1.78%
	Rate of PTSD among those with GERD and without indicated mental illness:	F = 683237 PP = 34.53%	F = 686626 PP = 34.70%	F = 697137 PP = 35.23%	F = 333956 PP = 16.88%	F = 749547 PP = 37.88
	Rate of PTSD among those without GERD and with indicated mental illness:	F = 98426 PP = 4.97%	F = 91751 PP = 4.64%	F = 75356 PP = 3.81%	F = 565123 PP = 28.56%	F = 27526 PP = 1.39%
	Rate of PTSD among those without GERD or indicated mental illness:	F = 1096170 PP = 55.39%	F = 1102845 PP = 55.73%	F = 1119240 PP = 56.56%	F = 629478 PP = 31.81%	F = 1167070 PP = 58.98%
PTSD & Peptic Ulcer Disease	Rate of PTSD among those with both PUD and indicated mental illness:	F = 7825 PP = .40%	F = 9310 PP = .47%	F = 6992 PP = .35%	F = 34039 PP = 1.72%	F = 3822 PP = .19%
	Rate of PTSD among those with PUD and without indicated mental illness:	F = 45843 PP = 2.32%	F = 43838 PP = 2.22%	F = 46676 P = 2.36%	F = 19629 PP = .99%	F = 49843 PP = 2.52%
	Rate of PTSD among those without PUD and	F = 191676 PP = 9.69%	F = 179809 PP = 9.07%	F = 155541 P = 7.86%	F = 981437 PP = 49.59%	F = 58468 PP = 2.95%

	with indicated mental illness:					
	Rate of PTSD among those without PUD or indicated mental illness:	F = 1733564 PP = 87.60%	F = 1745433 PP = 88.20%	F = 1769701 PP = 89.43%	F = 943805 PP = 47.69%	F = 1866774 PP = 94.33%
PTSD & Functional Dyspepsia	Rate of PTSD among those with both FD and indicated mental illness:	F = 17396 PP = .88%	F = 19022 PP = .96%	F = 15894 PP = .80%	F = 68454 PP = 3.46%	F = 5748 PP = .29%
	Rate of PTSD among those with FD and without indicated mental illness:	F = 91814 PP = 4.64%	F = 90188 PP = 4.58%	F = 93316 PP = 4.72%	F = 40756 PP = 2.06%	F = 103459 PP = 5.23%
	Rate of PTSD among those without FD and with indicated mental illness:	F = 182107 PP = 9.20%	F = 170617 PP = 8.62%	F = 146639 PP = 7.41%	F = 947025 PP = 47.86%	F = 56545 PP = 2.86%
	Rate of PTSD among those without FD or indicated mental illness:	F = 1687593 PP = 85.28%	F = 1699083 PP = 85.86%	F = 1723061 PP = 87.07%	F = 922680 PP = 46.63%	F = 1813155 PP = 91.62%
PTSD & Crohn's Disease	Rate of PTSD among those with both Crohn's and indicated mental illness:	F = 1747 PP = .09%	F = 1537 PP = .08%	F = 1539 PP = .08%	F = 6922 PP = .35%	F = 485 PP = 0%
	Rate of PTSD among those with Crohn's and without indicated mental illness:	F = 9886 PP = .50%	F = 10096 PP = .51%	F = 10094 PP = .51%	F = 4711 PP = .24%	F = 11148 PP = .56%
	Rate of PTSD among those without Crohn's and with indicated mental illness:	F = 197756 PP = 9.99%	F = 188102 PP = 9.51%	F = 160994 PP = 8.14%	F = 1008454 PP = 50.96%	F = 61808 PP = 3.12%

	Rate of PTSD among those without Crohn's or indicated mental illness:	F = 1769521 PP = 89.42%	F = 1779175 PP = 89.91%	F = 1806283 PP = 91.28%	F = 958723 PP = 48.45%	F = 1905469 PP = 96.29%
PTSD & Ulcerative Colitis	Rate of PTSD among those with both UC and indicated mental illness:	F = 3115 PP = .16%	F = 2875 PP = .15%	F = 2752 PP = .14%	F = 12554 PP = .63%	F = 1092 PP = .06%
	Rate of PTSD among those with UC and without indicated mental illness:	F = 19010 PP = .96%	F = 19250 PP = .97%	F = 19373 PP = .98%	F = 9572 PP = .48%	F = 21043 PP = 1.06%
	Rate of PTSD among those without UC and with indicated mental illness:	F = 196388 PP = 9.92%	F = 186764 PP = 9.44%	F = 159781 PP = 8.07%	F = 1002922 P = 50.68%	F = 61211 PP = 3.09%
	Rate of PTSD among those without UC or indicated mental illness:	F = 1760397 PP = 88.96%	F = 1770021 PP = 89.44%	F = 1797004 PP = 90.81%	F = 953863 PP = 48.20%	F = 1895574 PP = 95.79%
PTSD & Diverticular Disease	Rate of PTSD among those with both DD and indicated mental illness:	F = 32312 PP = 1.63%	F = 35184 PP = 1.78%	F = 27567 PP = 1.39%	F = 163949 PP = 8.28%	F = 16258 PP = .82%
	Rate of PTSD among those with DD and without indicated mental illness:	F = 250296 PP = 12.65%	F = 247424 PP = 12.5%	F = 255041 PP = 12.89%	F = 118659 PP = 6.00%	F = 242520 PP = 12.26%
	Rate of PTSD among those without DD and with indicated mental illness:	F = 167221 PP = 8.45%	F = 154455 PP = 7.81%	F = 134966 PP = 6.82%	F = 851527 PP = 43.03%	F = 46035 PP = 2.33%

	Rate of PTSD among those without DD or indicated mental illness:	F = 1529111 PP = 77.27%	F = 1541847 PP = 77.91%	F = 1561336 PP = 78.90%	F = 844775 PP = 42.69%	F = 1650267 PP = 83.39%
PTSD & Constipation	Rate of PTSD among those with both Constipation and indicated mental illness:	F = 34907 PP = 1.76%	F = 41689 PP = 2.11%	F = 31462 PP = 1.59%	F = 121087 PP = 6.12%	F = 15933 PP = .81%
	Rate of PTSD among those with Constipation and without indicated mental illness:	F = 166182 PP = 8.40%	F = 159390 PP = 8.05%	F = 169617 PP = 8.57%	F = 79992 PP = 4.04%	F = 185146 PP = 9.36%
	Rate of PTSD among those without Constipation and with indicated mental illness:	F = 164603 PP = 8.32%	F = 147950 PP = 7.48%	F = 131071 PP = 6.62%	F = 894389 PP = 45.20%	F = 46360 PP = 2.34%
	Rate of PTSD among those without Constipation or indicated mental illness:	F = 1613225 PP = 81.52%	F = 1629881 PP = 82.36%	F = 1637760 P = 82.76%	F = 883442 PP = 44.64%	F = 1731471 PP = 87.50%
PTSD & IBS	Rate of PTSD among those with both IBS and indicated mental illness:	F = 18111 PP = .92%	F = 12553 PP = .63%	F = 16720 PP = .84%	F = 59166 PP = 2.99%	F = 3260 PP = .16%
	Rate of PTSD among those with IBS and without indicated mental illness:	F = 90697 PP = 4.58%	F = 96255 PP = 4.86%	F = 91996 PP = 4.65%	F = 49642 PP = 2.51%	F = 105548 PP = 5.33%
	Rate of PTSD among those without IBS and with indicated mental illness:	F = 181392 PP = 9.17%	F = 177086 PP = 8.95%	F = 145723 PP = 7.36%	F = 956310 PP = 48.33%	F = 59033 PP = 2.98%

	Rate of PTSD among those without IBS or indicated mental illness:	F = 1688710 PP = 85.34%	F = 1693016 PP = 85.56%	F = 1724379 P = 87.14%	F = 913792 PP = 46.18	F = 1811069 PP = 91.52%
PTSD & Nausea/Vomiting	Rate of PTSD among those with both Nausea / Vomiting and indicated mental illness:	F = 85179 PP = 4.30%	F = 88884 PP = 4.49%	F = 75138 PP = 3.80%	F = 331142 PP = 16.73%	F = 31947 PP = 1.61%
	Rate of PTSD among those with Nausea / Vomiting and without indicated mental illness:	F = 450612 PP = 22.77%	F = 446907 PP = 22.58%	F = 460641 PP = 23.28%	F = 204649 PP = 10.34%	F = 503844 PP = 25.46%
	Rate of PTSD among those without Nausea/Vomiting and with indicated mental illness:	F = 114324 PP = 5.78%	F = 100755 PP = 5.09%	F = 87397 PP = 4.42%	F = 684334 PP = 34.58%	F = 29346 PP = 1.48%
	Rate of PTSD among those without Nausea/Vomiting or indicated mental illness:	F = 1328795 PP = 67.15%	F = 1342364 PP = 67.83%	F = 1355724 PP = 68.51%	F = 758785 PP = 38.34%	F = 1412773 PP = 71.39%