The Influence of Elective Surgery on Health in Veterans with Chronic Posttraumatic Stress Disorder

by

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Dissertation submitted in partial fulfillment of
the requirements for the degree of Doctor of Philosophy in
Nursing in the Graduate School
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ABSTRACT

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Abstract

Posttraumatic stress disorder (PTSD) is common, often chronic, and has been associated with greater risk of postoperative mortality in veterans. Therefore, the purpose of this dissertation was to determine if elective outpatient surgery had a persistent and deleterious effect on the physical or mental health of veterans, and also to explore factors that contributed to health change after outpatient elective surgery in veterans with PTSD. A longitudinal, mixed method, quasi-experimental, nonequivalent control group study was conducted. Physical and mental health, depressive symptom severity, posttraumatic symptom severity, and pain severity were measured in 29 veterans with PTSD before undergoing outpatient elective surgery, one week after surgery, one month after surgery, and three months after surgery. For comparison, parallel data were collected from a control group of 31 veterans with PTSD at enrollment, one week after enrollment, one month after enrollment, and three months after enrollment. Subjects who displayed clinically significant or distressing changes in health status after surgery were interviewed to identify factors associated with postoperative health change.

Subjects in the surgical group reported significant declines in subjective physical and mental health at one week, but not one or three months, after outpatient elective surgery. Depressive symptom severity and posttraumatic symptom severity were unchanged after surgery. Subjects reported that this physical and mental distress was driven by acute postoperative pain, but that underlying chronic pain remained influential throughout their postoperative course.

For my father

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1. The Influence of Elective Surgery on Veterans with Chronic PTSD: A Statement of the Problem

The purpose of this dissertation is to describe the state of the science about surgery and anesthesia in veterans with chronic posttraumatic stress disorder (PTSD), to relate that science to the greater body of literature about PTSD, to identify gaps in the literature describing the surgical population of patients with PTSD, and to propose an approach to extend our knowledge about this highly vulnerable population.

1.1 Surgery in the Patient with Preexisting Illness

Considerable effort has been devoted to defining patient populations at risk for poor outcomes after surgery. The process of surgery is divided into the phases of preoperative preparation, intraoperative management, and postoperative care. Collectively, these phases are called the perioperative period, and their collective execution is known as perioperative care. A relatively large volume of research has been conducted with patients with preexisting physical illness to define their risk of adverse perioperative outcomes and form evidence-based recommendations for their perioperative care. As a result of this research, evidence-based guidelines exist for the preoperative preparation, intraoperative management, and postoperative care of patients with chronic cardiac (Fleisher et al. 2006, Eagle et al. 2002), pulmonary (Yamakage, Iwasaki, and Namiki 2008, Qaseem et al. 2006), and neurological (Lieb and Selim 2008) comorbidities.

1.1.1 Surgery in the Patient with Preexisting Mental Illness

In contrast, relatively little research has been conducted to define perioperative risk and inform evidence-based recommendations for the perioperative care of patients with preexisting mental illness. This is problematic because literature suggests that surgical patients with preexisting mental illness demonstrate different patterns of preoperative physical comorbidity, different postoperative pain management needs, and experience different risks after surgery.

For example, patients with schizophrenia demonstrate greater prevalence of preexisting cardiac problems (Curkendall et al. 2004, Goff et al. 2005); respiratory problems (Copeland et al. 2007), obesity and diabetes (McEvoy et al. 2005); use less analgesia after surgery (Kudoh, Ishihara, and Matsuki 2000); are more likely to develop delirium (Kudoh et al. 2002); respiratory failure, pulmonary emboli, venous emboli, or sepsis after surgery; and demonstrate greater risk of postoperative mortality than patients without schizophrenia (Daumit et al. 2006). Patients with major depressive disorder are more likely to develop postoperative delirium than patients without major depressive disorder, especially when antidepressant medications were withheld before surgery (Kudoh, Katagai, and Takazawa 2002). Relatively little research has investigated the impact of surgery on patients with other mental illness such as bipolar disorder or posttraumatic stress disorder (PTSD; Copeland et al. 2008). These findings suggest that population-specific research is needed to identify the risks of undergoing surgery and define evidence-based strategies for the perioperative care of patients with other pre-existing mental illnesses.

1.2 Posttraumatic Stress Disorder

Posttraumatic stress disorder (PTSD) is an anxiety disorder characterized by avoidant behavior, physiological reactivity, emotional numbing, intrusive thoughts, and unwanted recurrent memories that develop after exposure to a traumatic event and persist for at least one month (American Psychiatric Association 2000). The lifetime prevalence of PTSD in the United States is estimated to be 6.8% (Kessler et al. 2005). The prevalence is greater in military veterans, with 9% to 43% demonstrating the disorder depending on the method used to diagnose PTSD and the veteran's era of service (Vasterling et al. 2010, Hoge and Castro 2006, Hoge et al. 2004, Dohrenwend et al. 2006, Blake et al. 1990).

1.2.1 PTSD as a Chronic Illness

Despite the availability of evidence-based treatment, there is evidence that PTSD may become a chronic disorder for many patients. Psychological symptoms of PTSD exist along a continuum of severity (Blake et al. 1995) and evidence-based treatment can reduce symptom severity below the diagnostic threshold for many patients (Foa et al. 2009). However, many patients experience multiple cycles of symptom recurrence in the years and decades after the traumatic experience despite the availability of efficacious treatments. For example, a longitudinal study (Solomon and Mikulincer 2006) of Israeli combat veterans who participated in the 1984 Lebanon conflict demonstrated a 38% incidence of PTSD one year after exposure and 19% incidence of PTSD 20 years after exposure to combat. This finding suggests that only half of those veterans who developed PTSD went on to experience complete and sustained resolution of symptoms. Similar results have been reported in U.S. veterans.

Perconte, Griger, and Bellucci (1989) reported that 55% of Vietnam veterans who demonstrated significant posttraumatic symptom improvement after 4 weeks of inpatient treatment were rehospitalized for posttraumatic symptom recurrence within two years. Aging and cognitive decline may also affect PTSD severity, as several case reports describe sudden onset or relapse of previously well-controlled posttraumatic symptoms in older veterans with new-onset cognitive impairment (Hamilton and Workman 1998, Mittal et al. 2001). Therefore, data suggests that some patients with a history of PTSD may never be completely free of the disorder (Foa et al. 2009).

1.2.2 PTSD, Comorbidity, and Health Risk Behaviors

Studies of outpatients with PTSD have demonstrated greater than national average prevalence of diabetes, asthma, stroke, myocardial infarction, cancer, and cirrhosis, (David et al. 2004, Buckley et al. 2004). The relationship between PTSD and the accumulation of these chronic conditions is likely mediated by health risk behaviors. Patients with preexisting PTSD report little physical exercise and greater than national average prevalence of tobacco use, drinking, and drug use (Buckley et al. 2004, Anthony, Warner, and Kessler 1994). At present, it is unknown whether the prevalence of concurrent substance abuse disorders in patients with PTSD represents self-medication of PTSD symptoms, or a vulnerability of the patient that facilitates the development of both substance use disorder and PTSD (Brown and Wolfe 1994). The presence of these comorbidities and health risk behaviors would place any patient at greater risk for poor outcomes after surgery (Wolters et al. 1996).

1.2.3 PTSD and Depression

Posttraumatic stress disorder and major depression are highly comorbid. Studies suggest that 50-82% of patients meeting criteria for PTSD also met criteria for major depression (Breslau et al. 2000, Bleich et al. 1997, Brown et al. 2001). In addition, persons who developed PTSD after exposure to a traumatic event were also at significantly greater risk of developing comorbid major depression (Breslau et al. 2000). A portion of the relationship between PTSD and major depression can be attributed to the similarity of posttraumatic and depressive symptoms. Depression and PTSD share the symptoms of loss of interest in significant activities, insomnia, and difficulty concentrating (American Psychiatric Association 2000), and items assessing these symptoms appear on measures of both depression and PTSD. However, studies on pairs of twins who served in the military during the Vietnam era have shown that PTSD and depression may share a common genetic liability. Pairs of monozygous twins were more likely than pairs of dyzygous twins to develop comorbid PTSD and depression when controlling for various life experiences, including exposure to traumatic events (Koenen, et al., 2008). Such findings have led some authors to suggest that PTSD and depression after trauma may be part of a single, larger, 'posttraumatic syndrome' with shared vulnerabilities that may arise from a genetic basis (Breslau et al. 2000, Koenen et al. 2008).

1.2.4 PTSD and Cognitive Function

In addition to greater prevalence of comorbidity and health risk behaviors, patients with PTSD demonstrate differences in cognitive function and neuroanatomy compared to their peers without PTSD. Some studies have reported that lower scores on measures of cognitive functioning were associated with the development of PTSD and severity of posttraumatic symptoms after exposure to trauma, as well as an inverse relationship between current and premorbid intelligence and posttraumatic symptom

severity (Macklin et al. 1998, McNally and Shin 1995, Vasterling & Brailey, 2005). However, longitudinal observational studies cannot determine a direction of causality between intelligence and PTSD, and the generalizability of these findings is unknown. Early research with survivors of the Cocoanut Grove Club fire clearly demonstrated that even very intelligent persons developed symptoms consistent with PTSD when exposed to a sufficiently horrific experience (Adler 1943).

Advances in neuroimaging techniques may shed more light on the relationships between cognitive functioning and PTSD. Meta-analyses of neuroimaging studies have reported a consistent and inverse relationship between PTSD severity and hippocampal volume (Karl et al. 2006), and studies of monozygous twins discordant for PTSD suggest that smaller hippocampal volume may be a premorbid marker of risk of developing PTSD after trauma exposure (Pitman et al. 2006). However, studies of the relationship between brain volume and cerebrospinal fluid volume in patients with PTSD suggest that generalized white matter atrophy may occur after exposure to trauma (Villarreal et al. 2002). These examples demonstrate that the relationships between PTSD, cognitive function, and neuroanatomy are complex, temporally ambiguous, and most likely bidirectional.

Although the direction of causality is ambiguous, studies have reported that outpatients with PTSD demonstrated worse performance on certain neuropsychological tests. After controlling for exposure to trauma, patients with PTSD performed worse than patients without PTSD on tasks that required the respondent to immediately learn and retain new information for a short period of time, manipulate that information in a meaningful way, and produce a response based on the

manipulated information (Beckham, Crawford, and Feldman 1998, Gilbertson et al. 2001, Hart et al. 2008). As the tasks used to test neuropsychological function closely parallel those used to test intelligence, these findings suggest that although lower intelligence scores may be observed in subjects with PTSD, the cognitive deficits are concentrated in specific domains rather than global intelligence (Gilbertson et al. 2001, Hart et al. 2008). This finding is important, because worse performance on measures of cognitive functioning may place the patient with PTSD at greater risk for cognitive decline after surgery (Millar, Asbury, and Murray 2001), which is associated with functional impairment and greater mortality (Monk et al. 2008, Steinmetz et al. 2009, Phillips-Bute et al. 2006).

1.2.5 PTSD and Subjective Health Status

The adverse relationship between PTSD and health also extends to subjective health. Outpatients with PTSD rate their subjective physical functioning, general health, and ability to perform physical roles in daily life significantly lower than population norms (Buckley et al. 2004). A possible explanation for this finding is that patients with PTSD demonstrate systematic cognitive biases that make them more likely to interpret ambiguous internal or external stimuli as negative or threatening (Constans 2005), and therefore interpret internal and external health-related cues in a more negative light. As a result, patients with PTSD perceive their health as worse than that of their peers without PTSD. This is significant, as subjective assessments of health are well-established predictors of mortality (Idler and Benyamini 1997, Idler and Kasl 1991, Fan et al. 2004), possibly through a vicious cycle in which negative health

perceptions lead to greater distress and greater perceptions of disability (Farmer and Ferraro 1997).

1.2.6 PTSD and Mortality

Outpatients with PTSD demonstrate greater risk of all-cause mortality than their peers without PTSD. Studies of Vietnam-era veterans have demonstrated that, since the war, those with PTSD were more likely to die from cardiovascular as well as external causes, including suicide, homicide, and accidents, than those without PTSD (Boscarino 2008a, 2006b, 2008b, 2006a). As noted, this greater mortality is likely mediated by health risk behaviors because outpatient Vietnam veterans with PTSD also demonstrated greater prevalence of tobacco, ethanol, and illicit substance use (Boscarino 2006b).

1.2.7 Previous Studies on Surgery in the Context of Preexisting PTSD

The most recent systematic review of the literature could only identify 12 studies published between 1966 and 2007 that reported perioperative outcomes from noncardiac surgery in patients with preexisting mental illness (Copeland et al. 2008). In that review, the authors located 10 publications that included patients with schizophrenia and 2 publications that included patients with major depression. The authors concluded that patients with schizophrenia and major depression demonstrated patterns of comorbid physical illness, medication use, and postoperative complications that necessitated specific perioperative risk counseling and management, but were unable to locate any publications that included subjects with bipolar disorder or PTSD undergoing noncardiac surgery. Therefore, a systematic

review of the literature is needed to assess and summarize the state of the science about surgery and anesthesia in the context of preexisting PTSD.

1.2.8 Conclusions

As a population, patients with PTSD demonstrate greater prevalence of several comorbidities and health risk behaviors that increase their risk of mortality, and also likely contribute to greater risk of poor outcomes after surgery. Given the results of previous research into the impact of surgery on patients with other mental illnesses, it is vital that research be undertaken to improve our understanding of this highly vulnerable population.

1.3 Specific Aims

Posttraumatic stress disorder is common, can be chronic, and has been associated with greater prevalence of comorbidities and health risk behaviors that increase risk of morbidity and mortality. Extending the science about the effects of surgery on the patient with PTSD is vital because many surgeries are *elective*, meaning that such surgeries may potentially be deferred if truly associated with greater risk of poor recovery. Patients with PTSD will always need to undergo non-elective surgeries to preserve life and limb, but the risks and benefits of elective surgery in this population need to be better understood so that clinicians and patients can make informed decisions. Therefore, the specific aims of this dissertation are to:

1. Review the state of the science describing surgery and anesthesia in the context of preexisting PTSD.

2. Identify research methods and study design(s) that would extend the science about the outcomes and risks of elective surgery and anesthesia in the setting of preexisting PTSD.

3. Utilize the identified methods and study design(s) to describe the effects of elective surgery and anesthesia on the mental and physical health of the patient with preexisting PTSD.

4. Utilize the findings of that study to identify factors associated with suboptimal recovery from elective surgery and anesthesia that will inform future studies of this population.

1.4 Review of the Literature

Despite the prevalence of preexisting PTSD, evidence that PTSD can be a chronic illness that never fully resolves, and evidence that other preexisting psychiatric illnesses influences perioperative outcomes, few studies have examined the effect of preexisting PTSD on the risks of undergoing surgery and anesthesia (Copeland et al. 2008). Therefore, the purpose of this literature review was to examine studies reporting the outcomes and experiences of patients with preexisting PTSD at the time they presented for surgery, determine what is known about surgery and anesthesia in the context of preexisting PTSD, and identify opportunities for future research.

1.4.1 Methods

MEDLINE, PsychINFO, and the Cumulative Index to Nursing and Allied Health Literature were searched to identify articles, abstracts, or dissertations for inclusion in this review of the literature on the perioperative outcomes of patients with pre-existing PTSD. The MEDLINE search utilized the Medical Subject Heading

(MeSH) term "perioperative period" or "surgery" and the MeSH term "stress disorder, post traumatic" or the keywords "post traumatic stress disorder" or "PTSD". The PsychINFO and CINAHL searches combined the keywords "surgery" and "posttraumatic stress disorder." The search was retrospectively truncated at 1980, the year PTSD was introduced as a diagnosis (American Psychiatric Association, Task Force on Nomenclature and Statistics, and American Psychiatric Association, Committee on Nomenclature and Statistics. 1980), and included all articles added to the databases through 03 March 2011. The search was limited to articles published in English. Additional searches were also performed on abstract archive websites of the American Association of Nurse Anesthetists and American Society of Anesthesiologists to identify peer-reviewed papers and posters presented at annual meetings. As of 03 March 2011, this search strategy yielded 176 peer-reviewed articles and abstracts.

Titles and abstracts of these 176 articles were evaluated for inclusion in this review of the literature. Inclusion criteria were databased or case report articles that described preoperative, intraoperative, or postoperative findings from one or more adult subjects with a diagnosis of PTSD or a screening test score indicative of PTSD at the time surgery was performed. Exclusion criteria were articles that reported PTSD only as an outcome of surgery, articles that only included children, and articles specifically investigating psychological trauma secondary to parturition or termination of pregnancy.

1.4.2 Results

Nine published articles, one case report, and four databased abstracts met criteria for inclusion. Several of these articles reported data from the same studies: (a) Four published articles reported different analyses of one study of patients undergoing coronary artery bypass graft surgery (Oxlad et al. 2006a, b, Oxlad and Wade 2006, 2008) and; (b) four databased abstracts reported different analyses of a single study of patients captured by an electronic clinical database (Brzezinski et al. 2009a, b, d, c). The remaining five published articles reported results from unique samples of patients (Dao et al. 2010, Hudetz et al. 2010, Ikossi et al. 2010, Schreiber et al. 2004, Page et al. 2009), and the subject of the case report was not included in any other study (Crosby et al. 2007). Therefore, although no data were published in duplicate, these 14 articles represented data from just eight unique samples, one of which consisted of a single subject.

The articles and abstracts were reviewed, categorized, and entered into a database to allow cross-comparison of surgical population, sample size, method of defining PTSD status, variables of interest, and findings (Gerrard 2007); these are presented in Table 1. The findings of this literature review were synthesized and used as the basis for an article describing the perioperative implications of posttraumatic stress disorder (Wofford, Hertzberg, and Vacchiano In press), which is presented as Chapter 2 of this dissertation.

Table 1. Studies describing the perioperative outcomes or care of patients with preexisting PTSD

Article	Design	Sample size: Total	Sample size: Number with PTSD	Surgical population	Method of determining PTSD status	Independent variable(s)	Dependent variable(s)	Findings
Dao, et al.(2010)	Cross-sectional, retrospective	62665	9202	National (US), CABG	ICD-9-CM Code	Presence of depression and/or PTSD diagnoses	In-hospital mortality	Prevalence of depression, PTSD, and comorbid depression/PTSD per ICD-9-CM codes significantly greater in deceased patients compared to living patients
Ikossi, Maldonado, Hernandez-Boussard, and Eisenberg, (2010)	Longitudinal, retrospective	102	24	Veteran (US), gastric bypass	Chart review	PTSD diagnosis	Hospital LOS, early complication rate, mean weight loss at one year	NSD between patients with and without PTSD in hospital LOS, early complication rate, or mean weight loss at one year after gastric bypass
Hudetz, et al. (2010)	Longitudinal, prospective	86	30	Veteran (US), CABG	Chart review	Presence of PTSD, depression, and/or alcohol dependence	Change in nonverbal memory, verbal memory, and executive function from pre- to post-op.	Presence of PTSD associated with more frequent decline in cognitive function after CABG

Table 1. Studies describing the perioperative outcomes or care of patients with preexisting PTSD

Article	Design	Sample size: Total	Sample size: Number with PTSD	Surgical population	Method of determining PTSD status	Independent variable(s)	Dependent variable(s)	Findings
Brzezinski, Marmar, Cason, Au, and Wallace (2009a)	Cross-sectional, retrospective	10252	789	Veteran (US), all elective surgery	Chart review	PTSD diagnosis	1 or 5 year mortality	Presence of PTSD associated with significantly greater 1 or 5 year mortality after elective surgery
Brzezinski, Marmar, Cason, Au, and Wallace (2009b)	Cross-sectional, retrospective	1764	134	Veteran (US), emergency surgery	Chart review	PTSD diagnosis	Number of non-emergency, major surgeries per subject from 1996-2008	Presence of PTSD associated with significantly greater number of surgeries per subject over time period
Brzezinski, Marmar, Cason, Au, and Wallace (2009d)	Cross-sectional, retrospective	17813	1571	Veteran (US), emergency surgery	Chart review	PTSD diagnosis	Number of emergency, major surgeries per subject from 1996-2008	NSD between veterans with and without PTSD in number of non-emergent major surgeries over time period
Brzezinski, Marmar, Cason, Au, and Wallace (2009c)	Cross-sectional, retrospective	17813	1571	Veteran (US), elective surgery	Chart review	PTSD diagnosis	Prevalence of diabetes, hypertension, hypercholesterol-emia, depression, and tobacco, alcohol or drug abuse	PTSD associated with greater prevalence of diabetes, hypertension, hypercholesterolemia, depression, and tobacco, alcohol and drug abuse

Table 1. Studies describing the perioperative outcomes or care of patients with preexisting PTSD

Article	Design	Sample size: Total	Sample size: Number with PTSD	Surgical population	Method of determining PTSD status	Independent variable(s)	Dependent variable(s)	Findings
Page, Kleiman, Asmundson, and Katz (2009)	Cross-sectional, prospective	447	65	Civilian (CA), major surgery	PCL-C	Presence of pain before major surgery	Factor structure of PTSD symptoms	Different factor structures between patients with and without pain before major surgery
Oxlad and Wade (2008)	Longitudinal, prospective	119	9	Civilian (AU), CABG	PDS	Optimism, illness representation, subjective health, types of coping	Severity of anxiety, depressive, and posttraumatic symptoms 6 months after CABG	Severity of anxiety, depressive, and posttraumatic symptoms 6 months after CABG predicted by different combinations of pre- and postoperative optimism, social support, avoidance coping, re-appraisal coping, illness representation, and subjective health status
Crosby, Mashour, Grodin, Jiang, and Osterman (2007)	Case report	1	1	Civilian, unspecified	Not specified	N/A	N/A	Case report of patient with preexisting PTSD who experienced a flashback accompanied by severe agitation after anesthesia

Table 1. Studies describing the perioperative outcomes or care of patients with preexisting PTSD

Article	Design	Sample size: Total	Sample size: Number with PTSD	Surgical population	Method of determining PTSD status	Independent variable(s)	Dependent variable(s)	Findings
Oxlad, Stubberfield, Stuklis, Edwards, and Wade (2006a)	Longitudinal, prospective	104	8	Civilian (AU); CABG	Modified PDS	Medical comorbidity, severity of anxiety, depressive, and posttraumatic symptoms before and immediately after CABG	Readmission to hospital for heart-related issues within 6 months of CABG	Cardiac-related admissions predicted by anxiety severity immediately after CABG.
Oxlad, Stubberfield, Stuklis, Edwards, and Wade (2006b)	Longitudinal, prospective	119	9	Civilian (AU); CABG	Modified PDS	Severity of anxiety, depressive, and posttraumatic symptoms before CABG	Hospital LOS after CABG	Severity of preoperative anxiety, depressive, and posttraumatic symptoms not predictive of postoperative LOS
Oxlad and Wade (2006)	Cross-sectional, prospective	119	9	Civilian (AU); CABG	Modified PDS	Illness perception, social support, subjective health, and coping	Severity of preoperative anxiety, depressive, and posttraumatic symptoms	Before CABG, avoidance coping mediates relationship between illness perception and posttraumatic symptom severity, and relationship between poor subjective health and depressive and posttraumatic symptoms

Table 1. Studies describing the perioperative outcomes or care of patients with preexisting PTSD

Article	Design	Sample size: Total	Sample size: Number with PTSD	Surgical population	Method of determining PTSD status	Independent variable(s)	Dependent variable(s)	Findings
Schreiber, Soskolne, Kozohovitch, and Deviri, (2004)	Longitudinal, prospective	63	23	Holocaust survivors (IS); CABG	IES	Global mastery, posttraumatic symptom severity, holocaust experience (ghetto, concentration camp, or other)	Subjective health	Posttraumatic symptom severity had significant effect on preoperative subjective health, pain, mobility, and energy level; posttraumatic symptom severity had significant effect on postoperative subjective health, emotional and social functioning

Note: PTSD = Posttraumatic stress disorder; CABG = Coronary artery bypass graft surgery; US = United States; ICD-9-CM = International Classification of Diseases, 9th Edition, Clinical Modification; LOS = Length of stay; NSD = No significant difference; PCL-C = Posttraumatic Check List – Civilian; PDS = Posttraumatic Diagnostic Scale; IES = Impact of Events Scale; CA = Canada; AU = Australia; IS = Israel.

2. The Perioperative Implications of Posttraumatic Stress Disorder

There are no established guidelines for the perioperative management of the patient with posttraumatic stress disorder (PTSD; Copeland et al. 2008). Studies suggest that patients with PTSD exhibit patterns of comorbidity, substance use, and psychoactive medication use that must be accounted for when planning an anesthetic. In addition, patients with PTSD can be very anxious during the perioperative process, and that anxiety can be ameliorated if the anesthetist adheres to certain basic tenets when interacting with the patient before and after surgery. Therefore, the purpose of this journal course is to familiarize the practicing nurse anesthetist with the perioperative implications of PTSD and suggest strategies for caring for patients with the disorder. To accomplish this purpose, this journal course will: (a) describe the epidemiology, phenomenology and treatment of PTSD; (b) systematically review the prevalence of PTSD in patients presenting for surgery, the comorbidities associated with PTSD, the relationship between PTSD and postoperative morbidity and mortality, and the potential effects of surgery on posttraumatic symptom severity, and; (c) suggest general strategies for interacting with and providing anesthesia care for the patient with PTSD.

2.1 Posttraumatic Stress Disorder

Posttraumatic stress disorder is an anxiety disorder that develops after exposure to a traumatic event. Approximately 6.8% of the US population will be diagnosed with PTSD at some point in their lives (Kessler et al. 2005). There are 17 recognized symptoms of PTSD, divided into three clusters (Table 1; American

Psychiatric Association 2000). In order for a patient to be diagnosed with PTSD, he or she must: (a) have been exposed to a traumatic event that evoked intense feelings of fear, hopelessness, or horror; (b) demonstrate at least one clinically significant symptom of reexperiencing, three clinically significant symptoms of avoidance or emotional numbing, and two clinically significant symptoms of persistent arousal; (c) have symptoms that persisted for at least one month, and; (d) have symptoms that adversely impacted functioning or resulted in significant distress (American Psychiatric Association 2000).

Although a clinician may not encounter a patient with PTSD until decades after the traumatic event, posttraumatic symptoms may still affect that patient's care. For many patients PTSD can become a chronic disorder that persists for decades, waxing and waning in severity (Solomon and Mikulincer 2006, Perconte, Griger, and Bellucci 1989). In addition, age-related cognitive decline may be associated with recurrence of clinically significant posttraumatic symptoms after decades of symptom remission (Mittal et al. 2001).

Studies account for PTSD in surgical patients by describing either the prevalence of a PTSD diagnosis amongst participants or the severity of posttraumatic symptoms in all subjects. When reporting the prevalence of PTSD, researchers identify and count patients who have been diagnosed with PTSD per the criteria set forth by the American Psychiatric Association (Brzezinski et al. 2009a, d, Dao et al. 2010, Hudetz et al. 2010, Ikossi et al. 2010). A limitation of studies describing the prevalence of PTSD is that a diagnosis of PTSD does not indicate the clinical severity of

posttraumatic symptoms at the time of surgery, as this diagnosis may have been made by a clinician months or years before the patient presents for surgery.

Table 2. Symptoms of posttraumatic stress disorder

Symptom Cluster	Symptom
Reexperiencing	Intrusive recollection
	Recurrent distressing dreams
	Flashbacks
	Psychological distress on exposure to trauma-related cues
	Physiological reactivity to trauma-related cues
Avoidance and emotional numbing	Avoidance of trauma-related thoughts, feelings, or conversations
	Avoidance of people, places and activities that are reminders of the trauma
	Inability to recall an important aspect of the trauma
	Diminished interest or participation in significant activities
	Feelings of estrangement or detachment from others
	Inability to experience positive feelings
	Sense of foreshortened future
Persistent arousal	Difficulty sleeping
	Irritability or outbursts of anger
	Difficulty concentrating
	Hypervigilance
	Exaggerated startle response

Source: From American Psychiatric Association. Desk Reference to the Diagnostic Criteria from the DSM-IV-TR. Washington, DC: American Psychiatric Association; 2000: 218-220.

In contrast, studies describing the severity of posttraumatic symptoms utilize posttraumatic symptom severity scales such as the Impact of Events Scale, the Post-traumatic Diagnostic Scale, or the PTSD Checklist-Civilian (Martin et al. 2010, Oxlad et al. 2006b, Schreiber et al. 2004, Page et al. 2009). Posttraumatic symptom severity scales are self-report instruments that require the respondent to subjectively rate the severity

of some or all of the 17 symptoms of PTSD. Patients reporting a posttraumatic symptom severity exceeding a certain threshold are likely to have PTSD, but a clinician must confirm the diagnosis because severity scores do not assess the exposure to a traumatic event or relative distribution of symptoms across clusters (Table 1) required to diagnose a patient with PTSD. Therefore, a limitation of studies describing only posttraumatic symptom severity is that they only estimate the true prevalence of PTSD, because measures of posttraumatic symptom severity are insufficient in isolation to diagnose PTSD. In addition, severity scales may be strongly affected by the presence of depression, as depressive symptoms overlap with posttraumatic symptoms (American Psychiatric Association 2000).

Dual representation is a predominant theory of how a patient develops and maintains PTSD after exposure to a traumatic event (Brewin, Dalgleish, and Joseph 1996). Dual representation theory posits that memories of a traumatic event exist in the form of verbally and/or situationally accessible memories. Verbally accessible memories are voluntarily accessible and have manageable emotional impact when recalled. In contrast, situationally accessible memories are accessed involuntarily in response to reminders of the trauma or during states of intense arousal, and are accompanied by an emotional state similar to that experienced during the traumatic event.

Posttraumatic stress disorder develops when situationally accessible memories of a traumatic event are accompanied by incomplete verbally accessible memories of that event. When triggered by reminders of the trauma or heightened states of emotional arousal, unopposed situationally accessible memories produce intense

emotional and somatic states similar to those experienced during the trauma, resulting in an over-generalized fear response. Cognitive and exposure therapies for PTSD assist the person to form verbally accessible memories of the information held in situationally accessible memories by talking about, imagining, or actually being exposed to trauma-related cues (Brewin 2001).

Although cognitive and exposure therapies are the mainstays of treatment, many patients with PTSD will receive some form of pharmacotherapy (Table 2). The first line medications for the treatment of PTSD are the selective serotonin reuptake inhibitors (SSRIs; Baker, Nievergelt, and Risbrough 2009). When SSRIs and time are ineffective in decreasing the severity of posttraumatic symptoms, additional medications may be added (Baker, Nievergelt, and Risbrough 2009).

Table 3. Medications used in the treatment of posttraumatic stress disorder and its comorbid conditions and symptoms

Drug Class	Medications	Notes and Anesthetic Safety Considerations
Selective serotonin reuptake inhibitors (SSRIs)	Sertraline[a]; paroxetine[a]; fluoxetine; citalopram; escitalopram; fluvoxamine	1st line treatment; preoperative withdrawal associated with greater risk of delirium in patients with depression (Kudoh, Katagai, and Takazawa 2002); administration of methylene blue associated with serotonergic crisis (Gillman 2006)
Selective norepinephrine reuptake inhibitors (SNRIs)	Venlafaxine; duloxetine	1st or 2nd line treatment; no anesthetic safety considerations noted
Monoamine oxidase inhibitors	Phenelzine	Rarely used secondary to side effects and dietary concerns; avoid ephedrine, meperidine, tramadol, methadone, and dextromethorphan due to risk of precipitating serotonergic crisis (Gillman 2005)
Tricyclic antidepressants	Imipramine; amytryptaline; desipramine; nortryptiline; doxepin	3rd line treatment for patients refractory to SSRIs/SNRIs; exaggerated response to sympathomimetic agents have been reported (Tung et al. 1981); Risk of prolonged QTc interval with nortryptiline (van Noord et al. 2009)
Tetracyclic antidepressant	Mirtazapine	2nd line treatment or adjunct treatment for insomnia; no anesthetic safety considerations noted
Monocyclic aminoketone antidepressant	Bupropion	3rd line treatment or adjunct for added antidepressant effect; lowers seizure threshold
Serotonin modulators	Trazodone; nefazodone	Adjunct therapy for insomnia; no anesthetic safety considerations noted

Table 3. Medications used in the treatment of posttraumatic stress disorder and its comorbid conditions and symptoms

Drug Class	Medications	Notes and Anesthetic Safety Considerations
Alpha antagonists	Prazosin	Adjunct therapy for nightmares; no anesthetic safety considerations noted
Anticonvulsants	Lamotrigine; tiagabine; topiramate; sodium valproate/valproic acid; carbamazepine	Third line treatment or adjunct for irritability, impulsivity and pain; no anesthetic safety considerations noted
Benzodiazepines	Alprazolam; lorazepam; clonazepam; diazepam; temazepam	Ineffective in the treatment of symptoms of reexperiencing, emotional numbing, and avoidance (Friedman 2003) but may be added as adjunct therapy for insomnia, irritability, anxiety, and panic; effects will be additive with sedatives administered perioperatively
Atypical antipsychotics	Quetiapine, ziprasidone; olanzapine; respiridone; aripiprazole	Adjunct treatment of insomnia, irritability, anger, anxiety, impulsivity and psychotic symptoms; refractory hypotension reported after spinal anesthesia with respiridone (Tarres and Villalonga 2005); Risk of prolonged QTc interval (van Noord et al. 2009)

Source: Data adapted from Baker, D. G., C. M. Nievergelt, and V. B. Risbrough. 2009. "Post-traumatic stress disorder: emerging concepts of pharmacotherapy." *Expert Opinion on Emerging Drugs* no. 14 (2):251-72.

[a] = Only FDA approved medications for PTSD

2.2 Prevalence of PTSD in Surgical Patients

The prevalence of posttraumatic stress disorder in surgical patients is associated with the presence of chronic pain and risk of having been traumatized. In patients presenting for major noncardiac surgery, 8% to 15% were either previously diagnosed with PTSD (Brzezinski et al. 2009a, d) or reported posttraumatic symptoms severe enough to suggest a diagnosis of PTSD (Page et al. 2009). In addition, patients who reported the presence of chronic pain before major elective surgery were more likely to demonstrate posttraumatic symptom severity indicative of a diagnosis of PTSD than patients who denied chronic pain (23% versus 10%) (Page et al. 2009). The prevalence of PTSD in patients undergoing cardiac surgery varies according to geographic location and the likelihood of previous exposure to trauma based on life course. In 2006 approximately 15% of patients who underwent coronary artery bypass graft surgery (CABG) in the United States were previously diagnosed with PTSD, while in two studies in Australia only 1% to 8% of patients presenting for cardiac surgery reported posttraumatic symptoms severe enough to suggest a diagnosis of PTSD (Dao et al. 2010, Oxlad et al. 2006a, b, Oxlad and Wade 2008, Tully et al. 2011). However, the prevalence of PTSD in patients presenting for cardiac surgery was greater in populations with exposure to traumatic events, with 35% of a sample of military veterans previously diagnosed with PTSD and 36% of a sample of Holocaust survivors reporting posttraumatic symptoms severe enough to indicate of a diagnosis of PTSD (Schreiber et al. 2004, Hudetz et al. 2010). Therefore, PTSD was more prevalent in patients who reported chronic pain, and in patients who are members of populations with greater risk of exposure to traumatic events.

2.3 Preoperative Risk Factors associated with PTSD

Patients with PTSD who present for surgery demonstrate greater prevalence of cardiovascular risk factors, depression, and substance abuse. Patients with PTSD also present for surgery with worse cognitive function than patients without PTSD. The presence of these risk factors likely arises from a combination of health risk behaviors and genetic liabilities.

2.3.1 Cardiovascular Risk Factors

Patients diagnosed with PTSD prior to surgery demonstrated greater prevalence of cardiovascular risk factors and this finding is most likely attributable to health risk behaviors. In patients presenting for major elective surgery, patients with PTSD had greater prevalence of hypertension, diabetes, and hypercholesterolemia than patients without PTSD despite being an average of six years of age younger (Brzezinski et al. 2009d). Patients with PTSD presenting for major elective surgery also had greater prevalence of risky health behaviors including smoking, drug abuse, and alcohol abuse than patients without PTSD (Brzezinski et al. 2009d).

2.3.2 Depression

A number of studies have noted an association between PTSD and depression. Among patients who underwent major noncardiac surgery, the prevalence of depression was 36% in patients with PTSD and 3.5% in patients without PTSD (Brzezinski et al. 2009d). Among patients who underwent coronary artery bypass graft surgery (CABG), the prevalence of depression was 53% to 61% in patients with PTSD, compared to 17% to 26% in patients without PTSD (Dao et al. 2010, Hudetz et al. 2010). The relationship between PTSD and depression extends to symptom severity:

posttraumatic symptom severity and depressive symptom severity were significantly correlated (r = 0.54) in patients awaiting CABG (Oxlad et al. 2006b). These results indicate that patients presenting for surgery with PTSD were more likely to have comorbid depression, and patients with more severe posttraumatic symptom severity were likely to have more severe depressive symptoms.

A portion of this relationship can be attributed to the similarity of posttraumatic and depressive symptoms. Depression and PTSD share the symptoms of loss of interest in significant activities, insomnia, and difficulty concentrating (American Psychiatric Association 2000), and items assessing these symptoms appear on measures of both depression and PTSD. However, studies on pairs of twins who served in the military during the Vietnam era have shown that PTSD and depression may share a common genetic liability. Pairs of monozygous twins were more likely than pairs of dyzygous twins to develop comorbid PTSD and depression when controlling for various life experiences, including exposure to traumatic events (Koenen et al. 2008). Therefore, depressive symptoms and posttraumatic symptoms correlate, and this correlation may arise from a genetic basis.

2.3.3 Substance Use

Among patients presenting for surgery, patients with PTSD demonstrated greater prevalence of alcohol, tobacco, and other drug abuse than patients without PTSD. Before major elective surgery, veterans with PTSD demonstrated three times greater prevalence of smoking (37.1% vs. 11.6%), five times greater prevalence of alcohol abuse (25.8% vs. 4.4%) and more than three times greater prevalence of other drug abuse (57.7% vs. 14.6%), compared to veterans without PTSD (Brzezinski et al. 2009d). Before CABG, veterans with PTSD demonstrated more than twice the

prevalence of alcohol dependence (50% vs. 20%) than veterans without PTSD (Hudetz et al. 2010). These findings were consistent with studies of outpatients with PTSD. Outpatient veterans with PTSD reported approximately twice the national average prevalence of tobacco, alcohol, and drug use (Buckley et al. 2004), and outpatient civilians with PTSD were more likely to abuse tobacco and drugs other than alcohol (Breslau, Davis, and Schultz 2003). The prevalence of concurrent substance abuse disorders and PTSD may represent self-medication of PTSD symptoms, or a vulnerability of the patient that facilitates the development of both substance use disorder and PTSD (Brown and Wolfe 1994). Therefore, patients with PTSD are more likely to be engaged in some form of substance use regardless of the setting in which they are encountered.

2.3.4 Cognitive Function

In addition to greater prevalence of cardiovascular risk factors and depression, patients with PTSD also demonstrate worse preoperative cognitive function. Before CABG, patients with PTSD demonstrated worse cognitive functioning on measures of verbal memory in comparison to both patients without PTSD and nonsurgical controls of similar age (Hudetz et al. 2010). This finding was consistent with previous research regarding the relationship between PTSD and cognitive functioning in nonsurgical populations that suggest that cognitive capability was inversely related to posttraumatic symptoms (Macklin et al. 1998, McNally and Shin 1995, Vasterling and Brailey 2005). In particular, patients with PTSD performed worse than controls without PTSD on tasks that required the respondent to immediately learn and retain new information for a short period of time, manipulate that information in a meaningful way, and produce a response based on the manipulated information, a set

of tasks collectively known as executive function (Beckham, Crawford, and Feldman 1998, Gilbertson et al. 2001, Hart et al. 2008). These findings suggest that the cognitive deficits associated with PTSD are concentrated in specific domains rather than affecting overall intelligence, and result in the patient having decreased cognitive reserve (Gilbertson et al. 2001, Hart et al. 2008).

These differential patterns of cognitive function in patients with PTSD suggest that PTSD is associated with less cognitive reserve. Cognitive reserve refers to the hypothesis that premorbid cognitive abilities create a buffer against the sequelae of degenerative neurological processes like Alzheimer's Disease, allowing cognition to undergo a process of graceful degradation as damage or disruption progresses (Purves 2008). When less cognitive reserve is present, less damage or disruption is required to produce overt clinical signs of brain dysfunction like dementia or delirium. Cognitive reserve has been estimated with proxies such as performance during neuropsychological testing and educational level (Stern 2009), and these proxies of cognitive reserve have demonstrated predictive validity for both delirium and cognitive decline after surgery (Greene et al. 2009, Monk et al. 2008, Moller et al. 1998).

To date, only one study has investigated PTSD as a predictor of cognitive decline after surgery. One week after CABG subjects with preexisting PTSD were more likely to demonstrate a decline in nonverbal memory, verbal memory, and executive function than subjects without PTSD (Hudetz et al. 2010). This finding suggests that patients with preexisting PTSD may be more vulnerable to cognitive decline after surgery and is consistent with the cognitive reserve hypothesis.

2.4 Postoperative Mortality

In large studies, preexisting PTSD was associated with greater risk of short and long-term postoperative mortality (Dao et al. 2010, Brzezinski et al. 2009a). A significantly greater proportion of patients with a diagnosis of PTSD or comorbid PTSD and depression died in hospital after CABG compared to patients without PTSD (Dao et al. 2010). In addition, patients with PTSD were approximately three times more likely to die within one or five years of undergoing major elective surgery than patients without PTSD, even after controlling for other predictors of mortality such as age, hypertension, diabetes, hypercholesterolemia, depression, and tobacco use (Brzezinski et al. 2009a). However, the investigators did not report on the statistical effect of interactions among predictors of mortality; that is, they did not report whether greater mortality was related to specific combinations of mortality predictors in a given patient (Brzezinski et al. 2009d). In addition, no studies to date have compared survival in patients with PTSD who underwent surgery with survival of patients with PTSD who did not undergo surgery. Therefore, data suggests that there was an association between preexisting PTSD and postoperative mortality, but does not elucidate whether this greater mortality was related to the presence of specific combinations of comorbid cardiovascular risk factors, to the severity of comorbid illness that was not captured by the databases, or to an effect of PTSD that was independent of surgery.

The greater risk of postoperative mortality in patients with PTSD may be an epiphenomenon unrelated to surgery. Studies of Vietnam-era veterans have demonstrated that since the war those with PTSD were more likely to die from cardiovascular and external causes, including suicide, homicide, and accidents, than

those without PTSD (Boscarino 2008a, 2006b, 2008b, 2006a). As noted, this greater mortality is likely mediated by health risk behaviors (Boscarino 2006b). Therefore, studies that estimate the risk of postoperative mortality in patients with PTSD in comparison to patients without PTSD may be confounding maturation and history; that is, studies may confound the natural maturation of mortality in patients with PTSD with the historical effect of having surgery. Such a comparison may lead to data that suggests that patients with PTSD are exposed to greater risk of mortality by undergoing surgery, when actually they are at greater risk of mortality than their peers without PTSD but the magnitude of risk is relatively unaffected by surgery.

2.5 Other Postoperative Outcomes

Despite its association with postoperative mortality, the presence of PTSD or severity of posttraumatic symptoms was unrelated to many other common metrics of postoperative outcome. Hudetz et al. (2010) reported that a previous diagnosis of PTSD was unrelated to length of ICU stay and six month incidence of hospital readmission after cardiac surgery. In addition, Oxlad et al. found that posttraumatic symptom severity was inversely related to length of ICU stay and unrelated to risk of rehospitalization within six months of surgery (2006b, a). After gastric bypass surgery, a previous diagnosis of PTSD was unrelated to length of hospital stay, incidence of postoperative complications, and one-year weight loss (Ikossi et al. 2010). Therefore, PTSD has not been demonstrated to be a predictor of hospital length of stay, readmission rate, or certain surgery-specific outcomes after cardiac or gastric bypass surgery.

2.6 Surgery and Posttraumatic Symptom Severity

At present, the effect of surgery on severity of posttraumatic symptoms is largely unknown. In the only study to report pre- and post-surgical posttraumatic symptom severity scores, Holocaust survivors undergoing cardiac surgery did not experience a significant increase in posttraumatic symptom severity from immediately before surgery to six months after surgery (Schreiber et al. 2004). After gastric bypass surgery, outpatient medical records indicated that mental health clinicians' global impressions were that posttraumatic symptom severity had improved in 41%, worsened in 8.3%, and remained unchanged in 50% of patients with preexisting PTSD (Ikossi et al. 2010). Although these studies did not find that surgery was associated with increased posttraumatic symptom severity, a case report provides anecdotal evidence of possible acute posttraumatic symptom exacerbation by perioperative experiences (Crosby et al. 2007). A young woman, who developed PTSD as a result of sexual and physical assault during a civil conflict in her home country, developed acute agitation immediately after emerging from general anesthesia. The patient became physically violent towards staff and had to be physically and chemically restrained. The patient later reported that during the episode she re-experienced her prior abuse, and that she attacked staff members because she thought that they were her original persecutors (Crosby et al. 2007). Therefore, the potential exists for surgery and anesthesia to exacerbate posttraumatic symptom severity when some aspect of the perioperative experience is similar to the patient's traumatic experience.

2.7 Clinical Implications

For many patients, PTSD can be a chronic illness associated with the accumulation of risk factors across the life course. Therefore, members of populations at high risk of developing the disorder should be asked if they have PTSD. There is only anecdotal evidence of posttraumatic symptom exacerbation after surgery, so if a patient has PTSD then alterations in the anesthetic plan should focus on managing comorbidities rather than preventing hypothetical behavioral problems. The patient with PTSD should be carefully assessed for cardiovascular risk factors, substance use, depression, chronic pain, and baseline cognitive impairment before surgery, and discussions of perioperative risk should focus on the contribution of the specific risk factors present in that patient. The presence of chronic pain may necessitate multimodal pain management techniques after surgery. In addition, certain medications used to treat PTSD can catastrophically interact with drugs commonly administered in the perioperative period and must be accounted for when planning the anesthetic (Table 2). However, psychoactive medications should generally be continued throughout the perioperative period to avoid side effects from acute withdrawal (Kudoh, Katagai, and Takazawa 2002, Warner et al. 2006).

In general, patients with PTSD are anxious in unfamiliar environments and around unfamiliar people (Foa, Keane, and Friedman 2000). Therefore, the operating room team should establish trust and reassure the patient that the environment is as safe as possible. Team members should calmly and slowly approach the patient in his or her field of vision, introduce themselves by name, and explain their role in the perioperative process. At all times staff should minimize loud unexpected noises and movements, and wake or gain the attention of patients verbally rather than by touch.

Furthermore, the team should emphasize that their goal is to make the patient as comfortable and safe as possible throughout the process of having surgery, and includes managing the patient's pain and anxiety. The overall goal is to ensure the patient understands and can anticipate what will happen throughout the perioperative process.

During assessment it is reasonable to briefly ask about potential triggers: "Is there anything specific that makes you really anxious, so that we can avoid upsetting you?" However, extensive discussion of traumatic events and posttraumatic symptoms can exacerbate anxiety (Foa, Keane, and Friedman 2000) and is therefore not prudent or informative during the preoperative interview. If the patient does report specific triggers, then efforts should be made to avoid exposing the patient to situations that could precipitate acute anxiety. Benzodiazepines and other drugs that produce short-term amnesia should be used judiciously and with caution because the patient may become agitated if he or she loses orientation to place and time. If the patient becomes acutely anxious or has a flashback, the presence of a trusted family member, friend, or medical provider may help the patient restore and maintain his or her orientation to the present place (Crosby et al. 2007).

2.8 Conclusions

Patients with preexisting PTSD present for surgery with risk factors that predispose them to greater postoperative morbidity and mortality, including greater prevalence of cardiovascular risk factors, depression, substance abuse, and chronic pain than patients without PTSD. Patients with PTSD also perform worse on preoperative measures of cognitive function and may be at greater risk of cognitive decline after surgery, but this finding has only been investigated in patients

undergoing cardiac surgery. Patients with PTSD demonstrate greater risk of short-term mortality after cardiac surgery and long-term mortality after noncardiac surgery in large studies, but the mechanism by which PTSD influences risk of mortality after surgery is unclear. Anecdotal evidence suggests that the perioperative process can transiently exacerbate PTSD symptoms, but the effects of surgery and anesthesia on posttraumatic symptom severity has only been explored in patients undergoing CABG.

There are many unanswered questions about the effect of surgery on patients with PTSD. Accurate estimation of risk of postoperative morbidity and mortality in this population is further confounded by the patterns of risk factors associated with PTSD, and at present there are no good theories in the literature that explicate a causal process between preexisting PTSD and greater risk of long-term mortality after surgery. Therefore, future research should aim to better define the contribution of PTSD to postoperative morbidity and mortality and to identify the unique perioperative needs of patients with PTSD.

3. Studying the Effect of Surgery on the Health of the Patient with Preexisting Posttraumatic Stress Disorder

Posttraumatic stress disorder (PTSD) is common, can be chronic, and has been associated with greater risk of postoperative mortality. As reviewed in Wofford, Hertzberg, and Vacchiano (In press), patients with preexisting PTSD present for surgery with risk factors that predispose them to greater postoperative morbidity and mortality, including greater prevalence of cardiovascular risk factors, depression, substance abuse and chronic pain than patients without PTSD. Patients with PTSD also demonstrate greater risk of short-term mortality after cardiac surgery and long-term mortality after noncardiac surgery in large studies, but the mechanism by which PTSD influences risk of postoperative mortality is unclear.

Understanding the relationship between PTSD and postoperative mortality is further complicated because posttraumatic symptom severity does not appear to be associated with traditional measures of postoperative morbidity, such as the incidence of postoperative complications, hospital length of stay, or surgery-related readmission rates (Oxlad et al. 2006a, b, Ikossi et al. 2010). However, veterans with PTSD were at least three time more likely than veterans without PTSD to die within one or five years of undergoing elective major surgery (Brzezinski et al. 2009a). In addition, greater posttraumatic symptom severity was associated with worse emotional, sleep, socia1, and cognitive functioning after surgery (Schreiber et al. 2004, Hudetz et al. 2010).

These findings may indicate that the causal process that links PTSD to mortality in this population is not captured by the traditional postoperative outcome measures like complication rates, hospital length of stay, or surgery-related hospital readmission. Therefore, a study is needed to explore alternative mechanisms by which surgery

might adversely affect the health of the patient with PTSD independent of these classical indicators of postoperative morbidity.

One commonality of all of these studies was that their analyses compared the outcomes of patients with preexisting PTSD with the outcomes of patients without PTSD. However, longitudinal cohort studies that compare the risk of postoperative mortality in patients with PTSD to that of patients without PTSD may be confounding maturation and history; that is, studies may confound the natural maturation of mortality in patients with PTSD with the historical effect of having surgery. Such a comparison may lead to data that suggests subjects with PTSD are exposed to greater risk of mortality by undergoing surgery, when actually their risk of mortality is greater than that of their peers without PTSD but unaffected by surgery. Therefore, a gap in the literature is that the effect of surgery on the patient with PTSD is only known in comparison to the effect of surgery on the patient without PTSD, and not in comparison to the patient with PTSD who does not undergo surgery. This is an important distinction, because some surgeries are elective and may be deferred indefinitely. Therefore, a research study is needed to address that gap by comparing the health of patients with PTSD who undergo elective surgery with that of patients with PTSD who do not undergo surgery.

However, there are obstacles to comparing surgical and nonsurgical patients with PTSD. Obviously, nonsurgical patients do not generate traditional postoperative outcomes like hospital length of stay, postoperative complication rates, or surgery-related hospital readmission rates. Therefore, other meaningful outcome criteria must be selected upon which to compare surgical and nonsurgical subjects with PTSD. Mortality would be one such criterion; however, mortality is a very distal outcome,

requiring very long durations of data collection and very large sample sizes to study effectively. Subjective health status is another possible outcome upon which to compare surgical and nonsurgical subjects with PTSD. Subjective health is the patient's assessment of his or her own health status, and is a holistic concept that includes aspects of physical, mental, and social well-being (Covinsky et al. 1999, Smith, Avis, and Assmann 1999).

Subjective health status captures the adverse effects of surgical diagnosis-related pain and disability. Before common elective surgeries, patients report greater pain, worse physical role performance, and worse physical functioning that returns to or exceeds baseline within a few weeks or months after surgery (Wellwood et al. 1998, Burney and Jones 2002, Busija et al. 2008, Langenbach et al. 2008, Shi et al. 2009). Therefore, subjective health may be a means to measure the effect of surgery on the patient with preexisting PTSD. Subjective health also demonstrates predictive validity for mortality; numerous studies have demonstrated that both veteran and civilian outpatients with worse subjective health, or declines in subjective health over time, demonstrate greater risk of mortality (Idler and Benyamini 1997, Idler and Kasl 1991, Fan et al. 2004).

3.1 Trajectory Theory

The relationship of health change with time can be viewed within the context of the trajectory theory of chronic illness (Corbin and Strauss 1991, Corbin 1998). In trajectory theory, an individual's experience (i.e., trajectory) of chronic illness is unique, but will consist of nine distinct phases: pretrajectory, trajectory, stable, unstable, acute, crisis, comeback, downward and dying (as illustrated in Figure 1). The stable phase is characterized by illness symptoms that are well controlled, and unstable

phases occur when the individual is unable to control illness symptoms. Inability to control symptoms may lead to a crisis phase in which acute care is necessary. Crisis phases are followed by either comeback phases during which the individual's health and disability returns to a tolerable level, or a downward phase with progressive increases in disability and symptoms. The downward phase culminates in a dying phase. Each individual's trajectory is influenced by a multitude of factors, including the pathophysiology of the disease and the actions of the individual, the individual's support system, and actions of the health care team.

Surgery is a period of acute health instability for all patients, and subjective health status captures the adverse effects of surgery-related pain and disability. Patients undergoing surgery should experience an initial decline in subjective health status, followed by a return to baseline a few weeks or months after surgery (Wellwood et al. 1998, Burney and Jones 2002, Busija et al. 2008, Langenbach et al. 2008, Shi et al. 2009). Therefore, health trajectory can be operationalized with repeated measurements of subjective health status, itself an independent predictor of mortality.

Studies suggest that psychological distress has an adverse effect on health over time. Farmer and Ferraro (1997) reported a self-reinforcing relationship between chronic physical illness, psychological distress, and physical disability over time in older adults . In this study, repeated measurements of these variables over time demonstrated that more severe chronic physical illness was associated with greater anxiety and worry, greater anxiety and worry was associated with worse perceived disability, and worse perceived disability was associated with more severe chronic physical illness.

3.1.1 Postoperative Health Trajectory and PTSD

Patients with PTSD may be at even greater risk from the erosive effects of psychological distress on health over time. In outpatients, PTSD was associated with worse subjective health status, including greater pain, greater impairment of role performance, worse physical functioning, and worse overall physical health (Buckley et al. 2004). This finding may be the result of information processing biases in PTSD that cause the patient to negatively interpret ambiguous health cues (Constans 2005). Comorbid depression would likely further worsen the patient's interpretation of subjective health, as patients with depression also demonstrate attentional biases towards negative internal and external emotional cues (Leppanen 2006), which would worsen interpretation of the social and mood-related aspects of subjective health. Therefore, a study investigating the effects of surgery on the patient with PTSD should assess for changes in both posttraumatic and depressive symptom severity.

Within the framework of trajectory theory, the relative contributions of surgery, as well as distress in the form of posttraumatic symptom severity, depressive symptom severity, anxiety and pain, to health trajectory, may be analyzed. If patients with preexisting PTSD are harmed by elective surgery, or do not benefit from undergoing elective surgery, then they should display postoperative subjective health declines from which they do not recover.

3.2 Research Questions

The purpose of this study was to address two gaps in the literature about the effect of surgery on patients with PTSD. First, this study sought to quantify the effect of elective surgery on the physical and mental health of patients with PTSD. Second,

this study sought to explore what factors patients with PTSD felt were associated with improvements or declines in physical and mental health after elective surgery. The following were the research questions for this study:

1. Does undergoing elective outpatient surgery affect the physical health of patients with preexisting PTSD?

2. Does undergoing elective outpatient surgery affect the mental health of patients with preexisting PTSD?

3. What preoperative characteristics of the patient with preexisting PTSD predict mental and physical health change after elective surgery?

4. From the perspective of the patient with PTSD, what factors were associated with positive or negative health change after elective surgery?

3.3 Research Design and Methods

3.3.1 General Study Design

This was a longitudinal, quasi-experimental, concurrent, embedded mixed-methods study. To address research questions 1-3, subjective health, posttraumatic symptom severity, depressive symptom severity, situational anxiety, and pain severity were compared over a three-month period between a sample of subjects with pre-existing PTSD who underwent outpatient elective surgery and a sample of subject with pre-existing PTSD who did not undergo outpatient elective surgery. To address research question 4, those patients who demonstrated greater than one standard deviation of change in subjective health status scores from baseline, or reported substantial subjective physical and mental distress or improvement after elective surgery, were asked to participate in open-ended interviews. This use of purposive

deviant case sampling (Teddlie and Yu 2007) to obtain a sample for qualitative analysis allowed us to evaluate the effects of different levels of a known quantitative predictor (that is, subjective health status) with a more flexible qualitative research method, with the goal of explaining or describing the factors that contributed to the case becoming an outlier (Creswell 2009).

3.3.2 Setting and Sample

3.3.2.1 Setting

The setting for this research was the Durham Veterans Administration Medical Center (VAMC), a large tertiary care hospital that provides both perioperative and psychiatric care to the veteran population of much of northern North Carolina. Approximately 48 patients with PTSD undergo elective outpatient surgery at the Durham VAMC each month (T. Monk, MD, Durham, NC, personal communication, February 2010), making it an ideal location to recruit patients with preexisting PTSD undergoing elective outpatient surgery.

3.3.2.2 Sample

All subjects met the inclusion criteria: they were aged ≥ 18 with military service-connected lifetime or current PTSD status documented in the VA Computerized Patient Record System (CPRS), who were eligible for care at the Durham VAMC, community dwelling (that is, non-institutionalized), had not had surgery in the past year, were American Society of Anesthesiologists Physical Status Classification I to III (meaning an absence of life-threatening comorbidities), and could read and understand the English language as evidenced by ability to verbalize understanding of the consent form to the investigator. Subjects for the surgical group

were recruited from the preoperative clinic after they were scheduled for outpatient elective surgery. Subjects for the control group were recruited from the primary care and mental health clinics, and were not scheduled for elective surgery during their period of participation in the study. The rationale for these inclusion criteria were that all subjects were eligible for emergency mental health services at the Durham VAMC if necessary, and were not exposed to the confounding influence of other surgeries within the past year. Enrolling outpatients also allowed the results of the proposed study to potentially be generalized to the 62.7 % of surgical procedures performed on outpatients (Statistics 2010), and had the added benefit of disaggregating the effects of surgery and anesthesia from the potentially confounding influence of hospitalization.

Patients undergoing very minor, low risk surgical procedures such as phacotomy were excluded as minor procedures were scheduled to be performed under local anesthesia with sedation. Patients receiving very painful and extensive surgical procedures were also excluded, as they would be admitted to the hospital and exposed to the confounding influence of hospitalization as well as the effects of surgery and anesthesia. Otherwise eligible subjects with a history of dementia, organic mental disorder, schizophrenia, or current manic syndrome were excluded. These medical conditions affect the ability of the subject to cooperate during interviews and accurately recall health issues from the previous month. Subject with substance abuse/dependence other than alcohol/tobacco use were also excluded, as estimates for the effect of non-alcohol substance use on subjective health were not available in this population.

3.3.2.3 Sample size calculation

Power calculations indicated that a sample size of 60 (30 per group) was required to achieve at least 80% power to detect a medium to large effect size when testing the primary hypothesis that there would be a statistically significant difference in average change in subjective health from baseline to twelve weeks after surgery in patients undergoing elective surgery when compared to patients not undergoing elective surgery. Subjective health was defined as the subject's physical health component summary score on the Veterans Rand 36-item Health Survey (VR-36) (Kazis 2000). This power calculation was based on the assumptions that: (a) a type of hierarchical mixed effects model for repeated measurement known as random coefficients regression would be used to test for significant group differences in trajectory of change across time (group-by-time interaction); (b) the level of significance for the two-tailed statistical test would be 0.05, and; (c) an intention-to-treat analysis would be conducted. Assuming 70% within-person correlation across time points, a sample size of 30 per group would yield 80% power to detect an effect size of $f = 0.55$ when comparing the group-by-time trajectories; for f effect sizes, Cohen defines a medium effect size as 0.25 and a large effect size as 0.40 (Cohen 1988). When comparing between-condition differences at twelve weeks, a sample size of 30 per group would provide 80% power to detect an effect size of $d = 0.50$; for d effect sizes, Cohen defines a medium effect size as 0.50 and a large effect size as 0.80 (Cohen 1988). Thus, a sample size of 60 (30 per group) would provide 80% power to detect medium to large effects in terms of change in subjective health. A target sample size of 80, which represents an increase of 25% over the required sample size, was proposed to adjust for attrition so that there would be adequate power to conduct the primary

intent-to-treat analysis. Thus, 40 participants per group would provide at least 80% power to test for medium to large effect sizes.

3.3.3 Measures and Instruments

Data were collected using self-report instruments and structured clinical interviews. As part of each assessment the number of days since surgery for surgical patients and since enrollment for control group patients was recorded. In addition, the season in which each assessment occurred was recorded as a 4-level categorical variable (winter, spring, summer, or fall) for consideration as a covariate in analyses of mental health.

3.3.3.1 Demographics

Information including age, gender, ethnicity, educational level, planned surgical procedure, and outpatient medications were gathered from each subject at enrollment to allow sample description.

3.3.3.2 Subjective health

The Veterans Rand 36-item Health Survey (VR-36) (Kazis 2000) measures the subjective health concepts of physical functioning, role limitations due to physical problems, bodily pain, general health perception, vitality, social functioning, role limitations due to emotional problems, and emotional well-being using Likert-scale responses. The content of the VR-36 items are identical to those on the Medical Outcomes Study 36-Item Questionnaire (SF-36), but incorporate expanded five-point Likert scales to improve measurement of role functioning in the veteran population. Responses for each subjective health concept are averaged and compared to population norms to determine the score. In addition to the component scores, factor-based

composite T- scores can be calculated to measure the aggregate health concepts of overall physical subjective health status (Physical Component Summary, or PCS score) and mental subjective health status (Mental Component Summary, or MCS score). T-scores range from 0 - 100, with higher scores indicating better subjective health status (Williams et al. 2009, Smeeding et al. 2010, Kazis et al. 2004). The VR-36 and its parent instrument, the SF-36, have been extensively used to monitor the health of the veteran population, veterans with PTSD, and perioperative patients (Williams et al. 2009, Smeeding et al. 2010), and are recommended as measures of subjective health in veterans with PTSD by consensus of the Department of Veterans Affairs Research Office, the National Institute of Mental Health, and the U. S. Department of Defense (U.S. Department of Veteran Affairs Office of Research, National Institute of Mental Health, and U.S. Department of Defense. 2008).

3.3.3.3 Post-traumatic stress disorder severity

Posttraumatic symptom severity was measured with the Clinician Administered PTSD Scale (CAPS; Blake et al. 1995), a 30-item, semi-structured interview that uses directed questions with scoring criteria to both diagnose PTSD and measure PTSD severity. The PTSD severity score is determined by summing the ratings of 17 symptom criteria for frequency and severity on five-point Likert scales. Possible scores range from 0 to 136, with higher scores indicating greater PTSD severity. The CAPS is considered the "gold standard" for measurement of PTSD in veterans (Blake et al. 1995, Weathers, Keane, and Davidson 2001).

3.3.3.4 Depressive symptom severity

Depressive symptom severity was measured with the Geriatric Depression Scale (GDS; Yesavage et al. 1983). The GDS is a 30-item yes/no format questionnaire. Possible scores range from 0-30, with higher scores indicating greater depressive symptom severity. The GDS was selected for this study because the average veteran presenting for elective outpatient surgery at the Durham VAMC is 62 years of age, and with the hypothesis that the yes/no format of the questionnaire would reduce the common method variance of depressive symptoms with the VR-36 and State-Trait Anxiety Scale-State scale, both of which employed Likert-type items. Although developed to measure depressive symptom severity in older adults, the GDS demonstrates acceptable validity across the adult lifespan (Yesavage et al. 1982, Rule, Harvey, and Dobbs 1989).

3.3.3.5 Pain severity

Pain severity was measured with the Visual Analog Scale (VAS). The VAS consisted of a horizontal 100-millimeter line with the labels "no pain" and "the most pain you can imagine" at opposite ends. For the purpose of this study, subjects were asked to rate the average amount of pain they experienced over the previous 24-hour period by drawing a line perpendicular to the 100-millimeter scale denoting their pain severity. The score was the distance in millimeters from the end of the scale labeled "no pain" to the perpendicular line drawn by the subject. The VAS has used in many previous studies of postoperative pain (Breivik, Bjornsson, and Skovlund 2000).

3.3.3.6 Situational anxiety

Situational anxiety was measured with the State-Trait Anxiety Inventory-State scale (STAI-S; Spielberger et al. 1983). The STAI-S is a 20-item scale in which the subject rates his or her anxiety in the present and recent past using a 4-point Likert scale. Possible scores range from 20-80, with higher scores indicating greater anxiety. The STAI-S is a widely used measure of situational anxiety that has been translated into more than 40 languages (Lam, Michalak, and Swinson 2005, 109). The test-retest reliability of the STAI-S is purposely low to better capture the effect of situational factors on anxiety (Spielberger et al. 1983).

3.3.3.7 Qualitative interviews

All subjects who demonstrated ≥ 10 points of change in VR-36 scores from baseline or a previous assessment were approached to participate in an unstructured, interactive interview (Richards and Morse 2007). This criterion was selected because outpatient veterans who demonstrated ≥ 10 points of decline or improvement in VR-36 scores from baseline also demonstrated respectively greater or lesser risk of mortality over the subsequent year (Fan et al. 2004). Each interview began with the question: "Starting with the day you had surgery, tell me what has happened that made your health better or worse." Additional prompts were added and used as needed. All interviews were conducted in a quiet, private office at the Durham VAMC. Interviews were digitally audio recorded, transcribed verbatim, and redacted for identifying information by replacing named persons and locations with pseudonyms.

3.3.4 Procedures

3.3.4.1 Recruitment

After obtaining approval from the Durham VAMC and Duke University School of Nursing Institutional Review Boards, subjects for the control group were recruited from the Durham VAMC preoperative clinic. The researchers reviewed the CPRS problem list of patients scheduled for the preoperative clinic. Approximately 10 days in advance of their preoperative assessment, those patients who appeared eligible were mailed an informational letter describing the study, the time commitment, and the opportunity to opt out of being approached about participation during the preoperative visit. The letter also provided potential subjects with time to consider participation in the study, and allowed subjects to allot adequate time to complete enrollment if they desired to participate. Patients visited the D-VAMC approximately one week before surgery for pre-operative assessment. At that time, the Anesthesia Department Preoperative Clinic staff conducted a preoperative assessment and assigned each patient an American Society of Anesthesiologists Physical Status Classification, or standardized classification of health based on functional limitation. Patients who desired to participate were introduced to the investigators, who verified eligibility per inclusion/exclusion criteria and obtained informed consent.

Subjects for the control group were recruited by self-referral. Flyers were placed in the D-VAMC PTSD, mental health, and primary care clinics. Potential subjects contacted the investigators directly to indicate interest in participating and initiate enrollment. Investigators screened potential subjects over the phone, and arranged to meet interested and eligible potential subjects to obtain informed consent.

3.3.4.2 Data collection

Data collection was timed to provide parallel data from the surgical and control groups across the twelve weeks of enrollment. In the surgical group, data were collected on enrollment and at approximately one week, four weeks, and twelve weeks after surgery to coincide with the available research on health trajectory after outpatient elective surgery (Wellwood et al. 1998, Burney and Jones 2002, Busija et al. 2008, Langenbach et al. 2008, Shi et al. 2009). Enrollment for surgical group subjects occurred at the preoperative clinic appointment, approximately one week before surgery. In the control group, data were collected at the same time intervals. The measures collected at each time interval are presented in Table 1.

Immediately after verifying eligibility and obtaining informed consent, demographic information was collected from the subject and the VR-36, CAPS, GDS, VAS, and STAI-S were administered. At that time, subjects were also provided with a copy of the VR-36, the VAS, and a post-paid envelope. Subjects were compensated $50 for completing this assessment.

Approximately one week after surgery or enrollment, subjects in the surgical and control groups were asked to complete and return by mail the copy of the VR-36 and VAS they were given on enrollment. Subjects in the surgical group who completed and returned the VR-36 and VAS were compensated $25, and subjects in the control group who completed and returned the VR-36 and VAS were compensated $10. Subjects in the surgical group were compensated slightly more because of the added burden of completing the assessment one week after undergoing surgery, when postoperative pain and disability was particularly severe. Subjects in both groups were called one week after surgery or enrollment to remind them to complete and

return the instruments; subjects who did not return the VR-36 and VAS by 13 days after enrollment received an additional reminder call. Approximately four and twelve weeks after surgery or enrollment, subjects in both groups again returned to the Durham VAMC and completed the VR-36, CAPS, GDS, STAI-S, and the VAS. Subjects were compensated $50 for completing this assessment.

Subjects in both groups who completed all assessments were compensated $100 at the conclusion of their participation in the study. All informed consent, enrollment, and data collection was performed by a single study staff member, and took place in a private office at the Durham VAMC medical center, with the exception of the instruments returned by mail one week after surgery or enrollment, respectively.

Table 4. Schedule of assessments

			Assessment time point			
Construct	Instrument	Variable	Baseline	Week 1	Week 4	Week 12
Subject demographics	Subject information questionnaire	Demographic data	X			
Subjective health	Veterans RAND 36 item health survey (VR-36)	Physical and Mental Component Summary scores	X	X	X	X
PTSD severity	Clinician Administered PTSD Scale (CAPS)	Severity score	X		X	X
Depressive symptom severity	Geriatric Depression Scale (GDS)	Score	X		X	X
Pain severity	Visual Analog Scale (VAS)	Score	X	X	X	X
Situational anxiety	State-Trait Anxiety Inventory – State Scale (STAI-S)	Score	X		X	X
Factors influencing individual subjective health status change	Qualitative interview	Thematic content		X*	X*	X*

Note: "X" denotes measure administered at this time point; "*" denotes that qualitative interviews may be conducted in any surgical group subject demonstrating ≥ 10 point change in VR-36 score from the previous assessment

3.3.5 Quantitative Data Analysis

3.3.5.1 Data management

All quantitative data were double-entered into an Access database and converted into SAS 9.2 datasets for purposes of analysis, checked for missing or improperly entered values, and de-identified.

3.3.5.2 Statistical analysis

Prior to analysis, data were examined for normality and transformed as necessary. Non-directional statistical tests were conducted and the level of significance was 0.05 for each test. Due to the exploratory nature of this study, adjustment was not made for the multiple outcomes. The analysis was a modified intention-to-treat analysis that included all subjects enrolled in the study who had a baseline assessment, regardless of completion of the study.

For all analyses time was measured in days after surgery for surgical group subjects, and in days from enrollment for control group subjects. To decrease burden surgical group subjects underwent baseline assessment at the time of their preoperative appointment, approximately 1 week before surgery. However, for purposes of the data analysis the day of surgery was considered to be baseline, or day 1, for surgical group subjects, not the day of enrollment. For control group subjects the day of enrollment was considered to be baseline, or day 1.

Student *t*-tests for continuous measures and chi-square tests for categorical measures were conducted to test whether the surgical and control groups differed on key clinical and demographic characteristics and baseline scores for the specified outcome measures. If the groups differed significantly on a key baseline measure, then that baseline measure was examined as a potential covariate in subsequent analyses.

Note that the expectation was that the two groups would differ significantly in initial subjective health status (defined as VR-36 PCS and MCS scores) at baseline. This was addressed in the analytic approach described below.

3.3.5.2.1 Analysis of research question 1: Does undergoing elective outpatient surgery affect the physical health of patients with preexisting PTSD?

A random coefficients regression model approach, which is a type of hierarchical mixed effects model designed for longitudinal data, was used to test for differences in trajectories of change in longitudinal VR-36 PCS scores, which included assessments at baseline, four weeks, and twelve weeks in the two groups. The random coefficients regression model approach was applied because this model allows the intercept and slope of change for each patient to vary from baseline and from assessment to assessment. Therefore, the individual's trajectory of change over time interval was the dependent outcome (Brown and Prescott 2006). Originally used in econometrics and educational research, the random coefficients regression model approach is particularly advantageous in the present analysis because it allows assessment of the population-level effects of an intervention, as well as the effects of time-varying covariates within individuals, even when group members differ substantially in their initial level of the outcome of interest (Deleeuw and Kreft 1986).

Major advantages of a random coefficients regression model over a traditional repeated-measures analysis or examination of change score controlling for baseline was that the method: (a) provided improved estimates of individual effects; (b) allowed for missing data points over time; (c) adjusted for serial correlation (e.g., measurements not equally correlated across time); (d) allowed for incorporation of both time-independent and time-dependent covariates; (e) allowed for irregular measurement occasions (e.g., does not assume time intervals are equal), and; (f)

provided the ability to model patient-specific time trends (e.g., response to treatment or condition can be individualized).

Prior to constructing the random coefficients regression model of longitudinal PCS scores, mean PCS scores were graphed over time to visually examine the temporal pattern of change within each group over the course of data collection. If these graphs indicated that the temporal pattern change on mean PCS scores over time was non-linear, then quadratic, cubic, and square root polynomial effects of time would be tested.

The analytic model of longitudinal PCS scores included the following fixed effects: Group (surgical or control), time, the group-by-time interaction, and two covariates (age and gender). Random effects were subject and subject-by-time; intercepts and slopes were set to random. It was hypothesized that the two groups would have significantly different trajectories over time as evidenced by a significant group-by-time interaction. *A priori* contrasts of the trajectories generated by the model were conducted at one week, four weeks, and twelve weeks to test for significant differences in the groups at those time points.

Based on a review of the literature, it was expected that the surgical group would demonstrate lower PCS scores at baseline compared to the control group and would demonstrate a non-linear trend in PCS scores over time (Wellwood et al. 1998, Burney and Jones 2002, Busija et al. 2008, Langenbach et al. 2008, Shi et al. 2009). Subjective health scores would likely be lower in subjects scheduled to receive elective surgery, as such surgery is performed to improve physical health. Previous studies of physical subjective health change after outpatient elective surgery using the PCS demonstrated a transient decrease in physical subjective health status at four weeks

after surgery due to pain and functional limitation, followed by a return to baseline by twelve weeks after surgery (Wellwood et al. 1998, Burney and Jones 2002, Busija et al. 2008, Langenbach et al. 2008, Shi et al. 2009). In contrast, subjects in the control group should demonstrate stable or very slow change on PCS scores across the twelve-week study period. If PTSD did not have an adverse effect on subjective physical health recovery after surgery, then the surgical and control groups should differ significantly at baseline on PCS scores, but converge at 3 months as early declines in subjective health status between baseline and four weeks were offset by subjective health improvement between four and twelve weeks due to healing and the beneficial effects of the surgery. This was the expected trend after elective surgery. However, if elective surgery exerted a persistent adverse effect on the subjective physical health of the veteran with chronic PTSD, then surgical and control groups would differ significantly at baseline on PCS scores, and not converge at twelve weeks.

See Figure 1 for a graphical representation of these possible trends in subjective physical health status over time. The X-axis represents mean VR-36 PCS scores; the Y-axis represents weeks after baseline. The black line represents the expected mean VR-36 PCS scores over time of subjects in the nonsurgical group, demonstrating little to no change. The dotted grey line represents the projected mean VR-36 PCS scores over time of subjects in the surgical group if surgery if not associated with health decline; under this assumption, subjects are expected to experience an initial decline in subjective health followed by recovery to or beyond baseline. The dashed grey line represents the projected mean VR-36 PCS scores over time of subjects in the surgical group if surgery is associated with health decline; subjects experience an initial decline in subjective health status from which they do not recover.

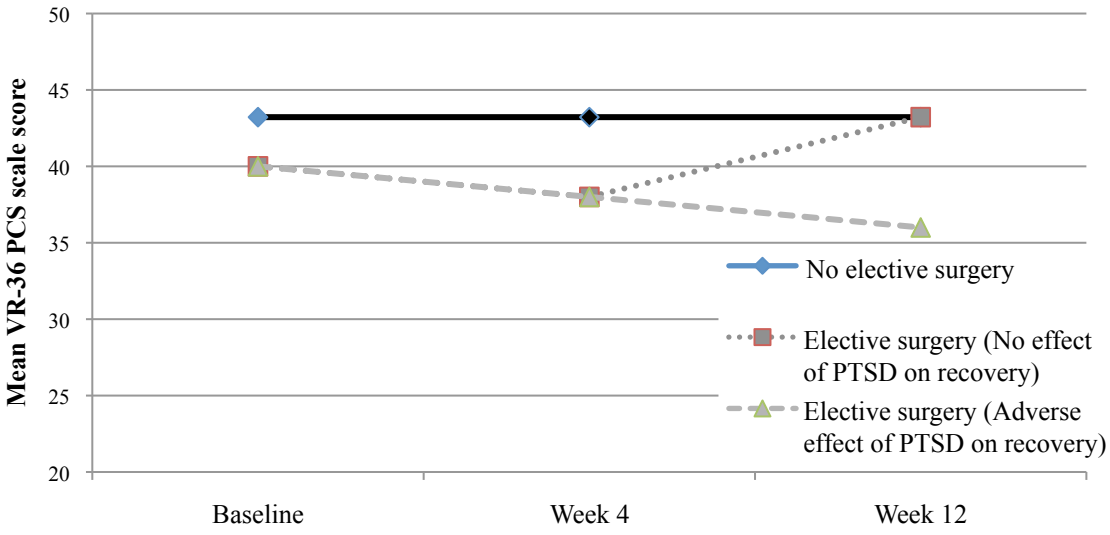

Figure 1. Projected trends of longitudinal VR-36 Physical Component Summary (PCS) scores in surgical and nonsurgical patients

3.3.5.2.2 Analysis of research question 2: Does undergoing elective outpatient surgery affect the mental health of patients with preexisting PTSD?

A series of random coefficients regression models were also used to test for differences in trajectories of change on longitudinal MCS scores, GDS scores, and CAPS severity scores. The random coefficients regression model of MCS scores included assessments at baseline, one week, four weeks, and twelve weeks in the two groups. The random coefficients regression models of GDS scores and CAPS severity scores included assessments at baseline, four weeks, and twelve weeks in the two groups. The random coefficients regression model approach was applied because such models allow the intercept and slope of the change for each patient to vary from baseline and from assessment to assessment. Therefore, the individual's trajectory of change in MCS scores, GDS scores, or CAPS severity scores over time interval was the dependent outcome for each analysis (Brown and Prescott 2006). The advantages of the random coefficients regression model approach were previously described in detail under the analysis of research question 1.

Prior to constructing each random coefficients regression model, the dependent variable (i.e., mean MCS scores, GDS scores, or CAPS severity scores) was graphed over time to visually examine the temporal pattern of change within each group. If these graphs indicated that the temporal pattern of change in longitudinal MCS scores was non-linear, then quadratic, cubic, and square root polynomial effects of time were tested.

Therefore, the analytic model of longitudinal MCS scores included the following fixed effects: group (surgical or control), time, the group-by-time interaction, and three covariates (age, gender, and season). Random effects were subject and subject-by-time; intercepts and slopes were set to random. It was hypothesized that the two groups would have significantly different trajectories over time as evidenced by a significant group-by-time interaction. In the event of a significant group-by-time interaction, contrasts of the trajectories generated by the model would be conducted at each time point to test for significant differences in the groups on MCS scores.

Separate random coefficients regression models were used to test for differences in trajectories of change in GDS scores and CAPS severity scores at baseline, four weeks, and 12 weeks after surgery or enrollment. Each analytic model of longitudinal GDS scores or CAPS severity scores included the following fixed effects: group (surgical or control), time, the group-by-time interaction, and two covariates (age and gender). Random effects were subject and subject-by-time; intercepts and slopes were set to random. It was hypothesized that the two groups would have significantly different trajectories over time as evidenced by a significant group-by-time interaction. In the event of a significant group-by-time interaction, contrasts of

the trajectories generated by each model were conducted at each time point to test for significant differences in the groups on GDS scores or CAPS severity scores.

3.3.5.2.3 Analysis of research question 3: What preoperative characteristics of the patient with preexisting PTSD predict mental and physical health change after elective surgery?

A series of random coefficients regression models were used to test for the effects of age, gender, baseline GDS scores, baseline CAPS severity scores, baseline VASP scores, or baseline STAI-S scores on trajectory of change on PCS or MCS scores at baseline, 1 week, 4 weeks, and 12 weeks in surgical group subjects only. Prior to constructing the random coefficients regression models, mean PCS or MCS scores were graphed over time to visually examine the temporal pattern of change within only surgical group subjects at baseline, one week, four weeks, and 12 weeks after surgery. If these graphs indicated that the temporal pattern of change in PCS or MCS scores over time was non-linear, then quadratic, cubic, and square root polynomial effects of time were tested.

Next, a set of random coefficients regression models of the PCS or MCS trajectory were applied to PCS or MCS scores at one week, four weeks, and twelve weeks in the surgical group only. Each analytic model included the following fixed effects: time and one of the candidate predictor variables (age, gender, baseline CAPS severity score, baseline GDS score, baseline VASP scores, or baseline STAI-S score). Random effects were subject and subject-by-time for all models. Any baseline predictor variable that was significant at the 0.10 level would be retained for further testing.

Next, all retained baseline measures were entered into the model simultaneously to examine the influence of each after controlling for all other

explanatory variables in the models. The independent variables included in these models were examined for multicollinearity and influential outliers. The final model included: (a) the fixed effects of time since surgery and baseline PCS or MCS score; (b) the random effects of subject and subject-by-time, and; (c) the main effects of baseline covariates that were significant at the 0.05 level after controlling for all other variables in the model and eliminating multicollinear variables.

3.3.6 Qualitative Data Analysis

3.3.6.1 Data management

Digital audio recordings of the interviews were labeled with the random number of the subject to whom they belonged, transcribed verbatim into Word documents on the VA secure server, checked for accuracy against the original recordings, and de-identified by assigning pseudonyms to any persons or places named during the interview.

3.3.6.2 Analysis of research question 4: From the perspective of the patient with PTSD, what factors were associated with positive or negative health change after elective surgery?

To answer this research question, qualitative content analysis was used to analyze the unstructured, interactive interviews collected from participants who demonstrated significant change in physical or mental health after surgery. After ensuring transcription accuracy, each interview was read, the topics described by the participant were identified, and an abstract of each topic was written. Within each topic the events, situations, thoughts, and feelings described by the participants were examined. These events, situations, thoughts, and feelings were compared within the same interview and across interviews with other subjects to arrive at codes, or

categories that were sufficient to encompass very similar topics but distinct from other topics. The thought process used to arrive at those codes was documented, and additional codes were created as necessary to encompass new topics described by participants (Sandelowski 1995). Ideally, each code could be distinctively depicted by quoting verbatim a statement from a participant in the context that participant intended (Sandelowski 1994). A researcher with extensive research in qualitative data analysis (JB) audited all analyses. The guiding principal of this data analysis was to construct a thorough description of the factors that subjects believed contributed to health change after elective surgery. Enrollment continued so long as surgical group subjects were available who met criteria for interview. After analysis of all interviews, the findings were summarized in lay language and mailed to participants as a member check to elicit their opinions (Carlson 2010). Participant responses to this member check were incorporated into the findings presented here.

3.4 Summary

This research design will allow quantification of the effects of common elective outpatient surgeries on the subjective health status of veterans with PTSD while exploring potential mechanisms for that effect. Veterans with PTSD have numerous reasons for recovering poorly from elective surgery, including greater prevalence of cardiovascular risk factors, depression, substance abuse and chronic pain, than patients without PTSD. Any or all of these risk factors and comorbidities could be associated with poor recovery in this population The use of this longitudinal mixed method design will also help guide interpretation of the results of the study, provide effect sizes to help estimate sample sizes for future studies, and suggest future avenues of research.

4. Causes of Change in Health Status after Elective Surgery in Patients with Preexisting Posttraumatic Stress Disorder

Posttraumatic stress disorder (PTSD) is common, can be chronic, and has been associated with greater risk of postoperative mortality. Characterized by avoidant behavior, physiological reactivity, emotional numbing, intrusive thoughts, and unwanted recurrent memories, PTSD is an anxiety disorder that develops after exposure to a traumatic event and persists for at least one month (American Psychiatric Association 2000). The lifetime prevalence of PTSD in the United States is estimated to be 6.8% (Kessler et al. 2005). The prevalence is greater in military veterans, with 9% to 43% demonstrating the disorder (Vasterling et al. 2010, Hoge and Castro 2006, Hoge et al. 2004, Dohrenwend et al. 2006, Blake et al. 1990). The greater prevalence of PTSD in military veterans means that at military treatment facilities and Veterans Affairs Medical Centers (VAMCs) a substantial number of patients presenting for surgery will have PTSD. For example, at one VAMC over a 12-year period, 9.4% of all elective surgical procedures requiring hospital admission were on patients with PTSD (Brzezinski et al. 2009b).

Although these veterans' symptoms may improve with treatment, our experience with the Vietnam veteran population has taught us that PTSD does not just "go away" with time. For example, a longitudinal study (Solomon and Mikulincer 2006) of Israeli combat veterans who participated in the 1984 Lebanon conflict demonstrated a 38% incidence of PTSD one year after exposure and 19% incidence of PTSD 20 years after exposure to combat. American veterans demonstrate similar

patterns of chronicity: Fifteen years after the end of the Vietnam War, 15-30% of Vietnam veterans still met diagnostic criteria for PTSD (Kulka 1990).

The prevalence of PTSD among surgical patients is troubling because PTSD has been associated with greater risk of long-term postoperative mortality (Dao et al. 2010, Brzezinski et al. 2009a). In veterans undergoing elective surgery requiring admission to the hospital, patients with PTSD were at least three time more likely than patients without PTSD to die within one or five years of surgery, despite controlling for other predictors of mortality such as age, hypertension, diabetes, hypercholesterolemia, depression, and tobacco use (Brzezinski et al. 2009a). In the 2006 Nationwide Inpatient Database, a significantly greater proportion of patients with a diagnosis of PTSD or comorbid PTSD and depression died in hospital after coronary artery bypass graft surgery (CABG) compared to patients without PTSD, even after controlling for age and burden of comorbidities (Dao et al. 2010).

However, the causal process that links PTSD to greater risk of postoperative mortality is unclear. In a sample of veterans undergoing gastric bypass surgery, preexisting PTSD did not affect length of hospital stay, the incidence of postoperative complications, or the mean amount of weight lost after one year (Ikossi et al. 2010). In a sample of patients undergoing CABG, posttraumatic symptom severity was not related to traditional measures of postoperative morbidity such as the incidence of postoperative complications, hospital length of stay, or surgery-related readmission rates (Oxlad et al. 2006a, b). These findings may indicate that the causal process that links PTSD to mortality in this population is not captured by the traditional postoperative outcome measures like hospital length of stay, complication rates, or surgical-diagnosis related hospital readmission.

The greater risk of postoperative mortality in patients with PTSD may be an epiphenomenon unrelated to surgery. Studies of Vietnam era veterans have demonstrated that since the war those with PTSD were more likely to die from cardiovascular and external causes, including suicide, homicide, and accidents, than those without PTSD (Boscarino 2008a, 2006b, 2008b, 2006a). Veterans with PTSD also demonstrate greater prevalence of comorbidities that increase their risk of mortality, such as diabetes, asthma, stroke, myocardial infarction, cancer, and liver cirrhosis, (David et al. 2004, Buckley et al. 2004). The relationship between PTSD and the accumulation of these chronic conditions is likely mediated by health risk behaviors. Patients with preexisting PTSD report little physical exercise and greater than national average prevalence of alcohol, tobacco, and drug use (Buckley et al. 2004, Anthony, Warner, and Kessler 1994, Boscarino 2006b). Depression is also highly comorbid with PTSD, likely because the disorders have overlapping symptoms and share some common neurochemical aberrations. Studies have reported a prevalence of preoperative comorbid depression of 36% to 61% in patients with PTSD, compared to 3.5% to 26% in patients without PTSD (Brzezinski et al. 2009d, Dao et al. 2010, Hudetz et al. 2010), and depression is an independent predictor of mortality in older adults (Schulz et al. 2000). The presence of these comorbidities and health risk behaviors would place any patient at greater risk for morbidity and mortality after surgery, regardless of PTSD status (Wolters et al. 1996).

4.1 Exploring the Health Effects of Elective Surgery on Veterans with Chronic PTSD

The existing studies demonstrate that postoperative outcome criteria other than hospital length of stay, surgery-related readmission rates, and surgical complication

rates must be investigated to better describe and understand the health effects of surgery on the patient with PTSD. Mortality would be one such criterion; however, mortality is a very distal outcome, requiring very long durations of data collection and very large sample sizes to effectively test hypotheses. Subjective health status is another possible outcome that could be used to describe health and measure health decline in this population after surgery. Subjective health is the patient's assessment of his or her own health status, and is a holistic concept that includes aspects of physical, mental, and social well-being (Covinsky et al. 1999, Smith, Avis, and Assmann 1999).

Both surgery and PTSD have independent effects on subjective health status. In outpatients, PTSD was associated with worse subjective health status, including greater pain, greater impairment of role performance, worse physical functioning, and worse overall physical health (Buckley et al. 2004). This finding may be the result of information processing biases in PTSD that cause the patient to negatively interpret ambiguous health cues (Constans 2005). Comorbid depression would likely further worsen the patient's interpretation of subjective health, as patients with depression also demonstrate attentional biases towards negative internal and external emotional cues (Leppanen 2006), which would worsen interpretation of the social and mood-related aspects of subjective health.

Subjective health status also captures the adverse effects of surgical diagnosis-related pain and disability. Before common elective surgeries, patients report greater pain, worse physical role performance, and worse physical functioning that return to or exceed baseline within a few weeks or months after surgery (Wellwood et al. 1998, Burney and Jones 2002, Busija et al. 2008, Langenbach et al. 2008, Shi et al. 2009). Therefore, subjective health may be a means to track the relative health effects of PTSD

and surgery in surgical patients with PTSD. Subjective health also demonstrates predictive validity for mortality: Numerous studies have demonstrated that outpatients with worse subjective health or declines in subjective health demonstrate greater risk of mortality (Idler and Benyamini 1997, Idler and Kasl 1991, Fan et al. 2004).

Although subjective health status can provide a means to describe *what* the effect of elective surgery is on health in veterans with PTSD undergoing elective surgery, it cannot suggest *why* those changes have occurred. The greater risk of mortality observed after elective surgery in veterans with PTSD could be associated with the surgery itself, with the underlying health problems and practices associated with having PTSD, or even with a complex combination of the two. In situations where the researcher is attempting to understand a complex situation about which little is known, premature attempts to reduce data to a set of statistically testable assumptions may preclude or obscure relationships among the phenomena under consideration (Richards and Morse 2007). In such situations, qualitative methods may provide the best means to describe the phenomena under consideration (Richards and Morse 2007). Therefore, the purpose of this study was to investigate reasons why patients with PTSD felt better or worse over time after having elective surgery.

4.2 Methods

Unstructured, interactive interviews (Richards and Morse 2007) were used to allow subjects with PTSD to describe factors associated with mental and physical health improvement and/or decline over time after elective outpatient surgery. Subjects were recruited using purposive deviant case sampling (Teddlie and Yu 2007). As part of a larger, longitudinal quasi-experimental study measuring the effect of

elective outpatient surgery on the mental and physical health of patients with PTSD at a large Veterans Affairs Medical Center (VAMC), subjects who demonstrated ≥10 points of improvement or decline from baseline in subjective health status were asked to participate in an unstructured, interactive interview. For the purposes of this study, subjective health status was defined as the participant's Mental Component Summary (MCS) or Physical Component Summary (PCS) scores on the Veterans Rand 36-item Health Survey (VR-36), a population specific variant of the Medical Outcomes Study 36-Item Health Survey. The criterion of ≥ 10 points was selected because a previous study in veteran outpatients demonstrated that this degree of change in PCS and/or MCS scores was associated with greater risk of 1-year mortality. During the course of the study several patients were noted to have very low MCS or PCS scores at baseline due to preexisting chronic mental and/or physical illness; because these patients had no room to demonstrate further decline in their health, the decision was made to interview them if they endorsed a particularly distressing subjective change in mental or physical health so that their experiences would not be lost from the study. For example, one participant was interviewed because of suicidal ideation culminating in a suicidal gesture, while another was interviewed who suffered a severe flashback in the recovery room. Participants who met these criteria were interviewed at one week, one month, and/or three months after surgery. Interviews were repeated whenever participants demonstrated ≥ 10 points of change in MCS and/or PCS scores, so long as the subject was available and willing to participate. This use of deviant case sampling to obtain a sample for qualitative analysis allowed us to evaluate the effects of different levels of a known quantitative predictor (that is, MCS and/or PCS scores) with a more

flexible qualitative research method, with the goal of explaining or describing the factors that contributed to the case becoming an outlier (Creswell 2009).

All subjects were aged ≥ 18 with military service-connected lifetime or current PTSD status documented in the VAMC Computerized Patient Record System, community dwelling (that is, non-institutionalized), underwent outpatient elective surgery within the prior three months, had not had undergone any other surgeries in the past year, and could read and understand English. Subjects were also American Society of Anesthesiologists Physical Status Classification I to III (meaning an absence of life-threatening comorbidities). Subjects with a history of dementia, organic mental disorder, schizophrenia, current manic syndrome, and current substance dependence other than alcohol/tobacco use were excluded.

The rationale for these inclusion criteria were that (a) all subjects were eligible for emergency mental health services at the Durham VAMC if necessary; (b) subjects did not have the potentially confounding risk of surgery within the past year; (c) patients undergoing very minor, low risk surgical procedures such as phacotomy were excluded as such procedures are performed under local anesthesia with sedation; and (d) patients receiving very painful and extensive surgical procedures were excluded, as they were admitted to the hospital. Enrolling outpatients allows the results of the proposed study to potentially be generalized to a larger population, as in the United States 62.7 % of surgical procedures are performed on (Statistics 2010). Enrolling outpatients also had the added benefit of disaggregating the effects of surgery and anesthesia from the potentially confounding influence of hospitalization.

4.2.1 Procedures

After receiving approval from the Institutional Review Board of the Durham VAMC, data were collected over a 14-month period using unstructured, interactive interviews. Each interview began with the question: "Starting with the day you had surgery, tell me what has happened that made your health better or worse." Additional prompts were added and used as needed. All interviews were conducted in a quiet, private office at the Durham VAMC. Interviews were digitally audio-recorded, transcribed verbatim, and redacted for identifying information by replacing named persons and locations with pseudonyms.

4.2.2 Data Analysis

After ensuring transcription accuracy, each interview was read and the topics described by the participant were identified, and an abstract of each topic was written. Within each topic the events, situations, thoughts, and feelings described by the participants were examined. These events, situations, thoughts, and feelings were compared within the same interview and across interviews with other subjects to arrive at codes or categories that were sufficient to encompass very similar topics but distinct from other topics. The thought process used to arrive at those codes was documented, and additional codes were created as necessary to encompass new topics described by participants (Sandelowski 1995). Ideally, each code could be distinctively depicted by quoting verbatim a statement from a participant in the context that participant intended (Sandelowski 1994). A researcher with extensive research in qualitative data analysis (JB) audited all analyses. The guiding principal of this data analysis was to construct a thorough description of the factors that subjects believe contributed to health change after elective surgery. Enrollment continued so long as

patients were available and consented to participate in interviews. After analysis of all interviews, the findings were summarized in lay language and mailed to participants as a member check to elicit their opinions (Carlson 2010). Participant responses to this member check were incorporated into the findings presented here.

4.3 Results

The sample consisted of 2 women and 12 men; 5 were African-American, 1 was a Pacific Islander, and 8 were Caucasian. All had at least a high school education, and half had attended between 1 and 4 years of college. Two participants were aged 30-39 years, 5 were aged 40-49 years, 1 was aged 50-59 years, and 6 were aged 60-69 years. Twelve participants lived with their spouse or significant other; 2 primarily lived alone but had children who resided with them on a part-time basis. As to employment status at the time of the study, 9 participants were either fully retired or medically disabled, three remained employed full- or part-time, and two were full-time students working toward college degrees. Additionally, all participants received varying amounts of disability pension compensation from the Veterans Administration or military retirement pay from the Department of Defense. The amount of time that had elapsed since participants experienced their traumatic event ranged from 4 and 45 years, with a mean of 24.4 years. Twelve of the 14 participants were diagnosed with some source of chronic pain at enrollment, but only 2 of the 14 participants sustained injuries during their traumatic experiences.

Interviews occurred 1-3 times per participant and lasted between 4 and 24 minutes. Although not an end point of enrollment, saturation occurred after analyzing the first interview of the twelfth participant, after which an additional two additional participants were interviewed to ensure that no new categories would emerge.

Participants identified four major categories of factors that influenced their physical and mental health during and after undergoing elective outpatient surgery: (a) preexisting chronic pain and disability; (b) the elective surgery itself; (c) the health care system, and; (d) friends and family.

4.3.1 Preexisting Chronic Pain and Disability

Almost all participants identified chronic pain and disability as factors that influenced their physical and mental health during recovery. This pain and disability predated the elective surgery and may or may not have been related to the purpose of the surgery. Regardless of its relationship to the reason for the patient electing to have surgery, this chronic pain continued to exert an independent, adverse effect on the health of participants as they recovered. One phenomenon observed in this sample was a shift in the content of the interviews over time: Among participants interviewed multiple times, content describing the impact of chronic pain and disability tended to appear in later interviews.

Participants described living with and managing back, neck, knee, and shoulder pain, as well as migraines. Regardless of the source, this chronic pain and disability aversely affected patient's mental and physical health throughout the process of recovering from surgery. One participant described living with chronic back pain and the accompanying disability:

> It's like there's no flow to my life, it's a bunch of stutter steps with feeling, the pain's good, and the pain's okay, and the pain's gone, oh no, the pain's bad…. I never know how it's going to be. It's the craziest thing. I mean, I can lay in my bed one day and get up feeling great, and lay in my bed another day, in the same position, but get up and feel like I was laying on rocks.

Managing this preexisting chronic pain and disability consumed a great deal of participants' attention and energy. Participants had developed highly individualized

paradigms for managing this chronic pain and the accompanying disability by taking both prescribed and over-the-counter medications; using non-pharmacological remedies like heat, cold, and pressure; and by seeking further care from their health care providers. Participants reported varying degrees of success in managing their chronic pain and disability. One participant described successfully using prescribed opiates for his chronic knee and leg pain:

> …for the past 30 years I have always managed my pain well, because I deal with the knee pain, and the gunshot wounds in my legs. I take 5 milligrams of Percocet a day….I haven't abused any drugs, or the pain medicine. I feel like whatever I'm doing is working and it's been well for me.

Another participant described his intentions to seek further care because his efforts to manage his chronic back pain using a combination of prescription medications and heat were unsuccessful:

> I'm going to have to talk to my primary care about changing something…he said once my body's adjusted to the meds, then it may take something else, like some morphine pills or something. I took Percocet twice yesterday just trying to get out of my recliner, and I could hardly get out of bed this morning. It was hard to make it here today…if it weren't for the heated seats in my truck, I wouldn't have made it.

4.3.2 Elective Surgery

Participants identified two main factors associated with the surgery that influenced their mental and physical health. These factors included the short-term acute pain and disability caused by the surgery and long-term impact of the surgery on their total burden of mental and physical distress.

4.3.2.1 Acute pain and disability

All participants described acute pain and disability from the surgery as adversely impacting their physical and/or mental health in the days and weeks after surgery. Among participants interviewed multiple times, content describing the

impact of acute pain and disability tended to appear in earlier interviews. Participants reported forming expectations about the degree of pain they expected to suffer based on prior experiences with surgery and information provided by their health care providers, but these expectations did not make the acute pain any less distressing. One participant said:

> There's been a lot of pain, an excessive amount compared to the left shoulder rotator cuff surgery I had three years ago, but there was much more extensive work done on this right one. Cutting a tendon, releasing it, working on the arthritis, and a rotator cuff repair. So, much more extensive than the last one. Very painful.

In addition, participants reported being unprepared for the duration of pain and disability after these comparatively 'minor' procedures. One participant described her experiences:

> It's only been two weeks, but I feel like my healing is going too slow. I want to just go ahead and heal, so I can get back to being myself and so that I can go back to doing everything that I feel that I need to do, or that I want to do.

Participants reported that this acute pain exacerbated their posttraumatic symptoms, causing them to experience flashbacks, intrusive memories, and irritability. Of note is that participants who discussed these experiences presented them in an order that indicated that pain preceded these acute changes in their mental health. In some cases participants attributed this experience to the similarity between their postoperative pain and their traumatic experiences. After foot surgery one participant described his experiences:

> Well, I've woken up in the night with the foot hurting so bad that it would place me in a bad situation…back in Vietnam, my feet would hurt so bad because I could never get them dry, you know…and lately I would wake up in the middle of the night with that falling off the shelf and taking me back… the pain brings on a lot, it tips the shelf and everything falls off…and I don't care what veteran with PTSD you talk to, he's lying if he says pain don't bring back memories.

In other cases, the relationship between pain and posttraumatic symptoms was less specific. The most common and distressing symptom associated with acute pain was irritability. One participant describes irritability associated with pain after surgery:

> After surgery I was hard, and I was sharp with everybody. I didn't want to be bothered, I didn't want nobody around me…I was in so damned much pain. And, I ain't going to lie to you, I've hurt before, but never this much.

In addition to acute pain, most participants reported suffering from acute disability in the days shortly after surgery. Once participant described his acute disability in the days shortly after surgery:

> …All of a sudden I was dependent on others to help me do things…Simple things like taking a shower, because I really couldn't move my left arm to do much, so I had to have somebody help me to scrub places that I couldn't reach. I was in bed for the first three days…I mean, I was getting up as much as I could, but I couldn't make lunch for myself, or make dinner for myself.

For many participants this acute disability precipitated or worsened depressive and/or posttraumatic symptoms. Participants reported being distressed by feelings of helplessness, blue mood, intrusive memories, and hypervigilance during the days immediately following surgery. Participants also described a relationship between acute physical disability and feelings of helplessness or hypervigilance. One participant described her feelings of helplessness shortly after surgery:

> I've been scared a lot… I feel vulnerable. I feel like if something happens, I can't take care of myself, I can't take care of my family…so, I'm not sleeping as well as I used to…because I'm so concerned about someone breaking into the house…you know, just anything could happen, and I'm defenseless.

Participants also described a relationship between acute pain and disability and intrusive memories. Participants reported being more distressed by intrusive memories because they were unable to participate in activities that they normally used

to distract themselves from this symptom. One participant who normally spent the majority of his day caring for his farm described his experiences shortly after surgery:

> I would be sitting around and in pain, and popping those pain pills and everything, and I would just start thinking about what I went through, and it just kind of stayed in my head, you know…it was like (reliving) everything I've been through in the 'Nam.

Participants coped with acute exacerbations in posttraumatic and depressive symptoms primarily by spending time with family members and pets, discussing their symptoms with their mental health provider at their next scheduled appointment, and resuming their normal activities as tolerated. Regardless of the amount of psychological distress they experienced, no participant reported using emergency mental health services in the days and weeks following surgery.

Much like chronic pain and disability, participants managed acute pain and disability by taking both prescribed and over-the-counter medications; using non-pharmacological remedies like heat, cold, and pressure, self-limiting their physical activity; and by seeking further care from their health care providers. Regardless of how distressing it was, this acute pain and disability typically abated with time with a commensurate improvement in psychological distress.

4.3.2.2 Impact of the surgery on total burden of physical and mental distress

As acute pain and disability resolved, participants began to describe the ultimate impact of the surgery on their physical and mental health. Participants were motivated to have surgery to decrease pain and disability, improve their cosmetic appearance, and/or set their mind at ease by getting a definitive diagnosis, and judged the effect of surgery on their health according to whether or not it accomplished their particular goals.

Participants for whom the surgery addressed a major source of chronic pain and disability were effusive about the positive benefit of surgery on their mental and physical health. One patient described the impact of an occipital nerve stimulator on his health:

> But the surgery has taken away…I would say it's up to 70-80% of the pain. I can go to sleep without the pain, you know, it don't wake me up…it's hard to explain. After 40-something years of the head pain, and suddenly it's gone… you can't describe it. I wish I could have done it a long time ago.

In contrast, patients for whom the surgery introduced a new source of chronic pain felt that the surgery had negatively impacted their health. One patient with new chronic pain after hernia surgery described the impact on his health:

> …and I'm wondering, now, if this is something that's just going to keep on going, if it's something that I'm going to have to live with, this pain in my abdomen. (Before surgery) I didn't have any pain on my right side, and now that's where it's all concentrated…I think, in retrospect, if this was something I could've lived with from now on, I wouldn't have had it done.

Participants had many sources of chronic pain and disability and the surgery could typically only address one source at a time; however, participants recognized and accepted any long-term improvements in pain and disability the surgery could provide. One participant who suffered from severe chronic back pain offered the following judgment about the impact of foot surgery on his health:

> (I had surgery) to get rid of some of the discomfort, and that has happened. Also to loosen up my foot so I could walk without specialty shoes or depending on the crutch so much…I'm walking better, but I still keep it (the cane) with me just in case I misstep or something.

4.3.3 Health Care System

Participants identified several factors associated with the health care system that influenced their mental and physical health during the process of undergoing and recovering from elective outpatient surgery. These factors included: (a) access to care

and resources; (b) the process of providing surgical and postoperative care, and; (c) the way health care staff interacted with participants.

4.3.3.1 Access to services and resources

In order to recover patients reported needing access to services and resources. Some patients had no problems getting what they needed from the care system, but other patients reported having a hard time getting things they needed to recover from surgery. Resources that patients reported having a hard time accessing included equipment such as boots, braces, and canes, as well as services such as physical therapy, pain management, and mental health services. The inaccessibility of these services and resources profoundly affected patients' health as they attempted to recover from surgery. A commonly reported experience was difficulty obtaining appropriate pain management services once surgery staff had discharged patients from follow-up. One patient described his experiences:

> …the last time I had pain medicine, I took it and I called back for more, the (orthopedic surgeon) said, 'We do not give pain medicine after six weeks." My response to that was, "That's not what they told me." I said, "They said they would take care of my pain, and at three months (the pain) should leave me." …And we had a round about it, and of course he didn't give me the pain medicine.

Other patients described being able to obtain pain medication, but found that the pain medication was inadequate or inappropriate given their history of chronic pain and daily analgesic consumption before surgery. One patient described his experiences:

> I've been on hydrocodone (for chronic back pain) since 2006…and to see them prescribe the same medication after the surgery…it should have been stronger. I brought that up to them during the surgery follow-up…and the guy said I needed to take it up with my primary care doctor so far as pain management.

Patients secured access to needed resources and services by calling their primary care manager or another staff member with whom they had a close relationship.

4.3.3.2 Process of providing care

Participants reported that their mental health was affected both before and after surgery by the way in which the system provided the surgical benefit and follow-up care. Patients were asked to arrive several hours before surgery, and then waited their turn for the operating room. Although they had an approximate time when their surgery should start, this was subject to change depending on the progression of preceding cases. Therefore, some patients felt 'lost' or 'forgotten' in the process of progressing from the same day surgery unit to the operating room. In some cases, patients became so anxious and distressed by this uncertainty that they threatened to leave without having surgery.

This phenomenon also occurred when receiving postoperative care; patients reported being placed in rooms in the clinic and then being forgotten. In these situations the volume of patients receiving surgical and postoperative care, and the relatively opacity of the traffic control process in the operating room and clinics create a situation in which patients feel lost and overlooked, causing the patient to experience serious but short-lived anxiety. In contrast, patients who received periodic reassurance from a staff member that all was well did not report feeling this way while awaiting surgery or follow-up care.

Some participants also described anxiety when unable to establish and maintain continuity of care. Because of the way in which both surgical and mental health services were provided, participants reported being unable to establish and

maintain trusting relationships with health care providers. One participant describes being unable to meet his surgeon until the morning before surgery:

> …I asked him point blank, I said, are you going to be the one that's doing the surgery? And he said, "Maybe, maybe not, I can't say, because when we're scheduled for surgery we don't know who we might be operating on (you)"…So, up till the actual surgery, I didn't know who the physician was.

This finding was not limited to surgical care. As noted, patients did not report using emergency mental health services despite being very distressed by depressive or posttraumatic symptoms. When asked why, one participant stated:

> I don't like going (to the emergency mental health clinic). They don't know you, and they don't know what you've been through. I'm okay talking to (my regular psychiatrist) because I've been seeing him for years, but to them in (the emergency mental health clinic) you're just another vet, so I don't like talking to them.

4.3.3.3 Interactions with staff members

Throughout the process of receiving surgery and postoperative care, patients felt that interactions with staff who appeared interested, caring, unhurried, and informative had a positive effect on their mental health. This feeling was so strong that some patients were not distressed with their overall care even if they had a lot of pain or postoperative complications. Some patients also preferred staff members who made appropriate physical contact when talking with them, such as touching them on the hand when explaining what would happen in surgery. One patient described his experiences after surgery:

> I can't complain about what they did because the doctors were concerned, and the nurses were concerned. …I feel like they have really took an interest, out of the thousands and thousands of the veterans that come in and have surgery, I mean, I'm not the only case, but for them to take an interest in my case, it really made me feel like they had my best interests at hand.

Even small expressions of interest and care on the part of staff members could exert a powerful beneficial effect on patients' mental health. One participant described

his feelings when a staff member called after working hours to let him know about the results of a biopsy:

> …the (day after surgery) at 5:30 the pathologist called me…he'd just received the results…I thought that was pretty astonishing. I'm not sure what kind of hours they work, but calling me at 5:30 to say "I just got these, and I thought you might want to know"…that brought tears to my eyes.

In contrast, patients reported feeling anxious when forced to interact with staff who seemed distracted, uninterested, unsympathetic and rushed.

Although participants preferred staff members who were forthcoming with information related to their care, the manner in which that information was delivered could result in greater anxiety. One participant describes his interaction with a staff member immediately before surgery:

> I went back into OR prep, and the anesthesiologist came back to talk to me. And he told me, "I'm going to take care of this, but right now they don't have the proper instruments in the OR, so we're waiting to put instruments together." …And, I'm laying there waiting for surgery, and I don't want to hear that these guys don't have their stuff in order.

This quote illustrates how the manner in which information is presented can make a difference in the patients' level of anxiety. The policy at this facility is that the patient cannot be placed under anesthesia until all needed equipment is in the operating room or immediately available. However, the manner in which this information was conveyed to the participant emphasized that the equipment was not available, rather than emphasizing that protocols were in place and working properly to ensure that the operating room was prepared to care for him.

Although frustrated by unsatisfactory interactions with staff members, some patients reported being afraid to confront staff for fear of being labeled as a 'problem.' Other patients reported setting 'ground rules' about communication when working

with a new staff member. One patient described his approach to ensuring staff listened to his needs:

> I explain to them, 'I'm very easy to get upset when you don't listen.' I try to hold back, but…I mean, I'm not going to do anything, but once I get upset, then my attitude changes. And then once my attitude changes, why, you get what you get.

However, the most common reaction to unsatisfactory interactions was to rationalize the staff member's behavior. Participants rationalized unsatisfactory interactions by attributing staff responses to high patient volume, differences of personality, or access to knowledge to which the participant was not privy. However, some participants rationalized unsatisfactory interactions by stating that they felt staff members were operating at the limits of their own competence. One participant described this feeling: " I…kind of disagree with him, but I also kind of agree with him, so I really didn't put on a show. I felt like he was doing all that he knew what to do."

In very rare cases, through no fault of their own, staff members who reminded patients of their traumatic experiences could trigger acute posttraumatic symptoms such as flashbacks. One participant who served in Vietnam described the effect of awakening in the recovery room with two Asian-American nurses standing over him:

> …when I come out of the anesthesia, I opened my eyes I seen two (Asian-American) ladies standing beside my bed, and it just freaked me out….they said that I began to go into defense mode, wondering if I was back in Vietnam, wondering if they was trying to hurt me, and wanting to defend everybody. It was like that they were standing there trying to determine what they were going to do with me, or to me. I was thinking that I was waiting for rescue, but the rescue wasn't coming because now they'd captured me.

4.3.4 Friends and family

Participants identified two major factors related to their friends and family members that influenced their physical and mental health after elective surgery: Physical assistance and emotional support.

4.3.4.1 Physical assistance

Family and friends helped patients take care of themselves right after surgery. Friends included both close personal friends and casual acquaintances from church or social clubs; family included spouses, unmarried significant others and children. This type of physical assistance included getting food, drink, and medications; performing personal hygiene tasks; and keeping their residence clean. One patient described receiving assistance with food preparation from his teenaged children in the days following surgery: "I couldn't make lunch for myself, or make dinner for myself…My kids tried to help me out, but that meant we were limited to what they could make, like spaghetti and macaroni and cheese." Patients who found themselves without this support struggled to meet their needs, even when their family members were away for only short periods of time. One patient described his experiences trying to care for himself in his wife's absence shortly after foot surgery:

> (Before my wife) went to work…she would lay me out my three oranges and my three apples, and I would have my TV controller, and I would get in my recliner with that foot up in the air…And if I needed anything, I found out that at that point in time crawling along on all fours was a good way to get around. So I did that, crawled along the carpet, for about 4 days…

4.3.4.2 Emotional support

Patients reported that the presence of emotional support from a friend or family member influenced their mental health after surgery. Interestingly, several patients cited pets as a source of this type of emotional support. Even being temporarily

deprived of emotional support could trigger profound feelings of distress. Patients asked about this phenomenon felt that being left alone and in pain gave them too much time to think about their problems. One patient described his mood after his girlfriend had to return to work:

> Monday morning my girlfriend had to go do her thing, so I was there by myself. I just couldn't get out of bed…I was just really depressed…I mean, really in a dark place…angry, and pissed off, mostly at myself, for not being able to do the things that I had been doing for myself for the past few years…but I wasn't able to do those, and I really just beat myself up for it. …You get back to, you know, that military aspect of, if you're not helping, you're hindering…and that's what I felt like, you know?

Participants indicated that family members and spouses remained a consistent source of emotional support throughout the study. Unfortunately, patients in pain were more irritable, which could cause family and/or friends to avoid the patient. In some cases this irritability was imperceptible to the patient until pointed out by someone else. In extreme cases excessive irritability could lead to friends disengaging from participants completely, triggering profound emotional distress for the participant. One patient described his emotional distress after his fiancé left him over concerns with his irritability and anger:

> I never put a lot of stock in that I was being mean until… my fiancé flat out told me, "your PTSD, you have a problem. You need to go get help"… (Since then) my fiancé and I have just been at it. This last week we had a knock down drag out…. it didn't need to get out of control. She tried to back off, and I didn't, and then I tried to back off, and she didn't…and now I think I've lost her. And, I'm hurt, I agonizing over that. I was suicidal for a period of time…it's been a mess.

4.4 Discussion

The factors identified by these 14 veterans as affecting their mental and physical health after surgery included chronic pain and disability, the elective surgery itself, the health care system, and family and friends. Patients elected to discuss these

factors in an order that suggested that they were most concerned with acute surgery-related pain and disability immediately after surgery, after which their attentions returned to their chronic pain and disability. Patients also elected to present these factors in an order that suggested that changes in their mental health were preceded and driven by changes in their physical health.

Some participants in this study often described surgery as an attempt to shape and manage the course of existing chronic pain and disability, while other described chronic pain and disability as a factor that complicated the management of acute surgical pain and disability. Other studies concur with the centrality of chronic pain as a factor influencing the health of veterans with PTSD. The prevalence of chronic pain in veterans seeking treatment for PTSD has been reported as 66%, even after excluding pain from injuries associated with the traumatic event (Shipherd et al. 2007). This relationship is not limited to veterans: Studies of preoperative civilian patients have reported a significant correlation between measures of pain severity and posttraumatic symptom severity (Martin et al. 2010).

Several models have been proposed to explicate the relationship between PTSD and chronic pain: (a) Shared Vulnerability (Asmundson and Katz 2009); (b) Triple Vulnerability (Barlow 2000); (c) Fear-Avoidance (Vlaeyen and Linton 2000), and; (d) Mutual Maintenance (Sharp and Harvey 2001). The Shared Vulnerability, Triple Vulnerability, and Fear Avoidance models all emphasize the role of avoidance of threatening stimuli as central to the relationship between PTSD and chronic pain (Asmundson and Katz 2009, Barlow 2000, Vlaeyen and Linton 2000). However, participants in the present study did not describe greater distress from avoidance-related posttraumatic symptoms in the days and weeks following surgery.

In contrast, the Mutual Maintenance model proposes that 7 factors play a role in the maintenance of both PTSD and chronic pain: (a) anxiety sensitivity that results in a tendency to catastrophize when faced with ambiguous situations; (b) physical pain that reminds the patient of traumatic experiences; (c) attentional biases that heighten patient vigilance towards potentially threatening or painful stimuli; (d) avoidant coping; (e) fatigue and lethargy that facilitate the development of depression; (f) preoccupation with fear and worry, and; (g) overwhelming cognitive burden from both disorders that limits the patient's ability to apply coping techniques (Sharp and Harvey 2001). Although the present study was not designed to assess or validate the Mutual Maintenance model, participants indicated that the burden of chronic and acute pain and disability prevented them from participating in activities that they normally used to ward off psychological distress. This finding both parallels, and suggests a temporal precedence within, the final factor of the Mutual Maintenance model such that pain impairs the patient's ability to cope with PTSD symptoms. Therefore, application and testing of the Mutual Maintenance model in future studies of postoperative recovery in patients with PTSD may improve our understanding of both the model and this specific population.

An experience described by participants was acute anxiety before surgery and exacerbated depressive and posttraumatic symptoms after surgery. Although anxious before surgery, participants indicated that this anxiety was self-limited and strongly linked to uncertainty about when they would actually go to surgery. This uncertainty was easily defused by communicating with the patient in an engaged, sincere manner, even if only to let him and her know that the nursing and surgical staff were aware of the situation. These findings suggest that the perioperative experience can be

improved for these patients by educating staff about specific interaction strategies that are reassuring to patients with PTSD. However, the nearly ubiquitous exacerbation of depressive and posttraumatic symptoms during the days and weeks following surgery exposes a serious gap in care. Especially troubling was that there was no evidence that patients would self-refer to existing emergency mental health services when severely distressed.

In contrast to the frequent descriptions of pain and disability-related posttraumatic and depressive symptom exacerbation in the days and weeks after surgery, only one participant described acute posttraumatic symptom exacerbations and accompanying behavioral disturbances during the process of receiving postoperative care. A growing line of research is investigating PTSD as a risk factor for emergence delirium or agitation in younger veterans with recent combat experience (McGuire 2012, McGuire and Burkard 2011). Emergence delirium is phenomenon in which the patient exhibits psychomotor agitation immediately after emergence from anesthesia, and an estimated 5-21% of all adult patients exhibit emergence delirium after noncardiac surgery regardless of PTSD status (Yu et al. 2010, Lepouse et al. 2006, Radtke et al. 2010). At the bedside the clinician has no means of distinguishing between the nonspecific agitation associated with emergence delirium and the acute anxiety and distress associated with PTSD-related flashbacks and dissociation.

The account of the participant who experienced a flashback in the recovery room suggests that aspects of the perioperative environment can remind patients of traumatic experiences and precipitate a flashback, and that the perceptual disturbances associated with recovering from anesthesia may contribute to the misinterpretation of innocuous environmental cues. Therefore, neurobehavioral disturbances immediately

after surgery may be the result of a complex and highly contextual interaction between PTSD and the residual effects of anesthesia. The rarity of neurobehavioral disturbances in this sample may indicate that veterans with long-standing, chronic PTSD and veterans recently diagnosed with PTSD constitute two distinct populations as to risk of emergence agitation. Further study is needed to determine if it is possible or necessary to distinguish between PTSD-related flashbacks and the more general psychomotor agitation associated with emergence delirium in order to develop an effective paradigm to prevent and manage the disorder.

Participants also described difficulties in accessing resources and services that were necessary for their recovery, including medical equipment, pain management, physical therapy, and mental health care. In every case, these resources were available from the health care system, but the participant was unable to access the resources either because of bureaucratic obstacles or a lack of clarity about which member of the health care team was responsible for meeting the participant's need. These findings suggest that patients would benefit from better coordination between surgery, primary care, physical therapy, and mental health, to ensure that the surgical benefit reaches its full potential, rather than becoming another source of distress for the patient. The best method for achieving this coordination would likely be through the adoption of a proven model of integrated care delivery, such as the Chronic Care Model (Wagner et al. 2001). Particular aspects of the Chronic Care Model that would remedy the concerns of participants in this study are: (a) well defined and distributed tasks across health care team members; (b) clinical case management services for particularly complex patients; (c) integration of specialist and primary care, and; (d) embedding of evidence-based practice guidelines into clinical care. The embedding of evidence-

based practice guidelines into clinical care is especially important, because there is an evidence based guideline for the management of chronic pain in the patient with PTSD (Gibson 2012), but there was no evidence in this study that surgeons adhered to it, or were even aware of its existence.

The erosive effect of posttraumatic symptoms on social support has also been described in the literature. Laffeye et al (2008) reported that more severe posttraumatic symptoms at baseline predicted a decrease in social support over time from nonveteran friends, but not relatives or fellow veterans. This partially concurs with the findings of the present study, in which some participants reliant on friends or a significant other to whom they were not married, found themselves without emotional support after surgery. Regardless of source, participants indicated that emotional support during recovery was protective against acute psychological distress.

The findings suggest three major avenues to address acute psychological distress after surgery. First, better pain management in the days immediately following surgery would allow patients to resume normal activities as soon as possible, thus accelerating their resumption of their habitual mechanisms for warding off psychological distress. Second, patients need access to a trusted mental health provider or peer support in case psychological distress becomes unbearable in the critical days after surgery and anesthesia. Third, further efforts need to be made to support the family member caring for the patient after discharge.

Only a small minority of participants felt that the elective surgery was ultimately detrimental to their physical and mental health. These participants typically described the surgical procedure as a new source of chronic pain and reported significant and ongoing problems obtaining access to physical therapy or

comprehensive pain management services. Likewise, a small minority of participants felt that the surgery significantly improved their physical and mental health by decreasing their total burden of chronic pain and/or disability. When coupled with participant reports that they were unprepared for the acute pain and disability after surgery, these findings suggest that patients would benefit from a frank discussion about the potential risks and benefits of elective surgery, focusing on what the surgery can accomplish to ameliorate their total burden of chronic pain and disability.

4.4.1 Strengths and Limitations

This small exploratory study used qualitative methods to generate data to guide the development of future research and theory. The chief weakness of this study was the inclusion of participants undergoing a variety of surgical procedures. The surgical procedures participants underwent were heterogeneous, so the degree of postoperative pain and disability was not consistent from one participant to another. However, every effort was made to strengthen the rigor of the study. The credibility of these findings were strengthened by audio recording all interviews, conducting multiple interviews with many participants, soliciting participant opinions about emergent themes, and soliciting participant opinions about study findings and conclusions. The dependability of these findings is supported by the decision trail cited within the methods section of this article.

Transferability of these findings will depend on the reader. The majority of surgical procedures performed in the United States are conducted on outpatients (Statistics 2010). However, these findings cannot reliably be extended to patients with PTSD who are hospitalized after surgery. In addition, these findings cannot be

extended to patients with acute rather than chronic PTSD, because all patients were interviewed a minimum of 4 years after experiencing a traumatic event.

4.4.2 Implications

These findings provide insight into the health effects of elective surgery and anesthesia in a sample of participants with PTSD. The foremost implication of these findings is the need for quality improvement projects to improve coordination of primary, surgical, and mental health care to provide holistic support to the patient after discharge from the hospital. Although important for all patients, this may be a critical factor in patients with PTSD because of the attendant risk of self-harm if the patient becomes acutely distressed and lacks support outside the health care system. Providers should also forewarn the patient and attendant family member or friend about the likelihood of increased depressive and/or posttraumatic symptoms in the days and weeks after surgery, and reiterate availability of emergency mental health services so that both patient and attendant are aware of whom to contact should the patient become acutely psychologically distressed after surgery.

5. Health Trajectory after Elective Surgery in Patients with Preexisting Posttraumatic Stress Disorder

Posttraumatic stress disorder (PTSD) is common, can be chronic, and has been associated with greater risk of postoperative mortality. Posttraumatic stress disorder is an anxiety disorder characterized by avoidant behavior, physiological reactivity, emotional numbing, intrusive thoughts, and unwanted recurrent memories that develop after exposure to a traumatic event and persists for at lease one month (American Psychiatric Association 2000). The lifetime prevalence of PTSD in the United States is estimated to be 6.8% (Kessler et al. 2005). The prevalence is greater in military veterans, with 9% to 43% demonstrating the disorder (Vasterling et al. 2010, Hoge and Castro 2006, Hoge et al. 2004, Dohrenwend et al. 2006, Blake et al. 1990).

This greater prevalence means that in certain populations a substantial number of patients presenting for surgery will have the disorder. At one Veterans' Administration Medical Center (VAMC) 9.4% of all major elective surgical procedures performed over a 12-year period were performed on patients with PTSD (Brzezinski et al. 2009b). In the National Inpatient Sample database for 2006, 14.7% of patients undergoing coronary artery bypass graft surgery also had a diagnosis of PTSD (Dao et al. 2010).

5.1 Health Effects of PTSD

Patients with preexisting PTSD demonstrate greater prevalence of baseline comorbidities and detrimental health practices that increase their risk of poor postoperative outcomes. Studies of outpatients with PTSD reported greater than national average prevalence of diabetes, asthma, stroke, myocardial infarction, cancer,

and liver cirrhosis (David et al. 2004, Buckley et al. 2004). The relationship between PTSD and the accumulation of these chronic conditions is likely mediated by health risk behaviors. Patients with preexisting PTSD report little physical exercise and a greater than national average prevalence of tobacco use, drinking, and drug use (Buckley et al. 2004, Anthony, Warner, and Kessler 1994). At present whether the prevalence of concurrent substance abuse disorders and PTSD is a form of self-medication of PTSD symptoms, or a vulnerability of the patient that facilitates the development of both substance use disorder and PTSD, is unknown (Brown and Wolfe 1994). Patients with PTSD also demonstrate greater prevalence of other mental illnesses. Depression is highly comorbid with PTSD, likely because the disorders have overlapping symptoms and share some common neurochemical aberrations. Studies reported a prevalence of preoperative comorbid depression in 36% to 61% of patients with preexisting PTSD, compared to 3.5% to 26% of patients without PTSD, and depression is an independent predictor of mortality in older adults (Schulz et al. 2000).

Given the prevalence of these comorbidities and health risk behaviors, patients with PTSD are at greater risk of mortality compared to those without PTSD. Studies of Vietnam-era veterans have demonstrated that since the war those with PTSD were more likely to die from cardiovascular and external causes, including suicide, homicide, and accidents, than those without PTSD (Boscarino 2008a, 2006b, 2008b, 2006a). As discussed previously, this greater mortality is likely mediated by health risk behaviors because outpatient Vietnam veterans with PTSD also demonstrated greater prevalence of smoking, ethanol use, and illicit substance use (Boscarino 2006b). The presence of these comorbidities and health risk behaviors would place any patient at

greater risk for poor outcomes after surgery regardless of PTSD status (Wolters et al. 1996).

5.2 Previous Research

Despite the prevalence of PTSD, relatively few published studies have examined the effects of surgery on patients' health in the context of preexisting PTSD. To date, studies have investigated postoperative health outcomes in patients with preexisting PTSD undergoing coronary artery bypass graft surgery (CABG), gastric bypass, and major elective surgery. In one study of patients undergoing CABG, posttraumatic symptom severity was found to have no effect on hospital length of stay, cardiac-related readmission, or psychological functioning six months after CABG, but was associated with more negative self-assessed health at six-months after surgery (Oxlad et al. 2006a, b, Oxlad and Wade 2008). However, only 9 of 119 subjects (7.5%) in that sample had clinically significant posttraumatic symptoms at any point in that study. In a sample of Holocaust survivors undergoing CABG, 36% of whom had clinically significant posttraumatic symptoms at baseline, greater posttraumatic symptom severity was associated with more postoperative difficulties with emotional functioning, sleep, and social functioning (Schreiber et al. 2004). Patients with preexisting PTSD were also more likely to demonstrate significant cognitive decline after CABG than patients without PTSD (Hudetz et al. 2010). Therefore, CABG did not appear to worsen posttraumatic symptom severity, but preoperative posttraumatic symptoms were inversely related to self-assessed postoperative health and associated with greater risk of postoperative cognitive decline.

The effect of PTSD on postoperative health has also received very limited investigation in patients undergoing noncardiac surgery. In a sample of veterans

undergoing gastric bypass surgery, preexisting PTSD did not affect length of hospital stay, the incidence of postoperative complications, or the mean amount of weight lost after one year (Ikossi et al. 2010). However, in veterans undergoing elective major surgery, patients with PTSD were at least three time more likely than patients without PTSD to die within one or five years of surgery (Brzezinski et al. 2009a). These findings may indicate that the causal process that links PTSD to mortality in this population is not captured by the traditional postoperative outcome measures like hospital length of stay, complication rates, or surgical-diagnosis related hospital readmission.

One commonality of all of these studies was that their analyses compared the outcomes of patients with preexisting PTSD with the outcomes of patients without PTSD. However, longitudinal cohort studies that compare the risk of postoperative mortality in patients with and without PTSD may be confounding maturation and history; that is, studies may confound the natural maturation of physical decline in patients with PTSD with the historical effect of having surgery. Such a comparison may lead to data that suggests that surgery is harmful to the health of patients with PTSD, when actually their health is worse than that of their peers without PTSD but relatively unaffected by surgery. A gap in the literature is that the effect of surgery on the patient with PTSD is only known in comparison to the effect of surgery on the patient without PTSD, and not in comparison to the patient with PTSD who does not undergo surgery. This is an important distinction, because some surgeries are elective and may be deferred indefinitely. Therefore, the purpose of this research study is to address that gap by comparing the health of patients with PTSD who undergo elective surgery with that of patients with PTSD who do not undergo surgery.

However, there are obstacles to comparing surgical and nonsurgical patients with PTSD. Obviously, nonsurgical patients do not generate traditional postoperative outcomes like hospital length of stay, postoperative complication rates, or surgery-related hospital readmission rates. Therefore, other meaningful outcome criteria must be selected upon which to compare surgical and nonsurgical subjects with PTSD. Mortality would be one such criterion; however, mortality requires very large sample sizes to test hypotheses because only 2.6% of Americans aged 45-84 years can be expected to experience mortality in a given year (Control 2010). Based on this average annual mortality rate, approximately 900 subjects evenly divided between those with and without PTSD would need to be followed for a year to detect a doubling in annual mortality due to PTSD (Agresti 2007). An alternative is to measure a patient attribute which has predictive validity for mortality, such as subjective health status (Idler and Benyamini 1997). Subjective health is the patient's assessment of his or her own health status, and is a holistic concept that includes aspects of physical, mental, and social well-being.

Both PTSD and surgery have independent effects on subjective health status. In veterans, PTSD was associated with worse subjective health status, including greater pain, greater impairment of role performance, worse physical functioning, and worse overall physical health (Buckley et al. 2004). This finding may be the result of information processing biases in PTSD that cause the patient to negatively interpret ambiguous health cues (Constans 2005). Comorbid depression would likely further worsen the patient's interpretation of subjective health, as patients with depression also demonstrate attentional biases towards negative internal and external emotional

cues (Leppanen 2006), which would worsen interpretation of the social and mood-related aspects of subjective health.

Subjective health status also captures the adverse effects of surgical diagnosis-related pain and disability. Before common elective surgeries, patients without PTSD reported greater pain, worse physical role performance, and worse physical functioning that returned to, or exceeded, baseline within a few weeks or months after surgery (Wellwood et al. 1998, Burney and Jones 2002, Busija et al. 2008, Langenbach et al. 2008, Shi et al. 2009). Therefore, subjective health may be a means to compare the relative effects of PTSD and surgery in surgical and nonsurgical patients with preexisting PTSD. Subjective health also demonstrates predictive validity for mortality; numerous studies have demonstrated that outpatients with worse subjective health or declines in subjective health demonstrate greater risk of mortality (Idler and Benyamini 1997, Idler and Kasl 1991, Fan et al. 2004).

5.3 Theoretical Frameworks

The relationship of health decline with time is best understood within the context of the trajectory theory of chronic illness (Corbin and Strauss 1991, Corbin 1998). In trajectory theory, an individual's experience (i.e., trajectory) of chronic illness is unique, but will consist of nine distinct phases: pretrajectory, trajectory, stable, unstable, acute, crisis, comeback, downward and dying (as illustrated in Figure 2). The stable phase is characterized by illness symptoms that are well controlled, and unstable phases occur when the individual is unable to control illness symptoms. Inability to control symptoms may lead to a crisis phase in which acute care is necessary. Crisis phases are followed by either comeback phases during which the individual's health and disability returns to a tolerable level, or a downward phase with progressive

increases in disability and symptoms. The downward phase culminates in a dying phase. Each individual's trajectory is influenced by a multitude of factors, including the pathophysiology of the disease and the actions of the individual, the individual's support system, and actions of the health care team.

Surgery is a period of acute health instability for all patients, and subjective health status captures the adverse effects of surgery-related pain and disability. Patients undergoing surgery should experience an initial decline in subjective health status, followed by a return to baseline a few weeks or months after surgery (Wellwood et al. 1998, Burney and Jones 2002, Busija et al. 2008, Langenbach et al. 2008, Shi et al. 2009). Therefore, health trajectory can be operationalized with repeated measurements of subjective health status, itself an independent predictor of mortality. Within this framework, the relative contributions of physical and mental distress in the form of posttraumatic symptom severity, depressive symptom severity, anxiety and pain to health change after surgery may be analyzed. If patients with preexisting PTSD are harmed by elective surgery, or do not benefit from undergoing elective surgery, then they should display postoperative subjective health declines from which they do not recover.

5.4 Research Questions

The purpose of this study was to investigate the effect of elective surgery on the mental and physical health of patients with pre-existing PTSD over a three-month period. The following were research questions for this study:

1. What are the effects of undergoing elective outpatient surgery on the physical health of patients with preexisting PTSD?

2. What are the effects of undergoing elective outpatient surgery on the mental health of patients with preexisting PTSD?

3. What preoperative characteristics of the patient with preexisting PTSD predict mental and physical health change after elective surgery?

We hypothesized that patients with preexisting PTSD who underwent elective surgery would demonstrate greater decline in subjective health and greater increases in posttraumatic and depressive symptom severity compared to patients with PTSD who did not undergo elective surgery over a three-month time period. We also hypothesized that more severe baseline posttraumatic and depressive symptoms, greater preoperative anxiety, and greater preoperative pain severity would be significant predictors of subjective health decline after elective surgery.

5.5 Research Design and Methods

5.5.1 General Study Design

This was a longitudinal, quasi-experimental, non-equivalent control group pilot study. Subjective mental and physical health status, posttraumatic symptom severity, depressive symptom severity, situational anxiety, and pain severity were compared over a three month period between a sample of veterans with pre-existing PTSD who underwent outpatient elective surgery and a sample of veterans with pre-existing PTSD who do not undergo outpatient elective surgery. Analysis addressing the first research question compared the change in physical subjective health over the three-month period of the study between the two groups. Analyses addressing the second research question compared the change in subjective mental health status, posttraumatic symptom severity, and depressive symptom severity over a three-month

period between the two groups. Analyses addressing the third research question evaluated the predictive value of baseline posttraumatic symptom severity, depressive symptom severity, preoperative situational anxiety, and preoperative pain severity for subjective health change in patients who underwent elective outpatient surgery.

5.5.2 Setting and Sample

5.5.2.1 Setting

The setting for this research was the Durham Veterans Administration Medical Center (VAMC), a large tertiary care hospital provides both perioperative and psychiatric care to the veteran population of much of northern North Carolina.

5.5.2.2 Sample

The sample consisted of patients aged ≥ 18 with military service-connected lifetime or current PTSD status documented in the VA Computerized Patient Record System (CPRS), who were eligible for care at the Durham VAMC, community dwelling (that is, non-institutionalized), had not had surgery in the prior year, and could read and understand the English language as evidenced by ability to verbalize understanding of the consent form to the investigator. Subjects for the surgical group were American Society of Anesthesiologists Physical Status Classification I to III (meaning an absence of life-threatening comorbidities) and scheduled for outpatient elective surgery under general anesthesia. Subjects for the control group could not be scheduled for surgery at the time of study enrollment. The rationale for these inclusion criteria are that (a) all subjects were eligible for emergency mental health services at the Durham VAMC if necessary; (b) subjects did not have the potentially confounding risk of surgery within the past year; (c) patients undergoing very minor, low risk surgical

procedures such as phacotomy were excluded as such procedures are scheduled for local anesthesia with sedation; and (d) patients receiving very painful and extensive surgical procedures were be excluded, as they will be admitted to the hospital and exposed to the confounding effects of hospitalization, above and beyond the effects of surgery and anesthesia.

Otherwise eligible subjects with a history of dementia, organic mental disorder, schizophrenia, or current manic syndrome were excluded. These medical conditions affect the ability of the subject to cooperate with interviews and accurately recall health issues from the previous month. Potential subjects with substance abuse/dependence other than alcohol/tobacco use were also excluded, as estimates for the effect of non-alcohol substance dependence on subjective health were not available in this population.

5.5.2.3 Sample size calculation

Power calculations indicated that a sample size of 60 (30 per group) was required to achieve at least 80% power to detect a medium to large effect size when testing the primary hypothesis that there would be a statistically significant decline in physical subjective health status from baseline to twelve weeks after surgery in patients with PTSD who underwent outpatient elective surgery when compared to patients with PTSD who did not undergo outpatient elective surgery. Physical subjective health status was defined as the subject's Physical Component Summary (PCS) score on the Veterans' Rand 36-Item Health Survey (VR-36; Kazis 2000, Kazis et al. 2004). This power calculation was based on the assumptions that: (a) a type of hierarchical mixed effects model for repeated measurement known as random coefficients regression would be used to test for significant group differences in

trajectory of change across time (treatment-by-time interaction); (b) the level of significance for the two-tailed statistical test would be 0.05, and; (c) an intention-to-treat analysis would be conducted. Assuming 70% within-person correlation across time points, a sample size of 30 per group would yield 80% power to detect an effect size of $f = 0.55$ when comparing the group-by-time trajectories; for f effect sizes, Cohen defines a medium effect size as 0.25 and a large effect size as 0.40 (Cohen 1988). When comparing between-condition differences at twelve weeks, a sample size of 30 per group would provide 80% power to detect an effect size of $d = 0.50$; for d effect sizes, Cohen defines a medium effect size as 0.50 and a large effect size as 0.80 (Cohen 1988). Thus, a sample size of 60 (30 per group) would provide 80% power to detect medium to large effects in terms of change in subjective health status.

5.5.3 Measures and Instruments

Data were collected using self-report instruments and structured clinical interviews. As part of each assessment the number of days since surgery for surgical patients and since enrollment for control group patients was recorded. In addition, the season in which each assessment occurred was recorded as a 4-level categorical variable (winter, spring, summer, or fall) for consideration as a covariate in analyses of mental health.

5.5.3.1 Demographics

Information including age, gender, ethnicity, educational level, marital status, planned surgical procedure, comorbidities, and outpatient psychoactive medications were gathered from each subject at enrollment to allow sample description and for consideration as covariates.

5.5.3.2 Subjective health

The Veterans Rand 36-item Health Survey (VR-36; Kazis 2000, Kazis et al. 2004) measures the subjective health concepts of physical functioning, role limitations due to physical problems, bodily pain, general health perception, vitality, social functioning, role limitations due to emotional problems, and emotional well-being using Likert-type responses. The content of the VR-36 items are identical to those on the Medical Outcomes Study 36-Item Questionnaire (SF-36), but incorporate expanded five-point Likert scales to improve measurement of role functioning in the veteran population. Responses for each subjective health concept are averaged and compared to population norms to determine the score. In addition to the component scores, factor-based composite T- scores can be calculated to measure the aggregate health concepts of overall physical subjective health (Physical Component Summary, or PCS score) and mental subjective health (Mental Component Summary, or MCS score) status. T-scores range from 0 - 100, with higher scores indicating better subjective health status (Williams et al. 2009, Smeeding et al. 2010, Kazis et al. 2004). The VR-36 and its parent instrument, the SF-36, have been extensively used to monitor the health of the veteran population, veterans with PTSD, and perioperative patients (Williams et al. 2009, Smeeding et al. 2010), and are recommended as measures of subjective health in veterans with PTSD by consensus of the Department of Veterans Affairs Research Office, the National Institute of Mental Health, and the U. S. Department of Defense (U.S. Department of Veterans Affairs Research Office, National Institute of Mental Health, and U. S. Department of Defense 2008).

5.5.3.3 Posttraumatic symptom severity

Posttraumatic symptom severity was measured with the Clinician Administered PTSD Scale (CAPS; Blake et al. 1995), a 30-item, semi-structured interview that uses directed questions with scoring criteria to both diagnose PTSD and measure PTSD severity. The CAPS severity score is determined by summing the ratings of 17 symptom criteria for frequency and severity on five-point Likert scales. Possible scores range from 0 to 136, with higher scores indicating greater PTSD severity. The CAPS is considered the "gold standard" for measurement of PTSD in veterans (Blake et al. 1995, Weathers, Keane, and Davidson 2001).

5.5.3.4 Depressive symptom severity

Depressive symptom severity was measured with the Geriatric Depression Scale (GDS; Yesavage et al. 1983). The GDS is a 30-item yes/no format questionnaire. Possible scores range from 0-30, with higher scores indicating greater depressive symptom severity. The GDS was selected for this study because the average veteran presenting for elective outpatient surgery at the Durham VAMC is 62 years of age, and with the hypothesis that the yes/no format of the questionnaire would reduce the common method variance associated with the use of instruments composed of Likert-type items such as the VR-36 and State-Trait Anxiety Scale-State scale. Although developed to measure depressive symptom severity in older adults, the GDS demonstrates acceptable validity across the adult lifespan (Yesavage et al. 1982, Rule, Harvey, and Dobbs 1989).

5.5.3.5 Pain severity

Pain severity was measured with a Visual Analog Scale (VAS). The VAS consisted of a horizontal 100-millimeter line with the labels "no pain" and "the most pain you can imagine" at opposite ends. For the purpose of this study, subjects were asked to rate the average amount of pain they experienced over the previous 24-hour period by drawing a line perpendicular to the 100-millimeter scale denoting their pain severity. The score was the distance in millimeters from the end of the scale labeled "no pain" to the perpendicular line drawn by the subject. The VAS has used in many previous studies of postoperative pain (Breivik, Bjornsson, and Skovlund 2000).

5.5.3.6 Situational anxiety

Situational anxiety was measured with the State-Trait Anxiety Inventory-State scale (STAI-S; Spielberger et al. 1983). The STAI-S is a 20-item scale in which the subject rates his or her anxiety in the present and recent past using a 4-point Likert scale. Possible scores range from 20-80, with higher scores indicating greater anxiety. The STAI-S is a widely used measure of situational anxiety that has been translated into more than 40 languages (Lam, Michalak, and Swinson 2005, 109). The test-retest reliability of the STAI-S is low due to the effect of situational factors on anxiety; therefore, it also gives some indication as to the longitudinal stability of testing conditions as the study progressed (Spielberger et al. 1983).

5.5.4 Procedures

5.5.4.1 Recruitment

After institutional review board approval, the list of patients scheduled for preoperative or PTSD clinic appointments were reviewed to identify eligible potential

subjects for the surgical and control groups, respectively. Those patients who appeared eligible were mailed an informational letter describing the study, the time commitment, and the opportunity to opt out of being approached about participation during the preoperative visit. At that appointment patients who desired to participate were introduced to the investigator, who verified eligibility per inclusion/exclusion criteria and obtained informed consent. Subjects for the control group were also recruited by self-referral. Flyers were placed in the PTSD, mental health, and primary care clinics, and potential subjects were asked to contact the investigators directly to indicate interest in participating and initiate enrollment.

5.5.4.2 Data Collection

Data collection was timed to provide parallel data from the surgical and control groups across the twelve weeks of enrollment. In the surgical group, data were collected on enrollment and at approximately one week, four weeks, and twelve weeks after surgery to coincide with the available research on health trajectory after outpatient elective surgery (Wellwood et al. 1998, Burney and Jones 2002, Busija et al. 2008, Langenbach et al. 2008, Shi et al. 2009). Enrollment for surgical group subjects occurred at the preoperative clinic appointment, approximately one week before surgery. In the control group, data were collected on enrollment and at approximately one week, four weeks, and twelve weeks after enrollment.

After verifying eligibility and administering informed consent, the primary investigator collected demographic information from the subject and administered the VR-36, CAPS, GDS, STAI-S, and the VAS. At that time, subjects were also provided with a copy of the VR-36, the VAS, and a post-paid envelope. Approximately one week after surgery or enrollment, subjects completed the VR-36 and the VAS and

returned it by mail to the investigators. Approximately four and twelve weeks after surgery or enrollment, subjects in both groups returned to the Durham VAMC and completed the VR-36, CAPS, GDS, STAI-S, and the VAS. All informed consent, enrollment, and data collection was performed by the primary investigator in a private office at the Durham VAMC, with the exception of the instruments completed by the subject at home an returned by mail one week after surgery or enrollment for members of the surgical and control groups, respectively.

5.6 Data Analysis

5.6.1 Statistical Analysis

Prior to analysis, data were examined for normality and transformed as necessary. Outcome variables that were transformed were GDS score (reflected and square root transformed) and VASP score (reflected and square root transformed). Non-directional statistical tests were conducted and the level of significance was 0.05 for each test. Due to the exploratory nature of this study, adjustment was not made for the multiple outcomes. The analysis was a modified intention-to-treat analysis that included all subjects enrolled in the study who had a baseline assessment, regardless of completion of the study.

For all analyses time was measured in days after surgery for surgical group subjects, and in days from enrollment for control group subjects. To decrease burden surgical group subjects underwent baseline assessment at the time of their preoperative appointment, approximately 1 week before surgery. However, for purposes of the data analysis the day of surgery was considered to be baseline, or day

1, for surgical group subjects, not the day of enrollment. For control group subjects the day of enrollment was considered to be baseline, or day 1.

Student *t*-tests for continuous measures and chi-square tests for categorical measures were conducted to test whether the surgical and control groups differed on key clinical and demographic characteristics and baseline scores for the specified outcome measures. If the groups differed significantly on a key baseline measure, then that baseline measure was examined as a potential covariate in subsequent analyses. Note that the expectation was that the two groups would differ significantly in initial subjective health status (defined as VR-36 PCS and MCS scores) at baseline. This was addressed in the analytic approach described below.

5.6.1.1 Analysis of research question 1: What are the effects of undergoing elective outpatient surgery on the physical health of patients with preexisting PTSD?

A random coefficients regression model approach, which is a type of hierarchical mixed effects model designed for longitudinal data, was used to test for differences in trajectories of change in longitudinal VR-36 PCS scores, which included assessments at baseline, four weeks, and twelve weeks in the two groups. The random coefficients regression model approach was applied because this model allows the intercept and slope of change for each patient to vary from baseline and from assessment to assessment. Therefore, the individual's trajectory of change over time interval was the dependent outcome (Brown and Prescott 2006). Originally used in econometrics and educational research, the random coefficients regression model approach is particularly advantageous in the present analysis because it allows assessment of the population-level effects of an intervention, as well as the effects of

time-varying covariates within individuals, even when group members differ substantially in their initial level of the outcome of interest (Deleeuw and Kreft 1986).

Major advantages of a random coefficients regression model over a traditional repeated-measures analysis or examination of change score controlling for baseline was that the method: (a) provided improved estimates of individual effects; (b) allowed for missing data points over time; (c) adjusted for serial correlation (e.g., measurements not equally correlated across time); (d) allowed for incorporation of both time-independent and time-dependent covariates; (e) allowed for irregular measurement occasions (e.g., does not assume time intervals are equal), and; (f) provided the ability to model patient-specific time trends (e.g., response to treatment or condition can be individualized).

Prior to constructing the random coefficients regression model of longitudinal PCS scores, mean PCS scores were graphed over time to visually examine the temporal pattern of change within each group over the course of data collection. These graphs indicated that the temporal pattern change on mean PCS scores over time was non-linear in the surgical group and non-existent in the control group. Specifically, a graph of mean PCS scores by group over time suggested that surgical group participants demonstrated an abrupt shift in both the level and rate of change on PCS scores following surgery, while control group participants demonstrated little to no change on PCS scores from baseline to 12 weeks after enrollment. Quadratic, cubic, and square root polynomial effects of time were tested and either found not significant or demonstrated convergence issues, likely due to the small number of subjects.

After review of the relevant literature about the analysis of such discontinuous phenomena, it was decided to apply techniques described by Singer and Willett (2003).

Specifically, surgical intervention was coded as a time-varying covariate that occurred between baseline and one week only to subjects in the surgical group. Therefore, the analytic model of longitudinal PCS scores included the following fixed effects: surgical intervention (exposed to surgery or not), time, the surgical intervention-by-time interaction, and two covariates (age and gender). Random effects were subject and subject-by-time; intercepts and slopes were set to random. It was hypothesized that the two groups would have significantly different trajectories over time as evidenced by a significant group-by-time interaction. *A priori* contrasts of the trajectories generated by the model were conducted at one week, four weeks, and twelve weeks to test for significant differences in the groups at those time points.

Based on a review of the literature, it was expected that the surgical group would demonstrate lower PCS scores at baseline compared to the control group and would demonstrate a non-linear trend in PCS scores over time (Wellwood et al. 1998, Burney and Jones 2002, Busija et al. 2008, Langenbach et al. 2008, Shi et al. 2009). Subjective health scores would likely be lower in subjects scheduled to receive elective surgery, as such surgery is performed to improve physical health. Previous studies of physical subjective health change after outpatient elective surgery using the PCS demonstrated a transient decrease in physical subjective health status at four weeks after surgery due to pain and functional limitation, followed by a return to baseline by twelve weeks after surgery (Wellwood et al. 1998, Burney and Jones 2002, Busija et al. 2008, Langenbach et al. 2008, Shi et al. 2009). In contrast, subjects in the control group should demonstrate stable or very slow change on PCS scores across the twelve-week study period. If PTSD did not have an adverse effect on subjective physical health recovery after surgery, then the surgical and control groups should differ significantly

at baseline on PCS scores, but converge at 3 months as early declines in subjective health between baseline and four weeks were offset by subjective health improvement between four and twelve weeks due to healing and the beneficial effects of the surgery. This was the expected trend after elective surgery. However, if elective surgery exerted a persistent adverse effect on the subjective physical health of the veteran with chronic PTSD, then surgical and control groups would differ significantly at baseline on PCS scores, and not converge at twelve weeks.

5.6.1.2 Analysis of research question 2: What are the effects of undergoing elective outpatient surgery on the mental health of patients with preexisting PTSD?

A series of random coefficients regression models were also used to test for differences in trajectories of change on longitudinal MCS scores, GDS scores, and CAPS severity scores. The random coefficients regression model of MCS scores included assessments at baseline, one week, four weeks, and twelve weeks in the two groups. The random coefficients regression models of GDS scores and CAPS severity scores included assessments at baseline, four weeks, and twelve weeks in the two groups. The random coefficients regression model approach was applied because such models allow the intercept and slope of the change for each patient to vary from baseline and from assessment to assessment. Therefore, the individual's trajectory of change in MCS scores, GDS scores, or CAPS severity scores over time interval was the dependent outcome for each analysis (Brown and Prescott 2006). The advantages of the random coefficients regression model approach were previously described in detail under the analysis of research question 1.

Prior to constructing each random coefficients regression model, the dependent variable (i.e., mean MCS scores, GDS scores, or CAPS severity scores) was graphed

over time to visually examine the temporal pattern of change within each group. These graphs indicated that the temporal pattern of change in longitudinal MCS scores was non-linear in the surgical group. Specifically, a graph of mean MCS scores by group over time suggested that surgical group participants demonstrated an abrupt shift in both the level and rate of change of MCS scores following surgery, while control group participants demonstrated a slow decline in MCS scores from baseline to 12 weeks after enrollment. Quadratic, cubic, and square root polynomial effects of time were tested and either found not significant or demonstrated convergence issues, likely due to the small number of subjects.

After review of the relevant literature about the analysis of such discontinuous phenomena, it was decided to apply techniques described by Singer and Willett (2003). Specifically, surgical intervention was coded as a time-varying covariate that occurred between baseline and one week only to subjects in the surgical group. Therefore, the analytic model of longitudinal MCS scores included the following fixed effects: surgical intervention (exposed to surgery or not), time, the surgical intervention-by-time interaction, and three covariates (age, gender, and season). Random effects were subject and subject-by-time; intercepts and slopes were set to random. It was hypothesized that the two groups would have significantly different trajectories over time as evidenced by a significant surgical intervention-by-time interaction. In the event of a significant surgical-intervention-by-time interaction, contrasts of the trajectories generated by the model would be conducted at each time point to test for significant differences in the groups on MCS scores.

In contrast, graphs of GDS scores and CAPS severity scores demonstrated little change over time regardless of surgical intervention. Quadratic, cubic, and square root

polynomial effects of time were tested and found not significant. Separate random coefficients regression models were used to test for differences in trajectories of change in GDS scores and CAPS severity scores at baseline, four weeks, and 12 weeks after surgery or enrollment. In each model, surgical intervention was coded as a time-varying covariate that occurred between baseline and one month only to subjects in the surgical group. Therefore, each analytic model of longitudinal GDS scores or CAPS severity scores included the following fixed effects: surgical intervention (i.e., exposed to surgery or not), time, the surgical intervention-by-time interaction, and two covariates (age and gender). Random effects were subject and subject-by-time; intercepts and slopes were set to random. It was hypothesized that the two groups would have significantly different trajectories over time as evidenced by a significant surgical intervention-by-time interaction. In the event of a significant surgical intervention-by-time interaction, contrasts of the trajectories generated by each model would be conducted at each time point to test for significant differences in the groups on GDS scores or CAPS severity scores.

5.6.1.3 Analysis of research question 3: What preoperative characteristics of the patient with preexisting PTSD predict physical and mental health change after elective surgery?

A series of random coefficients regression models were used to test for the effects of age, gender, baseline GDS scores, baseline CAPS severity scores, baseline VASP scores, or baseline STAI-S scores on trajectory of change on VR-36 PCS or MCS scores in surgical group subjects only. Prior to constructing the random coefficients regression models, mean PCS or MCS scores were graphed over time to visually examine the temporal pattern of change within only surgical group subjects at baseline, one week, four weeks, and 12 weeks after surgery. These graphs indicated that the

temporal pattern of change in both PCS and MCS scores over time was non-linear. Specifically, a graph of mean PCS and MCS scores suggested that surgical group participants demonstrated an abrupt shift in both the level and rate of change of PCS and MCS scores following surgery. Quadratic, cubic, and square root polynomial effects of time were tested and either found not significant or demonstrated convergence issues, likely due to the small number of subjects.

Because these subgroup analyses included only surgical group subjects, a time-varying covariate could not be used to capture the effect of surgery on the level and rate of change in PCS or MCS scores. Therefore, the data were left censored at one week after surgery to result in a linear trajectory of PCS or MCS scores from one week to 12 weeks after surgery, and the random coefficients regression model approach was applied to longitudinal PCS or MCS scores at one week, four weeks, and twelve weeks in the surgical group only. Quadratic, cubic, and square root polynomial effects of time were tested again and either found not significant or demonstrated convergence issues.

Next, a set of random coefficients regression models of the PCS or MCS trajectory were applied to PCS or MCS scores at one week, four weeks, and twelve weeks in the surgical group only. Each analytic model included the following fixed effects: time, baseline PCS or MCS scores, and one of the candidate predictor variables (age, gender, baseline CAPS severity score, baseline GDS score, baseline VASP scores, or baseline STAI-S score). Random effects were subject and subject-by-time for all models. Any baseline predictor variable that was significant at the 0.10 level would be retained for further testing.

Next, all retained baseline measures were entered into the model simultaneously to examine the influence of each after controlling for all other explanatory variables in the models. The independent variables included in these models were examined for multicollinearity and influential outliers. The final model included: (a) the fixed effects of time since surgery and baseline PCS or MCS score; (b) the random effects of subject and subject-by-time, and; (c) the main effects of baseline covariates that were significant at the 0.05 level after controlling for all other variables in the model and eliminating multicollinear variables.

5.7 Results

5.7.1 Subject Disposition

A total of 174 patients were screened for participation in the study, 91 for participation in the surgical group and 83 in the control group. A total of 29 patients provided informed consent and completed baseline assessment for participation in the surgical group. All 29 subjects went on to have surgical procedures as scheduled. The most common type of surgical procedure was orthopedic (n = 9), with the remainder evenly divided between general (n = 4), gynecology and urology (n = 4), plastic (n = 4), neurosurgery (n = 4), and oromaxillofacial/otolaryngology (n = 4). A total of 32 patients provided informed consent for participation in the control group; however, one subject disclosed misrepresenting exclusion criteria immediately after providing consent and was therefore dropped from the study before completing baseline assessment. Therefore, 31 control group subjects completed baseline assessment.

Of the 60 analyzable subjects, 58 (96.6%) provided data at 1 week, 55 (91.6%) provided data at 4 weeks, and 53 (88.3%) provided data at 12 weeks. A total of 7

(11.7%) participants withdrew or were lost to follow-up prior to completing 12-week assessment. The frequency of attrition was not significantly different between the surgical and control groups at 1 week (Fisher's exact test; p = .49), 4 weeks (Fisher's exact test; p = .35) or 12 weeks of study participation (Fisher's exact test, p = .43). Subjects who were lost to follow up were not significantly different from subjects who remained in the study with respect to age (WS = 230; n1 = 53, n2 = 7; p = .71), gender (Fisher's exact test; p = .99), years of education (WS = 171.5; n1 = 53, n2 = 7; p = .31), or baseline PCS, (WS = 198; n1 = 53, n2 = 7; p = .74), MCS (WS = 218; n1 = 53, n2 = 7; p = .93), GDS (WS = 252; n1 = 53, n2 = 7; p = .35), or CAPS severity scores (WS = 252; n1 = 53, n2 = 7; p = .15), indicating that missing data were missing at random. Screening, enrollment and retention in the surgical and control groups are graphically depicted in Figures 2 and 3, respectively.

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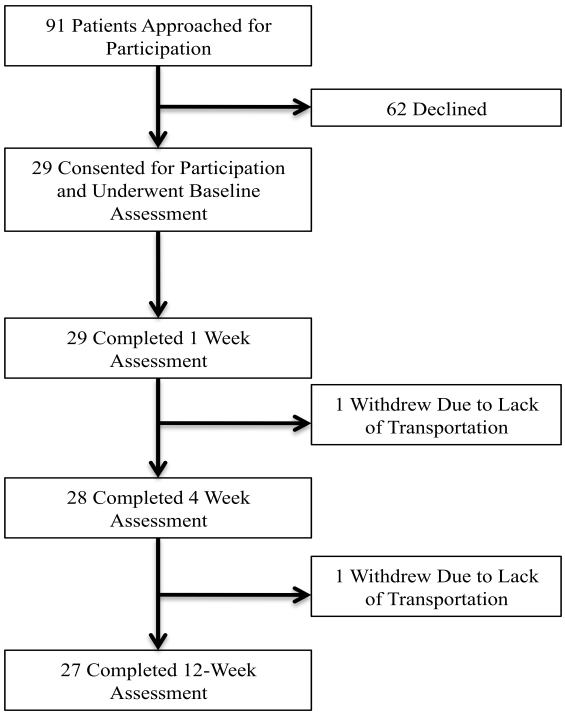

Figure 2. Subject flow through surgical group over 12 weeks

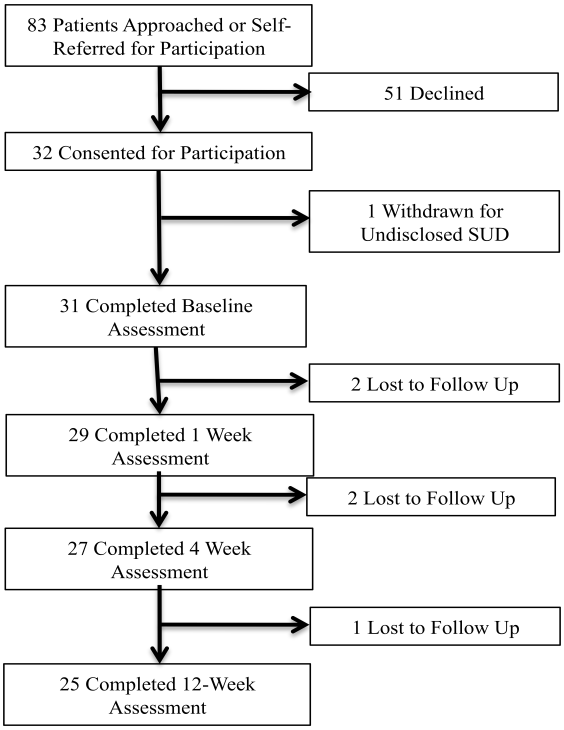

Figure 3. Subject flow through control group over 12 weeks

5.7.2 Baseline Characteristics

Demographics and comorbidities (Table 5) and psychoactive medication use (Table 6) were similar between surgical and control patients, with the exception that control patients were older, had suffered from posttraumatic symptoms for longer periods of time, and more likely to be taking tricyclic or tetracyclic antidepressants. Age was already included as a covariate in all analyses to control for its effect on physical and mental health status. Although not significant, the current use of tricyclic or tetracyclic antidepressants was considered as a potential covariate in subsequent analyses. At baseline there were no significant differences between surgical and control subjects in mean MCS, PCS, GDS, or CAPS severity scores (Table 7).

Table 5. Baseline sociodemographics and comorbidities

Variable	Surgical (n = 29)	Control (n = 31)	*p*
Age	51.8 ± 2.3	59.4 ± 1.5	< .01*
Education	13.2 ± 0.3	13.8 ± 0.4	.24
Duration of PTSD symptoms (in years)	24.8 ± 3.1	36.4 ± 1.9	< .01*
Male gender	25 (86 %)	27 (87 %)	.91
Ethnicity			.14
White	15 (52 %)	10 (32 %)	
African-American	13 (45 %)	21 (68 %)	
Pacific Islander	1 (3 %)		
Married	20 (70 %)	17 (55 %)	.26
Depression	18 (62 %)	25 (81 %)	.11
Bipolar disorder	1 (4 %)	1 (3 %)	.96
Other anxiety disorder	6 (21 %)	6 (19 %)	.90
Hypertension	18 (62 %)	24 (81 %)	.11
Myocardial infarction	2 (7 %)	2 (7 %)	.95
Arrthymia	1 (4 %)	1 (3 %)	.96
Chronic obstructive pulmonary disease	3 (10 %)	2 (6 %)	.61
Asthma	6 (21 %)	2 (6 %)	.11
Chronic bronchitis	4 (14 %)	3 (10 %)	.62
Obstructive sleep apnea	9 (31 %)	7 (23 %)	.46
Gastroesphageal reflux disease	12 (41 %)	13 (42 %)	.95
Cirrhosis	0 (0 %)	1 (3 %)	.33

Table 5. Baseline sociodemographics and comorbidities

Variable	Surgical (n = 29)	Control (n = 31)	*p*
Smoking (hx)	18 (32 %)	21 (67 %)	.65
Smoking (current)	10 (34 %)	9 (29 %)	.65
Ethanol abuse (hx)	15 (52 %)	19 (61 %)	.45
Ethanol abuse (current)	6 (21 %)	7 (23 %)	.86
Obesity	14 (48 %)	18 (58 %)	.45
Illicit substance use (hx)	5 (17 %)	11 (35 %)	.11
Type I diabetes	1 (3 %)	4 (13 %)	.19
Type II diabetes	5 (17 %)	4 (.13 %)	.64
Chronic pain	21 (72 %)	23 (74 %)	.88
Transient ischemic attack/cerebrovascular accident without sequelae	1 (3 %)	4 (13 %)	.19
PTSD at baseline[a]	24 (83 %)	26 (81 %)	.91

Note: Data are described as mean ± standard error of the mean or number (percent); PTSD = Posttraumatic Stress Disorder; hx = history

[a] Indicates the number (percent) of subjects meeting full diagnostic criteria for PTSD on the Clinician Administered PTSD Scale using the 'frequency ≥ 1, intensity ≥ 2' assessment criteria set forth in Weathers, Ruscio, and Keane (1999)

* Significant at $p < .05$).

Table 6. Psychoactive medication use

Medication	Surgical (n = 29)	Control (n = 31)	*p*
Selective serotonin reuptake inhibitors	11 (38 %)	15 (48 %)	.41
Tricyclic/tetracyclic Antidepressants	5 (17 %)	12 (39 %)	.06*
Anticonvulsants	4 (14 %)	4 (13 %)	.92
Benzodiazepine/sedative Hypnotic	7 (24 %)	4 (13 %)	.26
Atypical antipsychotic	7 (24 %)	4 (13 %)	.26
Other antidepressant	10 (34 %)	13 (42 %)	.55
Antihistamine	3 (10 %)	1 (3 %)	.27
Alpha antagonist	8 (28 %)	9 (29 %)	.90

Note: Data are described as number (percent)

* $p < .10$.

Table 7. Mean scores by group at baseline

Measure	Surgical (n = 29)	Control (n =31)	*t*	*df*	*p*
VR-36 Physical Component Summary (PCS) score	37.2 ± 1.5	37.7 ± 1.7	.25	58	.81
VR-36 Mental Component Summary (MCS) score	37.6 ± 2.1	34.3 ± 1.9	1.19	58	.24
Geriatric Depression Scale (GDS) score	18.3 ± 1.7	19.6 ± 1.4	.63	58	.53
Clinician Administered PTSD Scale (CAPS) severity score	69.6 ± 5.0	74.3 ± 4.0	.74	58	.46
State-Trait Anxiety Inventory, State (STAI-S) scale score	47.9 ± 2.9	47.3 ± 2.3	.87	58	.87
Visual Analog Scale for Pain (VASP) score	56.0 ± 5.2	46.9 ± 5.3	1.23	58	.22

Note; Data are described as mean ± standard error of the mean; VR-36 = Veterans Rand 36-Item Health Survey; PTSD = Posttraumatic Stress Disorder

5.7.3 Outcomes

Table 8 depicts the mean adjusted PCS, MCS, GDS, and CAPS severity scores (± standard error of the mean) at baseline, 1 week, 4 weeks, and 12 weeks after surgery or enrollment, respectively, in the surgical and control groups. Scores were adjusted for the fixed and random effects described in the data analysis. Table 8 also depicts Cohen's *d* effect sizes for the between-group difference in mean adjusted scores at each time point.

Table 8. Mean adjusted scores by group over 12 weeks after enrollment

		Mean adjusted score (± SE)			
Measure	Group	Baseline	Week 1	Week 4	Week 12
VR-36 Physical Component Summary (PCS) score	Surgical	37.0 ± 1.2	33.5 ± 1.2	35.0 ± 1.2	37.4 ± 1.5
	Control	37.7 ± 1.3	37.3 ± 1.0	37.1 ± 1.1	36.8 + 1.5
	Cohen's *d*	-.10	-.63	-.35	.07
VR-36 Mental Component Summary (MCS) score	Surgical	36.4 ± 1.6	33.6 ± 1.9	34.8 ± 1.8	36.7 ± 2.1
	Control	35.2 ± 1.4	36.5 ± 1.6	35.3 ± 1.5	33.3 ± 2.0
	Cohen's *d*	.15	-.40	-.08	.36
Geriatric Depression Scale (GDS) score	Surgical	17.9 ± 1.5	-	18.8 ± 1.5	18.5 ± 1.5
	Control	19.0 ± 1.1	-	19.2 ± 1.2	19.2 ± 1.2
	Cohen's *d*	-.05	-	-.07	-.02
Clinician Administered PTSD Scale (CAPS) severity score	Surgical	71.5 ± 4.1	-	71.5 ± 4.3	68.8 ± 4.6
	Control	72.9 ± 3.3	-	71.8 ± 4.0	70.6 ± 4.8
	Cohen's *d*	-.07	-	-.01	-.07

Note: Data are described as mean adjusted score ± standard error of the mean adjusted score; means are for predicted individual scores that have been adjusted for both fixed (surgical intervention, time, age, and gender) and random (subject) effects derived from the random coefficients regression model; mean MCS scores were also adjusted for fixed effect of season; SE = standard error of the mean; VR-36 = Veterans Rand 36-Item Health Survey; PTSD = Posttraumatic Stress Disorder; "-" indicates data were not collected for this outcome at this time point

5.7.3.1 Effect of elective surgery on physical health

Random coefficients regression analyses on longitudinal PCS scores identified a statistically significant effect of age (F = 5.20; df = 1,60.6; p = .03), surgical intervention (F = 14.01; df = 1,141; p < .00) and the surgical intervention-by-time interaction (F = 5.45; df = 1,58.8; p = .02), but not time (F = 3.30; df = 1,55.8; p = .07) or gender (F = 0.94;

df = 1,56.9; p = .34). As part of the random coefficients regression method, between-group contrasts were performed to compare the surgical and control participants at each scheduled assessment point along the predicted trajectories across time. Results indicated a statistically significant difference in which the PCS scale scores of the surgical group were significantly lower than those of the control group at 1 week (F = 14.01; df = 1,142; p < .00), but not 4 weeks (F = 3.41; df = 1,132; p = .07) or 12 weeks (F = 0.13; df = 1,50.8; p = .72) after surgery or enrollment, respectively. Mean adjusted PCS scores over time are depicted graphically in Figure 4. The intraclass correlation of the PCS score averaged .94 in surgical group subjects and .94 in control group subjects across the four scheduled assessments (baseline, 1 week, 4 weeks, and 12 weeks).

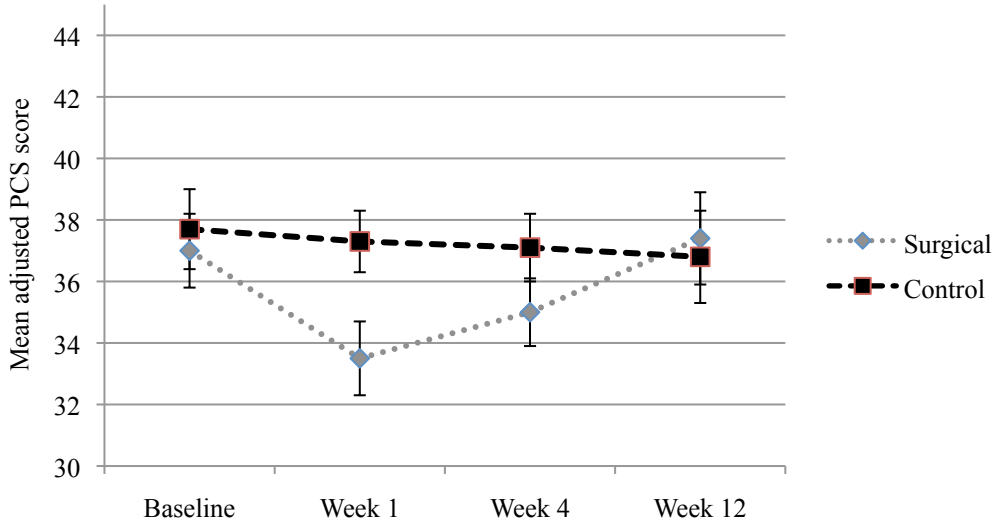

Figure 4. Mean adjusted VR-36 Physical Component Summary (PCS) scores over time

5.7.3.2 Effect of elective surgery on mental health

Random coefficients regression analyses on longitudinal MCS scores identified a statistically significant effect of age (F = 20.64; df = 1,57.6; p < .00), season (F = 2.82; df

= 3,136; p = .04), surgical intervention (F = 6.42; df = 1,138; p = .01) and the surgical intervention-by-time interaction (F = 7.07; df = 1,62.7; p < .00), but not time (F = 0.00; df = 1,48.5; p = .96) or gender (F = 0.35; df = 1,53.9; p = .56). As the surgical intervention-by-time interaction was significant, between-group contrasts were performed to compare the surgical and control participants at each scheduled assessment point along the predicted trajectories across time. Results indicated a statistically significant difference in which mean adjusted PCS scores of the surgical group were significantly lower than those of the control group at 1 week (F = 5.06; df = 1,138; p = .03), but not 4 weeks (F = .15; df = 1,134; p = .70) or 12 weeks (F = 2.12; df = 1,50.3; p = .15) after surgery or enrollment, respectively. The mean adjusted MCS scores over time are depicted graphically in Figure 5. The intraclass correlation of the MCS score averaged .94 in surgical group subjects and .92 in control group subjects across the four scheduled assessments (baseline, 1 week, 4 weeks, and 12 weeks).

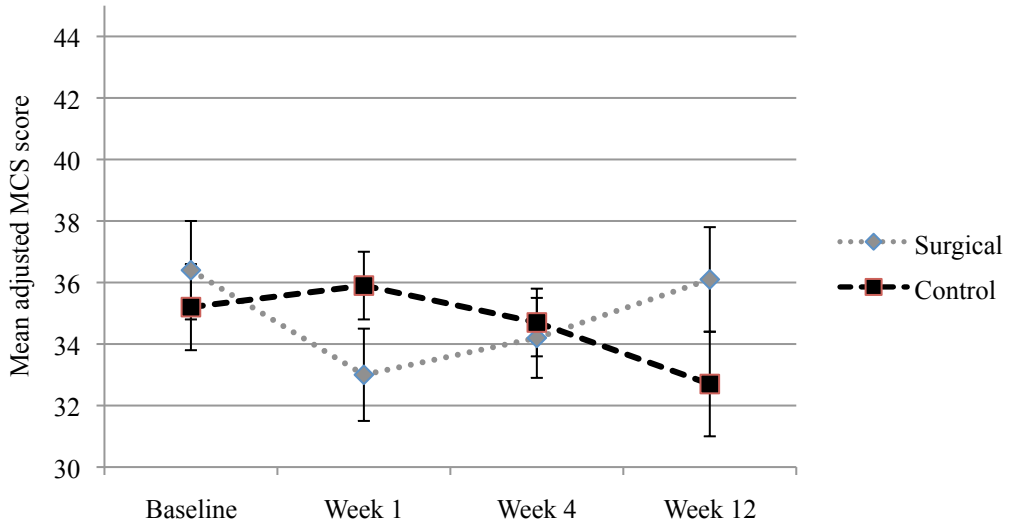

Figure 5. Mean adjusted VR-36 Mental Component Summary (MCS) scores over time

Random coefficients regression analyses on longitudinal GDS scores identified a statistically significant effect of age ($F = 25.27$; $df = 1,60.7$; $p < .00$), but not time ($F = 0.17$; $df = 1,67.5$; $p = .49$), surgical intervention ($F = .96$; $df = 1,69.5$; $p = .33$) or the surgical intervention-by-time interaction ($F = .13$; $df = 1,70.4$; $p = .72$). As the omnibus test of the surgical intervention-by-time interaction was not significant, no further analyses were performed on GDS score. The mean adjusted GDS scores over time are depicted graphically in Figure 6. The intraclass correlation of GDS scores averaged .95 in surgical group subjects and .90 in control group subjects across the three scheduled assessments (baseline, 4 weeks, and 12 weeks).

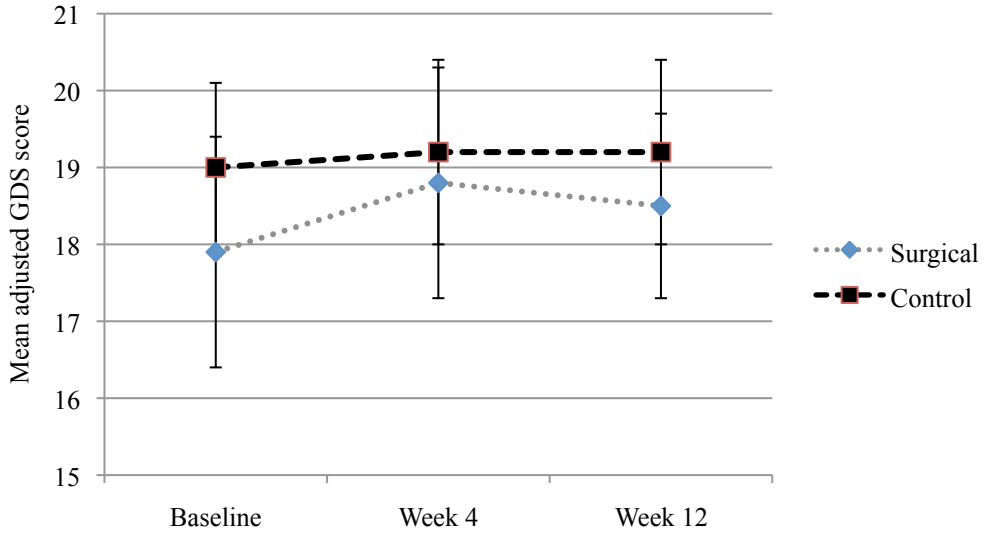

Figure 6. Mean adjusted Geriatric Depression Scale (GDS) scores over time

Random coefficients regression analyses on longitudinal CAPS severity scores identified a statistically significant effect of age ($F = 19.18$; $df = 1,59.7$ $p < .00$), but not time ($F = 0.57$; $df = 1,73.7$; $p = .45$), surgical intervention ($F = 0.16$; $df = 1,69.1$; $p = .69$) or surgical intervention-by-time interaction ($F = 0.09$; $df = 1,77.2$; $p = .76$). As the omnibus test of the surgical intervention-by-time interaction was not significant, no further analyses were performed on CAPS severity scores. The mean adjusted CAPS severity scores over time are depicted graphically in Figure 7. The intraclass correlation of CAPS severity scores averaged .93 in surgical group subjects and .92 in control group subjects across the three scheduled assessments (baseline, 4 weeks, and 12 weeks).

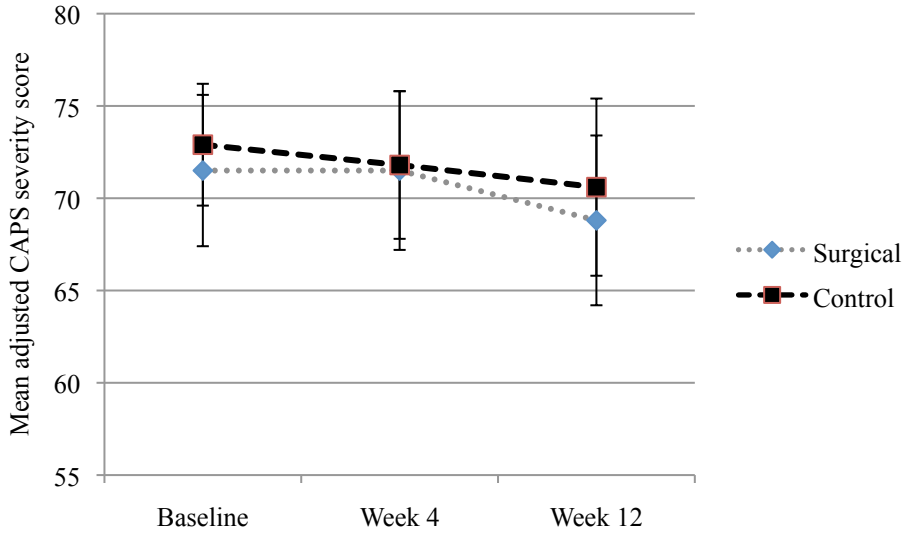

Figure 7. Mean adjusted Clinician-Administered PTSD Scale (CAPS) severity scores over time

5.7.3.3 Predicting physical and mental health change after elective surgery

Random coefficients regression analyses of longitudinal PCS scores in the surgical group only at 1 week, 4 weeks, and 12 weeks after surgery identified a statistically significant effect of day ($F = 5.67$; $df = 21.9$; $p = .03$) and baseline PCS score ($F = 65.55$; $df = 1,26.3$; $p = < .00$). None of the six covariates evaluated individually (age, gender, baseline GDS score, baseline CAPS severity score, baseline VASP score, or baseline STAI-S score) were significant at $p < .10$ after controlling for baseline PCS score.

Random coefficients regression analyses of longitudinal MCS scores in the surgical group only at 1 week, 4 weeks, and 12 weeks after surgery identified a statistically significant effect of baseline MCS score ($F = 20.44$; $df = 1,26.2$; $p = < .00$). Time was not statistically significant ($F = 1.21$; $df = 16.4$; $p = .29$) after controlling for baseline MCS score. Of the six covariates evaluated individually (age, gender, baseline

GDS score, baseline CAPS severity score, baseline VASP score, or baseline STAI-S score), only baseline GDS score was statistically significant ($F = 4.51$; $df = 1,25.8$; $p = .04$) after controlling for baseline MCS score. However, significant multicollinearity existed between baseline GDS score and baseline MCS score (mean variance inflation > 2). Therefore, baseline GDS score was eliminated from further consideration.

5.7.4 Adverse Events

Two surgical subjects experienced significant adverse events during study participation. One participant was unexpectedly admitted to the hospital for overnight observation after surgery due to concerns about sleep apnea, and one participant made a suicidal gesture 6 weeks after having surgery. Neither subject was permanently harmed by these events. No participant in the control group experienced any adverse events.

5.8 Discussion

The present study has expanded our understanding of the effects of common outpatient elective surgeries on veterans with chronic posttraumatic stress disorder (PTSD). The findings of this study suggest that surgery has a significant but short-lived adverse impact on the physical and mental subjective health status of veterans with chronic PTSD. This adverse impact peaks shortly after surgery, but resolves for the majority of patients within one month. We were unable to detect an effect on posttraumatic symptom severity or depressive symptom severity one month after surgery, possibly because the adverse effects had abated before these symptoms were reassessed. Finally, we were unable to assess the predictive validity of age, gender, preoperative posttraumatic symptoms, depressive symptoms, pain, and anxiety

severity for changes in mental and physical subjective health status over the three months of data collection. However, the most significant finding may be that the age- and gender-adjusted subjective mental and physical health scores of veterans with chronic PTSD were in the lowest 10% of the United States population (Kazis et al. 1998). This finding suggests a significant burden of physical and mental comorbidity regardless of surgical status, and that physical and mental comorbidity is likely the source of greater risk of postoperative mortality in veterans with PTSD.

The preoperative subjective physical health status of the subjects presenting for elective surgery was poor. At baseline, the mean PCS score for a veteran presenting for outpatient elective surgery was 37.0 after adjusting for age and gender. As the PCS is normalized to a mean of 50 and a standard deviation of 10, the veterans who underwent outpatient elective surgery while participating in this study were an average of 1.3 standard deviations below population norms. This is concerning, because a study of outpatient veterans reported that each 5-point increment below a PCS of 50 increased the odds ratio for risk of 1-year mortality by 1.27 compared to veterans within 5 points of the population mean (Fan et al. 2004). Similar findings were observed for subjective mental health status. At baseline, the mean MCS score for a veteran presenting for outpatient elective surgery was 36.4 after adjustment for age and gender, indicating that surgical group participants were 1.4 standard deviations below population norms. Fortunately, subjective mental health status appears to be less influential on risk of mortality: In outpatient veterans, each 5-point increment below a MCS of 50 increased the odds ratio for risk of 1-year mortality by 1.08 compared to veterans within 5 points of the population mean (Fan et al. 2004).

Therefore, the veterans in this study were at greater risk of mortality before they ever entered the operating room.

Participants in the surgical group also presented with clinically significant depressive and posttraumatic symptoms. The mean GDS score of veterans with chronic PTSD was 17.9 before surgery, indicating mild to moderate depression (Yesavage et al. 1983), while the mean CAPS severity score was 71.5 before surgery, indicating moderate to severe PTSD symptomatology (Weathers, Keane, and Davidson 2001). Therefore, patients with chronic PTSD continue to suffer from the psychiatric sequelae of their experiences, even 25 years after being exposed to a traumatic event.

On average, outpatient elective surgery affected both the physical and mental health of patients with chronic PTSD. The impact of elective outpatient surgery on physical subjective health status was transient. Surgical group subjects experienced a mean age-and-gender-adjusted decline of 3.5 points in PCS scores and 2.8 points in MCS scores that resolved by one month after surgery. For comparison, chronic lung disease has been estimated to result in a decline of 3.6 points in PCS score and major depression to result in a decline of 8 points in MCS score outpatient veterans (Kazis et al. 1998).

We were unable to detect an effect of outpatient elective surgery on depressive symptom severity or posttraumatic symptom severity. The lack of a significant effect of outpatient elective surgery on depressive and posttraumatic symptoms may have been due to the selected measurement points. In the present study we were unable to collect data on posttraumatic and depressive symptom severity one week after surgery because of concerns about excessive subject burden. Given that subjects reported significant decreases in subjective mental health status one week after surgery, a study

that collects data about posttraumatic and depressive symptoms within a week after surgery may detect a significant effect of surgery on the severity of these more specific psychiatric symptoms.

This inability to detect the predictive validity of baseline predictors for subjective health change was likely because of the small sample size remaining after removal of the nonsurgical subjects. The findings associated with research question 3 likely represent a combination of type I and type II error: Type I error in erroneously accepting the random coefficients regression model we were obligated to report, and type II error in erroneously excluding age, gender, baseline depressive symptom severity, baseline posttraumatic symptom severity, baseline pain severity, baseline and situational anxiety as predictors of physical or mental subjective health status over time after surgery. The size of the surgical subgroup was simply too small to both account for the non-linear trajectory of subjective health after surgery and evaluate the predictive validity of the covariates under consideration.

Limitations of the present study include the relatively small sample size, the limited duration of data collection, the pragmatic necessity of assessing surgical group subjects approximately one week before surgery, and the reliance on self-report measures to generate data. Limiting data collection to 12 weeks after surgery made the study practicable but means that we cannot rule out an adverse effect of elective surgery on long-term mortality in this population. To address the limited duration of data collection, future studies should attempt to follow patients for 1 to 5 years to further explore the impact of elective surgery on long-term mortality. The pragmatic necessity of assessing surgical group subjects 1 week before surgery was likely an additional source of random error, because events may have occurred to surgical

group subjects between baseline assessment and their day of surgery that were not accounted for by the study. Future studies should address this limitation by completing the baseline assessment as close to the day of surgery as possible.

The reliance on self-report measures could be addressed by incorporating clinician assessments of functional status. Clinician assessments of functional status were not practicable for this study because of the variety of surgical diagnoses included in the sample. However, future studies that enroll surgical subjects with a single surgical diagnosis, such as total knee replacement surgery, could incorporate any of several objective functional assessments in addition to patient self-reported physical functional status (Mizner et al. 2010).

Strengths of the present study include the use of previously validated measures, the inclusion of an appropriate comparison group to assess the effect of elective outpatient surgery on the mental and physical health of veterans with chronic PTSD, and the use of data analysis methods that allow the estimation of effects of both surgery (surgical intervention) and the healing process (surgical intervention-by-time interaction) while controlling for covariates such as age, gender, and seasonal fluctuations in mental subjective health status.

Note that we do not consider these results applicable to veterans who undergo more intensive or painful surgeries, those who are hospitalized after elective surgery, or those suffering from more acute exposure to traumatic events. Future studies should assess the impact of surgery and hospitalization on veterans with chronic posttraumatic stress disorder, and potentially include a control group of veterans without PTSD to provide a better estimation of the impact of PTSD on physical and

mental health after surgery. Future studies should also explore the effect of surgery on younger veterans, with more recent exposure to traumatic experiences.

The foremost implication of this study are that veterans with PTSD appear to be at greater risk for mortality at presentation for surgery due to poor baseline physical and mental health. On average, veterans with chronic PTSD can expect a significant but transient decline in their physical and mental subjective health after elective surgery, but should recover by one month after common outpatient elective surgeries. The present study found no evidence for a detrimental effect of outpatient elective surgery on physical or mental subjective health after three months. The present study also did not support a detrimental or beneficial effect of common outpatient elective surgeries on posttraumatic or depressive symptom severity in veterans with chronic PTSD, but this may have been due to the timing of data collection for these mental health issues.

6. The Influence of Elective Surgery on Subjective Health in Veterans with Chronic PTSD

The present study has expanded our understanding of the effects of common outpatient elective surgeries on veterans with chronic posttraumatic stress disorder (PTSD). The quantitative findings of this study suggest that surgery has a significant but short-lived adverse impact on the physical and mental subjective health status of veterans with chronic PTSD. This adverse impact peaks shortly after surgery, but resolves for the majority of patients within one month. We were unable to detect an effect on posttraumatic symptom severity or depressive symptom severity one month after surgery, possibly because the adverse effects had abated before these symptoms were reassessed. Finally, after controlling for age, gender, time, and baseline subjective physical and mental health status, we were unable to assess the predictive validity of preoperative posttraumatic symptom, depressive symptom, pain, and anxiety severity for changes in mental and physical subjective health status over the three months of data collection. This inability to detect the predictive validity of baseline measures for subjective health change was likely because of the small sample size remaining after removal of the nonsurgical subjects. However, the most significant finding may be that the age- and gender-adjusted subjective mental and physical health scores of veterans with chronic PTSD were in the lowest 10% of the United States population. This finding suggests a significant burden of physical and mental comorbidity regardless of surgical status, and that physical and mental comorbidity is likely the source of greater risk of postoperative mortality in veterans with PTSD.

The qualitative findings of this study support, elaborate, and expand upon the quantitative findings. Participants described significant subjective distress due to pain

and disability in the days and weeks after outpatient elective surgery. In many cases, patients felt that their pain management was complicated by a history of chronic pain syndrome. In particular, health care providers did not appear to account for opiate tolerance when prescribing analgesics for postoperative pain, nor establish a clear plan for transitioning responsibility for pain management back to the patient's primary care manager.

Participants also described significant psychological distress shortly after outpatient elective surgery, and attributed this psychological distress to the pain and physical disability that accompanied surgery. Participants indicated that this relationship between pain and physical disability and psychological distress might be driven by an inability to engage in normal activities they used to distract themselves from depressive and posttraumatic symptoms. Social support in the form of friends, family members, and pets helped patients cope with both physical and mental distress in the days and weeks after surgery. Unfortunately, psychologically distressed patients could become more irritable, and this irritability was often imperceptible to the patients. This irritability, and the lack of patient self-awareness regarding it, could result in an erosion of already strained relationships. In extreme cases, patients' social support systems could completely collapse, leaving the patient with little or no social support and vulnerable to risk of self-harm.

Participants also reported difficulties in interfacing with the health care system. The manner in which staff interacted with patients could result in short-lived psychological distress, particularly if patients could not establish a trusting, open, and reciprocal relationship with staff. Certain aspects of the perioperative environment that reminded patients of their particular traumatic experiences could acutely

exacerbate posttraumatic symptoms, but such incidents were rare and manageable with the assistance of a family member or friend trusted by the patient. Most distressing to patients were difficulties in accessing resources necessary for their postoperative recovery: Participants reported difficulties in obtaining mental health care, assistive devices such as braces, comprehensive pain management services, and physical therapy. In most cases participants felt uncomfortable in confronting health care providers about these unmet needs, and preferred to 'work around' these difficulties by contacting trusted staff members with a history of working with that particular patient.

6.1 Significance

The significance of this study lies in both the findings and the methodology. The findings are significant because they suggest that veterans with chronic posttraumatic stress disorder can undergo outpatient elective surgery with only transient adverse effects on their mental and physical health. However, the findings also suggest that substantial opportunities exist to improve the care of veterans with chronic PTSD before and after surgery.

In 2009, Brzezinski et al. reported that veterans with preexisting PTSD demonstrated greater one-year and five-year mortality after elective surgery compared to veterans without PTSD (Brzezinski et al. 2009a). Although PTSD was associated with multiple comorbidities in this sample (Brzezinski et al. 2009d), the effect of PTSD on mortality after elective surgery remained significant after controlling for other predictors of mortality such as age, diabetes, coronary artery disease, smoking, hypercholesterolemia, hypertension, and depression (Brzezinski et al. 2009d). The existing literature about surgical outcomes in veterans with preexisting PTSD did not

shed any light on potential causal mechanisms for this effect. Hudetz et al. (2010) reported greater risk of decrements in neuropsychological test performance in veterans with PTSD at one week after coronary artery bypass graft surgery (CABG), but adverse neuropsychological test performance at one week after surgery has not demonstrated an adverse effect on long-term mortality (Steinmetz et al. 2009). Ikossi et al. (2010) reported no significant differences after bariatric surgery between veterans with and without PTSD in length of postoperative hospital stay, early postoperative complications, or weight loss after one year. Other research efforts that enrolled subgroups of less than ten subjects with preexisting PTSD either reported no detectable effect of PTSD on any postoperative outcomes (Oxlad et al. 2006a, b, Oxlad and Wade 2006, 2008) or did not report subgroup analyses by PTSD diagnosis (Hudetz et al. 2007, Hudetz et al. 2009, Tully et al. 2010).

Therefore, there was mixed evidence in the literature for an adverse effect of PTSD on health after surgery. A preexisting diagnosis of PTSD was associated with greater risk of long-term postoperative mortality, but not with any adverse surgical outcomes that would suggest a causal process linking surgery and mortality. Exactly how to address the observed greater risk of mortality remains unclear, given the lack of known causal mechanisms linking elective surgery to mortality in veterans with PTSD.

One possible approach is to ignore the absence of known causal mechanisms and administer a non-specific therapy with broad effects. Brzezinski and other co-investigators at University of California - San Francisco have used this approach, and secured a two-year grant to conduct a randomized controlled trial to investigate the effect of prophylactic beta-blockade for veterans with PTSD undergoing elective

surgery ("Assistant Clinical Professor Marek Brzezinski Receives Grant to Study PTSD," 2009). This approach may demonstrate some success in reducing perioperative deaths due to cardiovascular morbidity, but has significant limitations. In addition to ignoring potential non-cardiac explanations for mortality in this population, prophylactic perioperative beta-blockade has also been associated with greater risk of 30-day all-cause mortality and stroke in a recent large phase III randomized clinical trial (Devereaux, et al., 2008).

An alternative hypothesis is that postoperative mortality in veterans with PTSD is an independent effect of having PTSD, rather than an interaction between PTSD and surgery. Studies in outpatients with PTSD support an independent effect of PTSD on postoperative mortality. Studies of Vietnam-era veterans have demonstrated that since the war those with PTSD were more likely to die from both cardiovascular and external causes such as suicide, homicide, and accidents, than those without PTSD (Boscarino 2008a, 2006b, 2008b, 2006a). This greater mortality is likely mediated by health risk behaviors, because outpatient Vietnam veterans with PTSD also demonstrated greater prevalence of smoking, ethanol use, and illicit substance use (Boscarino 2006b). The presence of these health risk behaviors would place any patient at greater risk for long-term mortality after surgery regardless of PTSD status (Wolters et al. 1996). Therefore, the greater risk of long-term postoperative mortality observed in veterans with PTSD is most likely an independent, adverse effect of PTSD rather than an interaction between PTSD and surgery, but several unanswered questions remained.

First, the relationship between PTSD and postoperative recovery, as compared to postoperative morbidity and mortality, is not known. An absence of indicators of

postoperative morbidity, such as hospital readmission, reoperations, etc., does not necessarily mean that the surgery was successful and resulted in the patient feeling better. This is concerning because studies suggest that psychological distress has an adverse effect on health over time. Farmer and Ferraro (1997) reported a self-reinforcing relationship between chronic physical illness, psychological distress, and physical disability over time in older adults. In that study, repeated measurements of these variables over time demonstrated that more severe chronic physical illness was associated with greater anxiety and worry, greater anxiety and worry was associated with worse perceived disability, and worse perceived disability was associated with more severe chronic physical illness. Therefore, a possibility exists that the high burden of preoperative physical comorbidities and cognitive biases associated with PTSD (Constans 2005) could interact with the acute physical distress associated with surgery to generate a spiral of disability-related health decline after elective surgery. If such an interaction existed, the patient with chronic PTSD would become progressively more disabled over time after surgery.

The findings of this study did not support the existence of such an interaction effect after common outpatient elective surgeries. After common elective outpatient surgeries patients with relatively severe preoperative PTSD symptoms experienced transient decrements in their mental and physical health, but recovered to baseline levels of health within one month. These data suggest that veterans with chronic PTSD can proceed with appropriate outpatient elective procedures without fearing permanent, detrimental effects to their physical or mental health from a catastrophic interaction of surgery and PTSD. However, they do remain at risk from the separate health effects of surgery and PTSD.

Second, the impact of elective surgery on posttraumatic symptom severity had not been previously described in the literature. Schreiber et al. (2004) reported that posttraumatic symptom severity in holocaust survivors did not change significantly from baseline to six months after cardiac surgery, but similar data had not been published for patients undergoing noncardiac surgery. The present study helps to address that gap in the literature by describing an absence of significant changes in posttraumatic symptom severity from baseline to three months after common outpatient elective surgeries.

Third, the population-specific postoperative needs of veterans with chronic PTSD had not been previously described. Compared to veterans without PTSD, veterans with chronic PTSD present for surgery with greater prevalence of diabetes, high blood pressure, depression, and high cholesterol, as well as greater prevalence of tobacco, alcohol, and illicit substance use (Brzezinski et al. 2009d). In addition, posttraumatic symptom severity has been associated with severity of chronic pain and pain-related disability in patients awaiting major surgery (Martin et al. 2010). Therefore, veterans with PTSD can be expected to have a high prevalence of comorbid conditions that could potentially be exacerbated by elective surgery and complicate postoperative recovery.

The findings of this study help to illuminate the population-specific needs of veterans with PTSD after elective outpatients surgery. Patients reported being physically distressed by a combination of postoperative and chronic pain, and felt that this physical distress precipitated psychological distress. Patients also described a need for the health care system to coordinate and ensure the timely delivery of postoperative services, to include comprehensive pain management, assistive devices,

and rehabilitative services. Finally, participants pointed out the need to prepare family members for the psychological distress experienced by the patient after elective surgery, and to support those family members while the patient recovered. Despite these distressing aspects of the perioperative experience, patients reported that outpatient elective surgeries were very beneficial to their physical and mental health if the surgery decreased their overall burden of chronic pain and disability.

The significance of the methodology lies in the use of general linear mixed modeling to analyze the behavioral outcomes over time after outpatient elective surgery. Surgery was associated with an abrupt shift in both the level and rate of change of physical and mental health. The representation of the surgical intervention as a time-varying covariate (Singer and Willett 2003) allowed the quantitative analysis of this study to estimate both the peak adverse impact of surgery and the rate of recovery back to baseline. Although this analytic technique has been used to analyze the impact of changing demographic factors such as educational acquisition, to my knowledge this is the first time it has been applied to assess the impact of surgical intervention on behavioral outcomes.

6.2 Strengths and Weaknesses

6.2.1 Feasibility

All studies must strike a balance between feasibility, interval validity, and external validity, and the decisions taken to ensure feasibility adversely impacted both the interval and external validity of the study. In particular, decisions that were incorporated to reduce the burden of participation, improve the available pool of potential subjects, and ensure subject access to emergency mental health services

weakened the study design. Finally, the conduct of the project by an active duty graduate student imposed a pragmatic limitation on the duration of participant follow-up in the postoperative period.

Concerns about subject burden in the surgical group precluded data collection immediately before and after surgery, and therefore may have adversely impacted internal validity. In particular, concerns about increasing preoperative anxiety meant that we were unable to collect baseline data in surgical group subjects on the day of surgery. The pragmatic necessity of assessing surgical group subjects at their preoperative appointment approximately one week before surgery could have been an additional source of random error, because events may have occurred to surgical group subjects between baseline assessment and their day of surgery that were not accounted for by the study. In addition, concerns about surgical group subject burden means that measures of posttraumatic and depressive symptom severity could not be collected one week after surgery. The presence of a significant detrimental effect of surgery on the mental subjective health status of surgical patients one week after surgery as measured by the Veterans Rand 36-Item Health Survey (VR-36) Mental Component Summary (MCS) score suggests that surgical group participants were more psychologically distressed at this time. This observation was supported by participant descriptions of greater distress from posttraumatic and depressive symptoms shortly after surgery. However, this acute distress had resolved by the time posttraumatic and depressive symptoms were measured one month after surgery. Therefore, it is possible that the findings of this study incorrectly conclude that posttraumatic and depressive symptoms were unaffected by outpatient elective

surgery simply because these symptoms were not measured when they were at their most severe.

Patients with a wide variety of surgical procedures were included to expand the pool of available potential subjects. This decision meant that the surgical stimulus was not consistent across subjects, and that the estimated effect of the surgery on subjective mental and physical health status represented a mean impact rather than the impact of any one particular surgical procedure. The variable impact of the surgical procedure on pain and disability was an additional source of random error, and may have lessened the internal validity of the study. In order to define the impact of a given surgical procedure it would be necessary to replicate the study using only patients who underwent a particular procedure.

The requirement that all subjects be entitled to use emergency mental health services at the Veterans' Affairs Medical (VAMC) Center without billing risk meant that a group of surgical subjects without PTSD could not be recruited. The purpose of the Veterans' Affairs (VA) health system is to provide care to all veterans, but there may be a fee when the care is for a non service-connected condition. Veterans are assessed on entering the VA system, and reassessed periodically over the remainder of their lives. According to the results of these assessments, veterans are assigned a proportion of service-connected disability ranging from 0 to 100 percent. Veterans with less than 100 percent service-connected disability are subject to financial means tests and may be at risk of being billed for emergency mental health services if their mental health issues are not service-connected. For example, a patient with a 30 percent service connection exclusively for a knee injury would be eligible for orthopedic services and surgery at the VAMC free of charge. If such a patient were

enrolled as a surgical group subject and found to be suicidal, then the VA would perform a means test and possibly charge a copay for providing emergency mental health services.

The inclusion of control group of patients without PTSD would have allowed the estimation of the impact of PTSD on the rate of recovery from elective surgery. At present, the findings estimate the rate of recovery from elective surgery (i.e., the surgical intervention-by-time interaction effect on physical and mental subjective health status) in veterans with PTSD, but whether this rate of recovery is similar to that of veterans without PTSD cannot be determined from the study as designed and conducted.

Finally, the nature of the primary investigator's military educational contract required the project to be conceived, funded, and carried to conclusion within three years. The implication of this time limit was that the study could not follow subjects for one and five years to determine the relative predictive validity of subject demographics, comorbidities, and subjective health measures for mortality. Although the subjective health measures do have predictive validity for mortality in veteran outpatients, it is not known at present if this predictive validity extends to veterans with chronic PTSD after outpatient elective surgery.

6.2.2 Internal Validity

Campbell (1957) described seven sources of unexplained and uncontrolled variance, or threats to internal validity, in behavioral research: (a) selection bias; (b) history; (c) maturation; (d) reactivity; (e) decay; (f) statistical regression, and; (g) mortality, also known as differential attrition. The internal validity of this study was threatened by issues of selection bias, history, and maturation, but relatively robust

against issues of reactivity, decay, statistical regression, and differential attrition. Where possible, analytic techniques were applied in this study to limit the impact of selection bias, history, and maturation.

6.2.2.1 Selection Bias

Selection bias effects internal validity when some aspect of how subjects are recruited or divided into treatment conditions results in systematic variance in outcome that is unrelated to treatment condition (Campbell 1957). To simplify, the groups were different at entry into the treatment condition, and that difference provides an alternative explanation for the findings. Selection bias is particularly insidious because it can combine with history, maturation, reactivity, decay, statistical regression, or differential attrition to produce unexpected interaction effects with synergistic influence on outcome. Selection bias can also have a large effect on the external validity of the research.

Selection bias was a threat to the validity of the present study. The best mechanism for reducing selection bias is randomization (Kish 1959), but randomization of patients to undergo or forego surgery was not feasible and unethical. Where treatment is pre-determined through subject choice or clinical requirement, the non-experimental or quasi-experimental cohort study becomes the only option. With quasi-experimental designs, random error is decreased and the statistical power of the research is increased if the two samples are similar in prognostic attributes. The best technique for ensuring baseline prognostic similarity in quasi-experimental studies using non-equivalent control groups is to match subjects between groups as closely as possible on known prognostic attributes (Polit and Beck 2010). Matching surgical and control subjects was not logistically feasible for the current study because of the time

limitation inherent in graduate work, but the similarity of the surgical and demographic groups in all baseline attributes except age and duration of PTSD symptoms supports the recruiting strategies used. A further effort to correct for the potential influence of selection bias was the use of age as a covariate in analyses of changes in mental and physical health after surgery.

6.2.2.2 History

History threatens internal validity when an event beyond the control of investigators exerts differential effects on treatment conditions (Campbell 1957). The threat of history to the internal validity of the present study is mixed. In support of the study, all data were collected from subjects from a single geographical area (northern North Carolina and southern Virginia) over a period of 14 months, meaning that participants were exposed to similar historical events over the duration of the study. A weakness of the study was that recruitment difficulties led to most of the surgical subjects being recruited in the first eight months of the study, while the majority of control subjects were recruited over the last four months of the study. Therefore, exposure to different environmental and societal stimuli over time was inevitable.

However, subjects in the surgical group demonstrated change over time in physical and mental health that was explainable in terms of the impact of the surgery, despite being enrolled and followed over nearly a year. In contrast, subjects in the control group demonstrated no discernible change over time in physical or mental health, as evidenced by the absence of a significant effect of time on physical health, mental health, depressive symptoms, or posttraumatic symptoms. In the present study, historical effects would have been staggered over time across the surgical group, producing greater random error, while historical effects would have been

minimized in the control group, resulting in less random error. While this phenomenon might have weakened the power of the study to detect changes in the mental and physical health of participants in the surgical group, it should not have systematically biased the direction of change after surgery because each subject was exposed to a slightly different set of historical effects over their participation in the study.

6.2.2.3 Maturation

Maturation affects internal validity when a variable systematically changes over time because of processes internal to the subject (Campbell 1957). Maturation can be part of normal development or the advancement of a pathological process (Polit and Beck 2010). Maturation is best controlled for experimentally by including a comparison group and by randomization. The subjects in this study could not be randomized, and the surgical and control groups were different in age and therefore possibly experiencing differential effects from maturation. However, age was included as a covariate in all analyses of mental and physical health over time.

6.2.2.4 Reactivity

Reactivity affects internal validity when the act of experimental measurement, as opposed to experimental manipulation, produces systematic changes in the outcome over time (Campbell 1957). When reactive measurement techniques cannot be avoided, a comparison or control group should be recruited so that the amount of reactivity can be estimated and statistically controlled (Polit and Beck 2010). In the present study, the minimal impact of reactivity was supported by the absence of a significant effect of time on mental and physical health of control group subjects. Were

reactivity a factor, control group participants would have demonstrated a systematic increase or decrease in measures of mental and/or physical health over time.

6.2.2.5 Instrument decay

In contrast to reactivity, decay effects internal validity when the act of measurement produces systematic change in the instrument over time (Campbell 1957). In human subjects research, decay occurs when data collectors can become fatigued, frustrated, apathetic, or just systematically biased in the application of research instruments, and injects greater random or systematic error into measurement. Instrument decay is best addressed experimentally through quality control processes that ensure measurement fidelity (Portney and Watkins 2009). In the present study, a single individual performed all testing, and all tests were administered in an identical order to all subjects throughout the study. Further evidence of the stability of testing conditions was the stable test-retest reliability of the instruments over time.

6.2.2.6 Statistical reversion toward the mean

Reversion or regression toward the mean affects internal validity when subjects initially display extreme performance on some measure (Campbell 1957). This is a statistical artifact that can lead to inaccurate conclusions that are most problematic when single group pretest-posttest designs are used. The present study controlled for statistical reversion toward the mean by using reliable instruments; using repeated measurements; including a control group; and enrolling subjects based on an established diagnosis of PTSD rather than a 'cut' score on a single screening test for posttraumatic stress disorder (Portney and Watkins 2009).

6.2.2.7 Differential attrition

Differential attrition occurs when some aspect of a subject or treatment condition produces systematic variance in the likelihood of subjects remaining in the study until data collection is complete (Campbell 1957). The present study guarded against differential attrition by minimizing and balancing the burden of study participation across groups and by conducting an intent-to-treat analysis that included data from all subjects, not just those who completed all data collection points (Portney and Watkins 2009). Evidence for a minimal effect of differential attrition in the present study can be found in the similarity of subjects in both numbers and demographic characteristics who withdrew from the surgical and control groups over time.

6.2.3 External Validity

The present study demonstrates reasonable external validity. The intent of the study was to establish inferences that could be applied by clinicians to veterans with a history of PTSD facing common elective outpatient surgeries, and the sample was recruited to address this intention. When providing perioperative care, surgical and anesthesia providers discover that a patient has PTSD by examining the patient's electronic medical record, and that criterion of a PTSD diagnosis in the patient's electronic medical record was used to establish eligibility in this study. Therefore, the mean scores on measures of physical and mental health before surgery reflected what perioperative health care providers might see in patients with a diagnosis of PTSD in their electronic medical record, rather than in participants who scored high on a measure of posttraumatic symptom severity on the day of their preoperative interview. In addition, the sample was heterogeneous with respect to gender, ethnicity, and surgical procedure.

The limitations of the external validity of the present study are implicit in the choice of subjects and setting. First, all patients were diagnosed with service-connected PTSD, meaning that the findings of the study cannot be extended to non-veteran patients with PTSD. Second, the long duration of posttraumatic symptoms reported by subjects in both the surgical and control group means that the results cannot be extended to veterans with more recent exposure to traumatic events. Third, the findings cannot be presumed to apply to patients admitted to the hospital after surgery. In particular, the high prevalence of depression, low cognitive reserve, and multiple medical comorbidities of veterans with PTSD would likely render them highly susceptible to postoperative delirium during a hospital admission, and postoperative delirium is associated with poor short and long-term outcomes after surgery (Marcantonio et al. 1994, Kat et al. 2008).

6.3 Recommendations

Future studies should seek to address the limitations of this study and expand the available literature about the effects of elective surgery on the patient with chronic PTSD. Recommendations to address the limitations of this study are to: (a) include a control group of surgical subjects without PTSD to allow better estimation of the effect of PTSD combined with surgical intervention on the physical and mental health of veterans; (b) collect data about posttraumatic and depressive symptom severity shortly after surgery to better estimate the peak impact of surgery on these constructs; (c) extend data collection beyond three months to evaluate the predictive validity of subjective health status for long-term morbidity and mortality; (d) match control and surgical subjects on key demographic variables, if possible, and; (e) enroll subjects undergoing a single surgical procedure, to better control the surgical stimulus and

further clarify the impact of posttraumatic and depressive symptom severity on physical and mental health after elective surgery.

6.3.1 Future Directions

Studies are only now beginning to explore the specific effect of surgery on the mental and physical health of veterans with chronic PTSD. Findings from this study suggest a need for further research to expand our knowledge about this potentially vulnerable population and quality improvement projects to improve the perioperative care delivered in our VA hospitals.

6.3.1.1 Future research

Future studies should seek to expand both the breadth and depth of our knowledge about the effects of surgery on the mental health of veterans with chronic PTSD. Studies should expand the breadth of our knowledge by investigating the effect of surgery on the mental and physical health of younger veterans with more recent exposure to traumatic events. A growing line of research is investigating PTSD as a risk factor for post-anesthesia emergence delirium or agitation in younger veterans with recent combat experience (McGuire 2012, McGuire and Burkard 2011). Emergence delirium is a phenomenon in which the patient exhibits psychomotor agitation immediately after emergence from anesthesia, and an estimated 5-21% of all adult patients exhibit emergence delirium after noncardiac surgery regardless of PTSD status (Yu et al. 2010, Lepouse et al. 2006, Radtke et al. 2010). However, a patient with PTSD who is experiencing trauma-related flashbacks and dissociation will display very similar behaviors (Crosby et al. 2007), and the bedside clinician with little personal knowledge of the patient has no means of distinguishing between the nonspecific

agitation associated with emergence delirium and the flashbacks and dissociation associated with PTSD.

The account of the participant in the present study who experienced a flashback in the recovery room suggests that aspects of the perioperative environment can remind patients of traumatic experiences and precipitate a flashback, and that the perceptual disturbances associated with recovering from anesthesia may contribute to the misinterpretation of innocuous environmental cues. Therefore, neurobehavioral disturbances immediately after surgery may be the result of a complex and highly contextual interaction between PTSD and the residual effects of anesthesia. The rarity of neurobehavioral disturbances in this sample may indicate that veterans with long-standing, chronic PTSD and veterans recently diagnosed with PTSD constitute two distinct populations as to risk of emergence delirium. Further study is needed to determine if it is possible or necessary to distinguish between PTSD-related flashbacks and the more general psychomotor agitation associated with emergence delirium, and whether any long-term physical and mental sequelae are associated with each phenomenon.

Studies should also be conceived to investigate the effect of major surgery on the mental and physical health of veterans with chronic PTSD. As noted, the high prevalence of depression, low cognitive reserve, and multiple medical comorbidities of veterans with PTSD would likely render them highly susceptible to postoperative delirium during a hospital admission, and postoperative delirium is associated with poor short and long-term outcomes after surgery (Marcantonio et al. 1994, Kat et al. 2008). In addition, major surgery would also impose a greater burden of postoperative pain and disability on patients, and the trends toward physical and mental recovery

observed in the present study may not hold true in patients undergoing more extensive and painful surgical procedures.

Studies should also be conducted to expand the depth of our knowledge about the interrelationships between posttraumatic stress disorder and its attendant comorbidities. In particular, the perioperative environment provides researchers with a significant opportunity to test models of the relationship between PTSD and chronic pain. At present it is unknown whether chronic pain exacerbates posttraumatic symptoms, if posttraumatic symptoms precipitate chronic pain, or if a common psychiatric or physiological liability facilitates the development of both disorders. The relationship between these disorders has thus far been impossible to parse out because of issues of temporal ambiguity. However the pain stimulus associated with surgery provides researchers with an opportunity to directly assess and manipulate this relationship.

For example, the Shared Vulnerability, Triple Vulnerability, and Fear Avoidance models all emphasize the role of anxiety sensitivity and avoidance of threatening stimuli as central to the relationship between PTSD and chronic pain (Asmundson and Katz 2009, Barlow 2000, Vlaeyen and Linton 2000). These models suggest that psychology drives the perception and response to pain in patients with chronic PTSD. Manipulation of the acute central hypothalamic-pituitary-adrenal axis response to the stress of surgery could be used to test the primacy of avoidant symptoms. Animal models have demonstrated that the injection of corticotrophin releasing factor into the amygdala was associated with increases in avoidant behavior (Liang and Lee 1988). From the experiences of participants in the present study, it is possible that the acute distress from posttraumatic and depressive symptoms

described shortly after surgery could be the result of further elevations in brain levels of CRF as the body attempted to mount a stress response to the physical insult of surgery. If a stress dose of hydrocortisone were administered to a patient to blunt the secretion of further CRF (Erkut, Pool, and Swaab 1998) during and immediately after surgery, then patients who received hydrocortisone should experience less of an increase in avoidant symptoms.

To test this theory, patients with PTSD and comorbid chronic back pain could be randomized to receive either hydrocortisone or a placebo before undergoing knee arthroscopy under nerve block, with postoperative analgesia provided with an indwelling nerve catheter for three days after surgery. If avoidance is central to the maintenance of both chronic pain and PTSD, then patients who receive hydrocortisone should require an unchanged amount of analgesia to treat their chronic back pain. In contrast, patients who receive a placebo should require more analgesia to manage their chronic back pain as avoidant symptoms increase due to excessive brain levels of CRF.

In addition, further studies should be conducted to expand the modalities available to manage postoperative pain for patients with chronic PTSD. In particular, future studies should explore the utility of non-opiate pain management modalities, including clonidine, dexmedetomidine, ketamine, indwelling nerve catheters, and alternative medical therapies such as acupuncture and acupressure. The role of non-opiate pain management modalities will likely be critical in this population because of the opiate tolerance associated with the long-term management of chronic pain.

6.3.1.2 Future quality improvement projects

Regardless of the clarity of the theories underlying the relationship between PTSD and chronic pain, the findings of the present study indicate that patients with

PTSD require more effective postoperative pain management after hospital discharge. The lack of effective post-discharge pain management reported by participants in the qualitative findings of the study was particularly troubling, because the facility had the resources to provide comprehensive pain management. The solution to this issue may be a simple quality improvement project to include postoperative pain management concerns in the Joint Commission-required preoperative checklist that is conducted before every surgery. This checklist requires that surgery, anesthesia, and the operating room nursing staff discuss matters such as required equipment and medications, as well as the patient's health status and postoperative disposition. The goal of this discussion is to identify any safety issues before they occur. While completing the preoperative checklist, anesthesia and surgery could engage in a dialogue to ensure that the surgeon is aware of the patient's history of chronic pain, has an effective plan to manage that pain after discharge, and has a plan to transition the patient's pain management needs back to his or her primary care manager within an appropriate time frame. If the surgeon is not comfortable with managing the patient's superimposed postoperative and chronic pain, a pain specialist could be consulted to make recommendations before the patient leaves the hospital. Similar checklists may need to be adopted at hospital discharge to ensure that patients have the assistive devices, rehabilitative consults, and follow-up appointments they require to support their recovery.

Improved patient access to pain management techniques would likely decrease patient distress and irritability after surgery and therefore decrease conflict with caregivers, but additional efforts beyond pain management should be made to shore up patients' social support after surgery. These efforts could take the form of quality

improvement projects to ensure that patients and family members are educated before surgery about the likelihood of acute psychological distress in the days and weeks after surgery. Such an educational offering would include the type and duration of symptoms to expect, as well as contact information for both routine and emergency mental health services.

The best means of addressing the difficulty patients reported with interacting with hospital staff is through education. Many non-psychiatric providers are not familiar with the wider implications of chronic mental health issues such as PTSD. Anecdotally, there is a perception within the anesthesia community that patients with PTSD are psychologically labile and at risk of becoming combative or violent in the perioperative setting. This perception may lead anesthetists to minimize interaction with patients with PTSD for fear of 'setting them off,' which is exactly the wrong approach according to the participants that were interviewed. When this preconception dominates, there is no hope for a frank discussion with the patient and proper consideration of the perioperative implications of PTSD.

Therefore, a reasonable goal is to demystify PTSD to a wider audience though publication and education. In a recent educational offering for anesthetists (Wofford, Hertzberg, and Vacchiano In press) we attempted to describe the phenomenology, etiology, treatment, and perioperative implications of PTSD, and offer general recommendations for interacting with the patient with PTSD who presents for surgery. We also hope that the publication of the qualitative findings of this study will further enhance non-psychiatric health care providers' understanding of the unique needs of veterans with chronic PTSD.

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Biography

Ken Wofford was born in New Orleans, LA, in 1973. The son of a career Sailor, he spent seven years of his childhood overseas before enlisting in the Navy as a Hospital Corpsman in 1992. He received his Bachelor's of Science in Nursing from Jacksonville University in 1997 and his Master's of Science in Nurse Anesthesia from Georgetown University in 2004. When not in school he has been stationed in diverse locations, including California, South Carolina, Guam, Okinawa, Florida, and Iraq.

His interest in research began during his anesthesia training, when he coauthored an article entitled "The effect of PENCAN needle orientation on spinal anesthesia outcomes." After returning from Iraq he became interested in studying the effect of surgery on mental health and cognition in vulnerable populations. Since entering the Ph.D. program at Duke University School of Nursing he has coauthored two articles: "Sorting through the confusion: Adverse cognitive change after surgery in adults," and "The perioperative implications of posttraumatic stress disorder."