EXPLORING VARIABLES OF POST-OPERATIVE DEPRESSION
IN CARDIAC SURGICAL PATIENTS

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EXPLORING VARIABLES OF POST-OPERATIVE DEPRESSION
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Evidence supports that both psychological and psychosocial factors, such as uncertainty and depression contribute to the incidence of poor health outcomes in cardiac patients undergoing surgery. Uncertainty and depression can illicit feelings of loss of control and have a direct effect on the health related quality of life of patients undergoing cardiac surgery. Known predictor variables were identified and proposals for further research were explored in order to establish a standard of care for this population related to their psychological health. This research attempts to highlight those variables that impact the long-term outcomes of cardiac patients. In addition, the role of serotonin levels is explored as a function of identifying depressive symptomatology before and after surgery. Pre-operative assessment of these variables may assist in the development
of interventional strategies that can be applied by health care providers in order to identify those patients at risk and to ultimately improve health outcomes.
DEDICATION

This dissertation is dedicated to my husband, Harry, whose support and patience through the long days, months, and years never wavered. Without his confidence in everything I do, this would have been impossible. Also, to my children, for giving me the time and space I needed – putting me first before themselves so I could achieve my goal. Lastly, all of my family and friends who stood by me with constant and lasting encouragement. Thank you.
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LIST OF ABBREVIATIONS

CABG: Coronary Artery Bypass Grafting
BDI: Beck Depression Inventory
MUIS: Mishel Uncertainty in Illness Scale
APA: American Psychological Association
CHAPTER ONE

Introduction

Coronary artery bypass grafting (CABG) surgery is the recognized treatment for those patients with symptoms of ischemic heart disease identified through coronary angiography not amenable to percutaneous intervention. The goals of the surgery are related to reducing morbidity and mortality from future coronary risk factors, improve quality of life, and prolong life expectancy (Hawkes, Nowak, Bidstrup, & Speare, 2006; McKenzie, Simpson, & Stewart, 2010). Through the literature, there is corroboration that psychosocial factors including those of uncertainty and depression contribute to the development of depressive symptomology. These factors along with a sense of loss of control have a direct effect on the individual's health related quality of life.

Psychological distress manifested by feelings of uncertainty and symptoms of depression have been reported as pre-operative correlates affecting health outcomes after surgery (Fitzsimons, Parahoo, & Stringer, 2000; Koivula, Tarkka, Tarkka, Laippala, & Paunonen-Ilmonen, 2002; McCormick, Naimark, & Tate, 2006). "Better understanding of the mood predictors, such as depression and anxiety, should help the identification and treatment of at-risk patients in this clinical population" (McKenzie et al., 2010, p. 75). In addition, a review of the literature examined the function of serotonin as a neurotransmitter in the body. Its correlation to depressive symptoms is not fully understood and warrants further exploration and assessment in this population (Elder & Mosack, 2011; Lacasse & Leo, 2005; Lemonick, 1997; Wankerl, Wust, & Otte, 2010).

Presently, most health care clinicians do not perform a focused assessment of the patient related to their psychological well-being with consideration to factors that could influence their recovery. Within the cardiac surgery population, there is no established
standard of care or core measure that assesses pre-cardiac surgery patients who are at risk for depression post-surgery.

The objective of this research inquiry was to evaluate associative factors in the pre-operative phase that could potentiate post-operative depression. Specifically, the research examined the influence among uncertainty and serotonin levels on post-operative depressive symptomology. This information demonstrated the need for development of future research into interventional strategies by health care clinicians to optimize patient outcomes.

The aim of the research was the investigation of pre-operative uncertainty, depression, and serotonin levels as associative factors of post-operative depression in the cardiac surgical population. Specifically, this inquiry explored the relationship between a pre-operative serotonin level, levels of uncertainty using Mishel's Uncertainty in Illness Scale (MUIS), and depressive symptomatology measured by Beck's Depression Inventory (BDI) as associative (predictive) factors in post-operative depression.

The long-term goal of this research would be to establish standards of practice based on the findings in order to provide guidelines for assessment, prevention and treatment in caring for patients undergoing cardiac surgery in order to lessen the negative impact of depression post surgically. The results of this inquiry support the call for research related to nursing strategies to guide practice, affect pre-operative teaching to the patient, and improve postoperative outcomes. The development of evidence-based practice will change the delivery of care.

The research questions that were addressed are:
1. What is the relationship between selected demographic variables and post-operative depression in a cardiac patient undergoing surgery?

2. What is the relationship between pre-operative serotonin levels and depression scores measured pre-operatively (Time 1), at 4 weeks post-operatively (Time 2), and at 12 weeks post-operatively (Time 3)?

3. What is the relationship between scores on the Beck Depression Inventory compared pre-operatively and post-operatively in the cardiac surgical patient?

4. What is the relationship between scores on the Mishel Uncertainty in Illness Scale in comparison to scores on the Beck Depression Inventory pre-operatively, at 4 weeks, and at 12 weeks post-operatively?

5. Is a combination of selected socio-demographic variables, pre-operative serotonin level, uncertainty, and depression scores a predictor of post-operative depression at 4 weeks and 12 weeks post-operatively?

**Background and Significance**

The investigation of uncertainty, depression, and their clinical sequelae in the cardiac surgical participants in this study focused on pre-operative evaluation with follow up during the post-operative course. Research in cardiac surgical patients demonstrated that post-operative depression is linked with an increase in morbidity, mortality, and increased readmissions for cardiac events (Blumenthal, et al., 2003; Oxlad, Stuberfield, Stuklis, Edwards, & Wade, 2006; Tully & Szackely, 2013). In addressing potential causes of depression, the effect of serotonin, a neurotransmitter, emerged as a potential correlate to symptoms of depression. Much of the research related to serotonin as a direct contributor has been controversial; centered mainly on therapeutic treatment
options after the diagnosis. The role serotonin levels may play in identifying those individuals at greater risk for depression related to illness or surgery is worthy of further exploration. A review of the literature examined the function of serotonin as a neurotransmitter in the body as well as associated research studies that have investigated the measurement of serotonin levels and depressive symptoms within cardiac disease processes (Lett et al., 2004; Meltzer, 1989; Sanner & Frazier, 2011).

Current literature described a relationship between post-operative psychological status and recovery in the cardiac patient (Blumenthal et al., 2003; Mallik et al., 2005; Pignay-Demaria, Lesperance, Demaria, Frasure-Smith, & Perrault, 2003). This research was conducted to explore the relationship between cardiac surgery and depression, along with potential predictor variables that may assist in the development of standards of health care practices for patients undergoing cardiac revascularization.

Theoretical Framework

The mid-range theoretical framework developed by Mishel guided this research study. The uncertainty in illness theory explains how a patient deals with illness related events and their outcomes. The theory is based on three themes, antecedents of uncertainty, which includes stimuli frame, cognitive capacities, and structure providers. These subtexts refer to how stimuli is perceived, information processed, and how outside support affects the patient in either a positive or a negative direction. Appraisal of uncertainty includes inference and illusion, which describes an evaluative process of uncertainty, based on personal experiences, knowledge, and constructed beliefs affecting outlook. Lastly, coping with uncertainty includes the concepts of danger, opportunity, coping and adaptation (Mishel, 1981, 1988; Mishel & Clayton, 2008). Each of these
processes influences the evolution of uncertainty into a positive or negative outcome. The uncertainty in illness theory highlights the process a patient may experience when dealing with either an acute illness or a chronic condition.
CHAPTER TWO

Chapter 2 includes the first manuscript. A thorough review of the literature was conducted and the manuscript was written to meet the requirements for the target journal. The manuscript was submitted, reviewed by the editorial board reviewers, and revisions are currently in process for resubmission.

Manuscript 1

Introduction

Coronary artery bypass grafting (CABG) surgery is the recognized treatment for those patients with symptoms of ischemic heart disease identified through coronary angiography not amenable to percutaneous intervention. The goals of the surgery are to reduce morbidity and mortality from coronary risk factors, improve quality of life, and prolong life expectancy (Hawkes et al., 2006; McKenzie et al., 2010). The literature clearly provides evidence that both psychological and psychosocial factors including those of uncertainty and depression may contribute to the incidence of poor health outcomes in this population (McCormick et al., 2006; White & Frasure-Smith, 1995). Uncertainty and depression can illicit feelings associated with a loss of control and have a direct effect on the health related quality of life beginning in the pre-operative phase and often continuing through the post-operative state (Fitzsimons et al., 2000; Gallagher & McKinley, 2009; So & La Guardia, 2011).

Psychological distress manifested by symptoms related to uncertainty and depression have been reported as pre-operative correlates affecting health outcomes after cardiac surgery and coronary angioplasty (Fitzsimons et al., 2000; Koivula et al., 2002; McCormick et al., 2006). Recognition of these psychological risk factors may assist the
clinician with early identification of patients at risk for depression within the cardiac surgical population (McKenzie et al., 2010).

This review explored the role of preoperative uncertainty and depression on quality of life in patients with coronary artery disease. Evidence of the negative effects of post-operative depression including an increase in morbidity, mortality, and readmissions for cardiac events was addressed (Blumenthal et al., 2003; Oxlad et al., 2006; Tully, Baker, Turnbull, Winefield, & Knight, 2009). An assessment of the patient and their psychological wellbeing with consideration of factors that may influence recovery in the post-operative period was reviewed. An examination of the role of serotonin, a neurotransmitter, which is often cited relative to depression, may assist to correlate findings with those of uncertainty and depression. This review examined the current state of science regarding the relationship between depression, uncertainty, serotonin, and patients undergoing cardiac surgery. The lack of pre-surgical assessment, which may result in negative health outcomes, presents a need for further research and evaluation of pre-operative psychological and psychosocial well-being in this population.

Cardiac Surgery and Depression

William Harvey, in 1628, first suggested the link between the "mind and the heart" in describing both positive and negative emotions with their correlational effects on the heart (Rumsfeld & Ho, 2005). However, it was not until over three centuries later that research studies began to establish sound evidence for this relationship. It was first reported in the 1980's that a relationship existed between cardiovascular patients with major depression and the increased risk of cardiovascular events, leading to major cardiac surgery, and increased mortality rates (Peterson et al., 2002).
The varying etiologies of post-operative depression include reports of anxiety, stress of cardiac surgery and patient co-morbidities (Hawkes et al., 2006; Timberlake et al., 1997). Researchers have reported pre-operative depression as a predictor of negative psychological effect in the post-operative phase. Similar results were found among pre-operative depression scores and quality of life scores after cardiac surgery (Mallik et al., 2005; Peterson et al., 2002; Timberlake et al., 1997; Tully et al., 2009).

In the early 1980's, Merle Mishel developed a theory related to uncertainty in illness and its effect on the overall well-being of the individual. Her initial work in uncertainty was influenced by the work of Lazarus (1974) on stress and coping. Further guided by the work of Bower (1978) and Shalit (1977), Mishel continued to investigate the importance of the cognitive state in stress response (Mishel & Clayton, 2008; Smith & Liehr, 2008). The theory of uncertainty in illness consists of three major themes that include antecedents of uncertainty, how past illness experiences affect patient ability to deal with present situation;” appraisal of uncertainty, which places value on present uncertainty, and coping with uncertainty for adaptation. (Mishel, 1981, 1988; Mishel & Clayton, 2008).

Personal experiences reflect behaviors exhibited as coping mechanisms to control environmental stimuli in terms of a diagnosis of acute illness or living with a chronic, sometimes life-threatening illness. Mishel defined uncertainty as an "inability to determine the meaning of illness-related events, occurring when the decision maker… is unable to predict outcomes accurately" (Alligood & Tomey, 2010, p. 601). This definition highlights the interpretation and understanding of the diagnosis by the individual. Mishel offers an assessment of cognitive aspects of uncertainty based on the
individual's inherent nature, exposure to previous stimuli, and their outcomes. She utilizes the terms *danger* or *opportunity* to evaluate whether a person demonstrates a positive or negative response to uncertainty as an indicator of each person's capacity for adaptation to illness (Mishel, 1988). Her research revealed the effects of uncertainty in many different disease populations including those with cardiac disease (Eastwood, Doering, Roper, & Hays, 2008; McCormick et al., 2006; White & Frasure-Smith, 1995).

In 2006, McCormick and colleagues conducted a cross-sectional, descriptive, correlational study investigating both psychological and physical factors influencing patients awaiting a cardiac surgical procedure. In this study, the theoretical framework of Mishel's Uncertainty in Illness provided the guiding principles in describing the manner in which patients assimilate information and develop an understanding of their illness. In this mixed methods study, forty-two patients were assessed for levels of uncertainty (Mishel's Uncertainty in Illness Scale), anxiety (Graphical Anxiety Rating Scale), symptom distress (symptoms frequency and symptom distress Scale), and functional status (Kansas City Cardiomyopathy Questionnaire Subscales). In addition, the influence of length of time waiting for surgery on psychosomatic condition was explored. Of those forty-two patients, twenty-six agreed to be interviewed regarding their experience while waiting for surgery.

The data revealed that length of time awaiting surgery and its effect on psychological factors did not reach statistical significance; however, based on interviews, responses, and extrapolated themes, the investigators concluded that patients experienced both positive and negative feelings based on the patient response at a particular moment. Highly significant correlations were found between functional status and anxiety,
symptom distress, and physical limitations. While no significant differences were observed between the length of time (<2 months, 2–4 months, and > 4 months), symptom frequency scores and anxiety, levels tended to increase with time along with a deterioration of social and physical functional status as waiting time increased. Findings suggest that regular assessment of symptoms and functional status during the waiting period may help to stabilize the patient's cardiac status. The researchers recommend that further research be conducted in a larger sample in a time series including both pre-operative and post-operative phases of care. This study highlighted the benefit of performing a baseline psychological profile prior to major cardiac surgery with continued evaluation through the post-operative period. This information may assist in identifying pre-operative characteristics of danger or opportunity that may affect patient outcomes (McCormick et al., 2006; Mishel, 1988).

Magni and colleagues (1987) conducted a prospective study, which revealed those patients with a higher psychological distress score prior to cardiac surgery were more likely to have higher scores on depression and anxiety one year after surgery. Ninety-nine patients were followed over the course of one year after their cardiac surgery. Approximately 25% of patients had continued symptom distress, high scores on anxiety and depression scales, at one year after surgery. These researchers also relayed the importance of the need for further preoperative evaluation and support prior to revascularization. Similarly, Frasure-Smith and colleagues (1993) reported an increased mortality among patients who were depressed at time of a cardiovascular event (Rumsfeld & Ho, 2005).
Another research study, nine hundred and sixty three patients requiring coronary artery bypass graft (CABG) were found to have higher scores of depression that translated into negative health outcomes after 6 months (Mallik et al., 2005). Patients underwent a baseline evaluation of both physical and psychological status prior to their scheduled procedure followed by an assessment utilizing a depression scale post-operatively. In this study, depression was characterized as an independent risk factor of poor health outcomes six months after coronary artery bypass surgery; demonstrating that depressive symptoms were a better measure of surgical health outcomes than co-morbidity factors such as left ventricular function, diabetes mellitus, heart failure, and myocardial infarction (Mallik et al., 2005).

Clearly, studies have shown the link between these pre-operative factors specific to stress of illness, uncertainty, and pre-operative depression and the overall quality of life of patients' post-operatively. These types of stressors, which can result in a life style change or modification, can trigger a depressive response. The adaptive or maladaptive response of the patient to the cardiac surgical procedure was the focus in addressing the problem and improving patient outcomes (Lauermann, 2000).

In 2011, Seriani discussed the diathesis-stress model of depression relating the genetic and biochemical (diathesis) individual response to stressful event. This relationship may consider the effect of uncertainty, baseline evaluation of depression, and the neurotransmitter serotonin in the pre-operative phase before cardiac surgery.

**Depression**

The common feature of all depressive disorders is the presence of sad, empty, or irritable mood, accompanied by somatic and cognitive changes that significantly affect
the individual’s capacity to function (APA-5, 2013, p. 155). The American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria is designed to be utilized by clinicians to assist in a more reliable diagnosis of mental disorders (2013). The DSM-5 assists in delineating depressive disorders based on symptoms that may limit a person's functional capacity. A sub-category of major depressive disorder labeled *Depressive Disorder Due to Another Medical Condition* allows for a consideration of symptoms and associated factors related to the specific episodes along with a timeline for evaluation (APA-5, 2013). A thorough assessment of a patient’s history of depression is warranted when determining their status related to depression at the time of cardiac surgery.

In a study by the Centers for Disease Control (2010), the World Health Organization in 2004 reported depression as the third leading cause of disability in higher income countries (USDOH, 2010). Similarly, in 2009, the Annals of Internal Medicine employed a task force, which revealed consistent findings labeling depression among the leading causes of disability in persons age 15 and older (US Preventive Task Force, 2009). The National Institute of Mental Health (NIMH) estimates that 1 to 5% of older adults experience depression and that number rises to 11.5% for hospitalized patients. Further data revealed that in 2012, an estimated 16 million adults (age 18 or older) experienced one major depressive episode; this accounts for 6.9% of all adults in the United States (NIMH, 2012). Early recognition and treatment play an integral role in overall patient health and outcomes.

Depression has been well documented when viewed within the context of medical healthcare with its effects on outcomes. Research is ongoing looking at underlying
causes of depression and its association with medical conditions. Symptoms typically associated with depression such as sadness, anxiety, fear, and loss of control are among the clinical signs either voiced or silenced by depression. Narrowing the focus of post-operative depression to its significance within the cardiac population demonstrated the interrelatedness of pre-operative evaluation and its association post-operatively in patients receiving cardiac care and undergoing cardiac revascularization (Gallagher & McKinley, 2009; Mallik et al., 2005; Peterson et al., 2002; Timberlake et al., 1997; Tully et al., 2009). Factors such as social support, psychological baseline, and physical response to the post-operative state play a role beginning at initial diagnosis through cardiac recovery and after care.

The Beck Depression Inventory (BDI) is a 21-question multiple-choice inventory that can be completed by the patient or by the clinician. The BDI is among the most widely used instruments for measuring the severity of depressive symptoms. The tool is designed for individuals 13 and older, with items relating to symptoms of depression including hopelessness and irritability, thought processes such as guilt or feelings of being punished, physical fatigue, weight loss or gain, and lack of interest in sexual activity. It utilizes evaluation of depressive symptomology with each category representing a specific expression of depressive behavior (Beck, 1972).

There is ample research and clinical evidence that the effects of illness on an individual may have undesirable consequences. Further areas of interest for exploration are the possible connection between pre-operative uncertainty in illness utilizing the theoretical framework established by Mishel; depression, measured by the Beck
Depression Inventory; and the measurement of serotonin levels within the cardiac surgery population.

**Serotonin**

In addressing potential causes of depression, the effect of serotonin, a neurotransmitter, emerged as a potential correlate to the diagnosis of depression. Much of the research related to serotonin as a direct contributor has been controversial; centered mainly on therapeutic treatment options after the diagnosis. The role serotonin levels may play in identifying those individuals at greater risk for depression related to illness or surgery is worthy of further exploration. A review of the literature examined both scientific details of the workings of serotonin as a neurotransmitter in the body as well as associated research studies that have investigated the measurement of serotonin levels and depressive symptoms within certain disease processes.

A person's genetic makeup coupled with the advent of a stressful situation has been linked with increased risk of depression. Each person is uniquely different in his or her truest form; abnormalities within this genetic makeup have been cause for investigation into the manifestations of one's behavior. The available amount of neurotransmitter within the synapses of certain areas of the brain makes a difference in expression of behavior. Genetic mutations of the serotonin molecule, called polymorphisms, are reflected in the gene description of the short or ‘s’ allele or the long ‘l’ allele where alleles represent different forms of the gene that can lead to variations in the structure of the protein resulting in changes in transmission of information (Medina, 2004, p. 18).
Elder and Mosack (2011) define and discuss important concepts in developing a basic understanding of genetics and depression. Hereditability is the amount of variation of a trait that can be attributed to genetic influences. Evidence has been presented linking individuals with the s allele as being at greater risk of developing depression related to environmental influences than those without this particular allele. If an individual carries either one s allele or two, the risk of major depressive disorder is greater (Elder & Mosack, 2011).

The role of neurotransmitters and their receptors play an integral role in areas related to brain activity and the body's response. This intricate network within the brain is responsible for maintaining homeostasis of neurologic activity throughout the body. Serotonin (5-HT) is discussed due to its association with behavior disorders at lower and higher levels ranging between depression and anxiety (Blows, 2000). 5-HTT, the serotonin transporter protein was reviewed related to its involvement in the transport and reuptake of serotonin. This information provided insight into the role of serotonin and its use in conjunction with psychometric tools to assist in the early identification of those patients at risk for post-operative depression in the cardiac surgical population.

Serotonin (5-HT) is important for its role in the cognitive and affective behaviors of mood, sleep, appetite, and body system functions. It is part of the amine group of neurotransmitters found within the raphe nuclei on the pons, medulla, and the brain stem (Blows, 2000; Valenzuela, Puglia, & Zucca, 2011). The serotonin pathway leads to neuronal pathways within our body with distribution areas in "multiple centers of the cerebrum, the limbic area, and the basal ganglia" (Blows, 2000, p. 234).
Serotonin is classified as a monoamine. An associated monoamine theory of depression, first discussed forty years ago, hypothesizes this link between decreased levels of circulating serotonergic activity as a causative factor related to depression (Sanner & Frazier, 2011).

Blows (2000) discusses the production of serotonin from the amino acid, tryptophan, which can be found in dietary sources. The passing of tryptophan through the blood brain barrier and its conversion to serotonin relies on the enzymatic processes occurring within the neuronal pathways. Deficiency in any of the vitamins that aid in the conversion may cause changes in behavior (Medina, 2004). Sanner and Franzier (2011) relate factors that may be a resultant cause of the deficiency; these include dietary depletion of tryptophan, inhibition of enzymatic processes of conversion, decrease in serotonin receptors or a non-working transport system. The 5-HT receptor sites and their pre-synaptic and post-synaptic function play an important role within these transport systems. The conversion process in which tryptophan is converted to 5-HT with subsequent metabolism allows for 5-HTT to perform as the transporter protein.

The 5-HTT gene is the transport protein for serotonin. It plays an essential part in "regulating the concentration of serotonin in the brain" (Medina, 2004, p. 17). The role of 5-HTT is in the reuptake of serotonin in the cell thereby maintaining a state of concentrated equilibrium that allows for expression of the gene.

Figure 1. Represents the activity within the transport system where serotonin is being released by the pre-synaptic area and binding with the receptors in the postsynaptic cells. It appears that any factor that may alter the course of activity via transport or
uptake would have an effect on the circulating levels of serotonin resulting in a potential change in behavior.

**Figure 1. Action of Serotonin and the Serotonin Transporter.**

![Image](https://dynamichealthresources.com)

Schematic drawing of the neurotransmitter serotonin being released from the presynaptic cell and binding to the receptors on the postsynaptic cell. 5-HTT encodes the protein labeled reuptake transporter. Image from [https://dynamichealthresources.com](https://dynamichealthresources.com). Permission granted by Dynamic Health Resources.

This information assisted in providing insight into the effect that serotonin has on individual behavior. Baseline psychosocial evaluation along with serotonin levels in the pre-operative phase may assist in identifying those at increased risk; individuals that may be on the cusp of uncertainty and depression before cardiac revascularization.

The cumulative result of the information provided within the review revealed components that may have an effect on the overall health outcomes of those individuals undergoing cardiac surgery. Further research into the components of uncertainty, depression, and serotonin level may lead the nursing health care team into strategic development of pre-operative tools to assist with early detection and intervention. These
areas were further explored to gain information and impart knowledge to improve health outcomes in this population.

Current practice guidelines and clinical pathways do not proactively assess patients who are awaiting surgery for history of depression or uncertainty. This accounts for a missed opportunity for early identification, education, and intervention (Blumenthal et al., 2003; Lett et al., 2004; Pignay-Demaria et al., 2003). There is no measurement tool in use pre-operatively to gauge those patients at potential risk for poor psychological outcomes after surgery, thereby affecting post-operative recovery and quality of life.

Nursing Implications

Evidence Based Screening and Assessment

Presently, most health care clinicians do not perform a focused assessment of the patient related to their psychological well-being with consideration to factors that may influence their recovery. Within the cardiac surgery population, there is no established standard of care or core measure, which assesses the pre-cardiac surgery patients with regard to risk for depression post-surgery. Because there are no established parameters for this particular assessment, the exploration of influencing factors was the focus of further investigation.

Call for Research

Current practice guidelines and clinical pathways do not proactively assess patients who are awaiting surgery for history of depression or uncertainty. Gallagher and McKinley (2009) discussed the need for a more proficient method of assessment and identification of psychological symptoms in this patient population that may affect outcomes. Not establishing guidelines for assessment and treatment of psychological
symptoms transpires into a missed opportunity for early identification, education, and intervention (Blumenthal et al., 2003; Lett et al., 2004; Pignay-Demaria et al., 2003). There is no standard measurement tool in use pre-operatively to gauge those patients at potential risk for poor psychological outcomes after surgery, thereby affecting post-operative recovery and quality of life. Panagopoulou and colleagues (2005) found that those individuals with psychological risk prior to cardiac surgery had worse health outcomes in the post-operative time period at one month and six months (Panagopoulou, Montgomery, & Benos, 2006). This finding speaks to the need to explore opportunities for risk stratification or modification within this population.

**Summary**

The number of coronary artery bypass graftings (CABG) in the United States, according to data from 2010, was approximately 395,000 not including valve procedures, or valve procedures plus CABG (www.cdc.gov). This information coupled with the literature that supports the evidence of depression in this population of patients presented an opportunity for further exploration into the role of pre-operative evaluation of uncertainty, depression and serotonin. Uncertainty, as discussed through the theoretical framework of Mishel, seeks to establish whether the patient views illness as a danger or opportunity. This information may assist in determining an individual's adaptation to illness. The BDI assesses severity of depressive symptoms by reviewing patient responses at the particular point in time in which the BDI is completed. The use of both of these tools offers valuable information that in conjunction with the biomarker measure of serotonin may assist in the development of a standard of care to recognize early signs and symptoms pre-operatively. This pre-operative evaluation may include nursing as an
important link in identifying those at risk, informing the health care team, and working on interventional strategies to promote positive health outcomes.
CHAPTER THREE

Research Design

A descriptive, correlational, prospective design was used to conduct this study. The relationships among specific variables as associative factors related to post-operative depression were explored. The importance of this study lies in the fact that at present, there is no standard of care in the evaluation of depressive symptoms as well as uncertainty in the cardiac surgical population pre-operatively and post-operatively.

This study examined depression scores with the use of the Beck Depression Inventory (BDI), levels of uncertainty as measured by Mishel's Uncertainty in Illness Scale (MUIS), along with the measurement of serotonin level, a neurotransmitter in the brain. These variables were explored relative to their impact on post-operative depression in patients undergoing cardiac surgery using a descriptive, correlational, prospective design.

Setting

The setting was the outpatient Cardiovascular Surgery Department at the University of Pennsylvania-Presbyterian Hospital in Philadelphia, Pennsylvania. The practice consults with more than 150 patients per month including pre-operative and postoperative patients. These numbers yield an elective surgical population of 50-72 surgeries per month.

Population

The population under study included participants undergoing elective cardiac surgical procedures for symptoms related to coronary artery disease and/or valvular heart disease. The inclusion criteria included men and women age 21 or older requiring cardiac
surgery; with no exclusions related to ethnicity, race, or religion. Exclusion criteria included those with a diagnosis of mental disorder, anti-depressant therapy, non-English speaking persons, and those diagnosed with a mental handicap.

**Power Analysis**

No previous research was conducted using the combination of variables explored, therefore, the two-tailed significance criteria was set at 0.05 and the power at .80. The results for the projected sample size that could achieve these criteria was 52 participants.

**Measurements**

**Demographics**

Demographic data including type of surgical procedure, gender, age, marital status, years of education, annual household income, history of depression, history of certain types cancer were collected (Appendix A). Variables measured included depressive symptomatology, levels of uncertainty, and serotonin levels. The predictor variables were uncertainty, depression and serotonin. The outcome variable was depression.

**Beck's Depression Inventory (BDI)**

The BDI (Appendix B) was utilized for the evaluation of depressive symptomatology. Permission for use was granted through the American Psychological Association (APA), which owns the copyright to the original scale. The BDI is based on categories of symptoms and attitudes (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961). Each category represents a specific expression of a depressive behavior. Behavior responses were scored on a self-report scale. The 21-question inventory had a maximum score of 63 and a minimum of zero. Depression scores were classified based on specific
parameters established within the BDI. Higher-level scores reflected greater depressive symptoms. These ranges reflected mild (11-16), moderate (21-30), severe (31-40), and over 40 classified as severe depression. Scores above 17 reflected a correlation with depressive symptoms that would require medical treatment. Beck and colleagues (1961) in their original work established reliability and validity through their administration of the scale and clinical acumen. The BDI has established itself as a reliable and valid standardized measure of assessment of depressive symptoms within a variety of populations. For example, many studies of post-operative outcomes for depression were evaluated using the BDI in a population of cardiac patients who had undergone CABG (Connerney, Sloan, Shapiro, Bagiella, & Seckman, 2010; Foss-Neradko, Stepnowska, & Piotrowicz, 2012; King, Colella, Faris, & Thompson, 2009).

The BDI was administered to the participant after informed consent had been obtained. This was a paper and pencil collection method with the questionnaire taking approximately 15 minutes to complete. An initial assessment was obtained on the scheduled day of pre-operative instruction and testing for the participant. Data were entered into a computer data system under the participant number for statistical analysis. Further administration of the tool took place at 4 weeks and 12 weeks post-operatively.

Mishel's Uncertainty in Illness Scale (MUIS)

The MUIS (Appendix C) was used to measure uncertainty in this population. The scale is based on her theory developed in 1981, which corresponds to an individual's adaptability to a diagnosis of illness and how the individual interprets and integrates this information. Uncertainty related to an illness may have a negative trajectory with physical and psychological effects on both the patient and the recovery process. MUIS, a
structured, self-administered tool, was utilized in the quantitative evaluation of participant responses related to illness. Based on a thirty-three question Likert scale, scores were analyzed on uncertainty related to "recognition, accommodation, and perception" (Mishel, 1982, p.259). In a previous study in a sample of forty-two patients undergoing elective CABG surgery, uncertainty measurements for those patients waiting surgery were at moderate levels with an associated decrease in quality of life (McCormick et al., 2006). Similarly, uncertainty and quality of life examined both pre and post coronary angiography at one year revealed that baseline uncertainty affected patient quality of life (Eastwood et al., 2008).

Permission (Appendix D) was obtained from Dr. Merle Mishel for use of her scale in this research study. The Adult Form of the MUIS had explicit instructions guiding the participant to evaluate how they were feeling on the particular day in which they were responding to the questionnaire. The scale required a response to each question. The 5-point Likert format ranges from (0) strongly disagree to (5) strongly agree. Cumulative scores obtained through the questionnaire ranged from 0-165, with higher scores indicating greater uncertainty. Cumulative numerical scores corresponded to mild (0-54), moderate (55-110), and high (111-165) levels of uncertainty.

A detailed report of the work conducted using the scale, including its reliability and consistency in different patient populations is offered in the tool's manual. The scale has many different forms and is used internationally in a wide variety of disease processes. The adult form, looking at the cardiac population, in terms of reliabilities and Coefficient Alpha for categories of ambiguity, complexity, inconsistency, and unpredictability within the questionnaire were in the range of 0.73-0.93 overall (Mishel
The questionnaire related to uncertainty in illness (MUIS) was administered by paper and pencil method to the patient at each established time point. Overall, total scores on the MUIS were utilized in the data analyses.

**Serotonin**

This neurotransmitter and biomarker, was collected via a blood sample at the time of patient's routine pre-operative blood work. Approximately, 4 ml of blood was drawn in a separate tube with preservative added to ensure stability of the specimen. The blood specimen was identified with the participant study number. No identifying information was labeled on the specimen. Specimens were discarded at the conclusion of the study by reference laboratory staff. These specimens were sent to ARUP, a national reference laboratory, for analysis. The reference range utilized by the lab was 50-220. The results of the blood studies were categorized as nominal data with scores falling within a range of low to high based on the parameters established by the lab.

**Research Procedure**

Once approvals from the appropriate Institutional Review Boards were obtained, recruitment activities began. Participants who met the inclusion criteria were identified through the cardiovascular office staff and surgeons within the department. Once identified, the study was explained and the patient's interest in participation was determined. Reassurance in the privacy and confidentiality of all matters related to the study were clearly outlined in the consent for participation. Participants were identified on all forms throughout the study by number only. Participants were asked to provide their address for future mailings related to the research study. Specific identifying numbers correlated name and address for the purpose of this future communication.
Participants were asked their preferred method of communication, via telephone or email, for follow-up with questionnaires if needed. Participants were not identified by name in any reports within the study. Participants were informed that they may withdraw from the study at any time and that any data collected to that point would be destroyed.

Patients scheduled for coronary artery bypass grafting, valve replacement, or both bypass grafting and valve replacement were identified as potential participants through the Cardiovascular Surgery Department. Upon meeting with the cardiovascular surgeon in consult, the opportunity to participate in the study was discussed with the patient by the surgeon. If the patient was agreeable to receive further information, this primary researcher or a research assistant was on hand to provide a detailed description of the study and answer any questions related to participation.

Data were gathered at set intervals established prior to the initiation of the study corresponding to the pre-operative phase, 4 weeks post-operatively, and 12 weeks post-operatively. Preoperative data were collected in the physician’s office in the surgical department. Surveys were distributed to participants at 4 weeks and 12 weeks after surgery, the 4 week surveys were either mailed back or brought with them to their four-week post-operative visit. The twelve-week survey was mailed back by the patient, as there was no in-person visit. Blood samples were collected in the outpatient lab center both preoperatively and at four weeks to determine serotonin levels. Patients did not return for in-person twelve-week visits, therefore serotonin levels could not be evaluated at this time point.

A research assistant was available to review the details of the study with each participant. This informational process took approximately 15 minutes. If the patient
agreed to participate in the study, the nurse practitioner working in the physician’s office then met with the participant and obtained informed consent (Appendix E). The demographic data sheet, the BDI, and the MUIS were explained to the participant and then administered by the nurse practitioner. The surgical date was then agreed upon by the patient and the surgeon.

The average time for completion of the demographic data and the two scales was approximately 30 minutes. Data were entered into a computer data system under the participant number for statistical analysis.

After discharge from the hospital, questionnaires were sent to the participant at home for completion with return postage guaranteed via USPS Priority Mail. Once the follow-up questionnaires were returned, questionnaires were stored in a locked cabinet and data were entered into a software program for statistical analysis on a password-protected computer.

A sample of blood to measure serotonin was obtained at the same time that standard pre-operative blood work as required by the hospital was collected by drawing an extra tube of blood from the patient, Blood specimens were sent by the University of Pennsylvania Hospital to ARUP, the off-site reference laboratory, for analysis through a specific research protocol. ARUP, the reference lab, was the designated off-site laboratory that conducted this specific test. Serotonin levels were measured by high-pressure liquid chromatography. A serum separator tube was used for collection. The cost to run this test was incurred by the primary research team. The expense through ARUP was $40.00 per specimen. This was the first of two blood draws required as part of
the research study. The second blood draw at 4-weeks post-operative was drawn and analyzed in the same way as the first blood draw.

**Data Analysis**

Data screening in this research analysis played an integral role in the accuracy of the reported data results. Tabachnik and Fidell (2013) discussed the importance of identification and resolution of factors that may produce erroneous results. Initially, a thorough review of completed demographic data and the two surveys collected was done prior to its inclusion in the database. An individual on the research team with data entry experience then checked and cleaned the data set. Missing data were assessed and consideration was given to factors that could reveal an arbitrary link or particular pattern within the data set. The final database was reviewed with the statistician to determine that data were entered properly and that missing data was handled properly.

Contact information was obtained to enable the research assistant to communicate with the participant at the designated time intervals if questionnaire data had not been returned. If participant wished results of the study, they were to contact the primary researcher.

IBM SPSS Version 23 was used for analysis of the data. Descriptive statistics were run on all variables, including frequencies and central tendencies of the variables of depression, uncertainty in illness, and serotonin with consideration of the dependent variable of depression scores. This information determined means and standard deviations for each predictor. Analysis also revealed the significant bivariate correlations within the data set.
To assure the integrity of the analysis, assumptions for multiple regression analyses were tested. Only those predictors that had relationships with the outcome were included in the model. Data were tested and met the assumptions of normal distribution. Tolerance values for all predictors were greater than 1-R² indicating that the assumption of no multicollinearity between the predictor variables was not violated. Adequate sample size would decrease the risk of Type II error. Multivariate linearity was assessed identifying the relationship between depression scores and the variables of uncertainty and serotonin.

Multiple regression analyses were used to determine if a relationship exists between the pre-operative measurements of depression, uncertainty in illness, and serotonin levels with the occurrence of post-operative depression in cardiac-surgical patients. The independent variables including depression, uncertainty, and serotonin were evaluated utilizing the tools previously discussed. Depression scores were classified based on the specific parameters established within the BDI guidelines. Cumulative scores for the Uncertainty in Illness scale were obtained through Likert scale format. In addition, serotonin levels were interpreted using nominal scores according to specific parameters identified by the laboratory.

Timeline

The recruitment phase took place over the course of approximately four months. Collection of data at specified intervals lasted 12 weeks' time. Data entry was ongoing through the research process. Once all data were collected, analysis of data and interpretation of statistical results were conducted. Dissemination of results will conclude with dissertation and manuscript submission of results of this study.
Protection of Research Participants

IRB approvals were obtained prior to the initiation of the study. Participants’ privacy and confidentiality were upheld at all times. All data collected from participants were stored in a locked filing cabinet in the primary investigator’s office. Human subjects were involved in recruitment and enrollment for this research study. Informed consent was explained to the participants. Those who wished to participate signed the consent form and a copy was given to them. Participation in this study was voluntary.

Participants could leave the study at any time for any reason without specification. Participating in this study had minimal risk but no greater than everyday activities. It is also important to note that an additional tube of blood was drawn along with the standard preoperative blood work required by the hospital for the first blood specimen required for this study. Therefore, participants did not need to experience any additional and/or potential discomfort associated with blood draws. The second specimen of blood obtained at the 4-week post-operative visit did require a blood draw.

Access to information related to this research study was limited to the principal investigator, research assistant, and the research chair affiliated with the University.
References


Lacasse, J. R., & Leo, J. (2005). Serotonin and depression: A disconnect between the advertisements and the scientific literature. *PLOS Medicine, 2*(12), e392. doi:10.1371/journal.pmed.0020392


Appendix A

Demographic Questionnaire
Demographic Questionnaire

ID #

1. Scheduled Procedure:
   CABG
   CABG plus Valve
   Valve Surgery Only

2. Gender
   a) Male
   b) Female

3. Age

4. Marital Status
   a) Single
   b) Married
   c) Divorced
   d) Widow/Widower
   e) Separated
   f) Living with significant other

5. Years of Education
   a) Some High School or less
   b) High School graduate
   c) Some college or associate degree
   d) College graduate/Bachelor's degree
   e) Post graduate/professional degree

Annual Household Income
   a) Under $15,000
   b) $15,000-$24,999
   c) $25,000-$34,999
d) $35,000-$49,999

e) $50,000-$74,999

f) $75,000-$99,999

g) $100,000 and over

Previous episodes of depression: Yes               No

Are you presently taking any anti-depressant medications?   Yes      No

If yes, please list._______________________________________

Do you have any history of stomach cancer or thyroid cancer? Yes    No

If yes, please explain. ____________________________________

Do you have any history of psychological disorders?   Yes    No

If yes, please explain. ____________________________________
Appendix B

Beck Depression Inventory (BDI)
Beck Depression Inventory
Please select the response that most closely states how you are feeling at the present time.

1. I do not feel sad.
   0 I do not feel sad.
   1 I feel blue or sad.
   2 I am blue or sad all the time and I can't snap out of it.
   3 I am so sad and unhappy that I can't stand it.

2. I am not particularly pessimistic or discouraged about the future.
   0 I am not particularly pessimistic or discouraged about the future.
   1 I feel discouraged about the future.
   2 I feel I have nothing to look forward to.
   3 I feel the future is hopeless and that things cannot improve.

3. I do not feel like a failure.
   0 I do not feel like a failure.
   1 I feel that I have failed more than the average person.
   2 I feel that I have accomplished very little that is worthwhile or that means anything.
   3 I feel I am a complete failure as a person.

4. I am not particularly dissatisfied.
   0 I am not particularly dissatisfied.
   1 I don't enjoy things the way I used to.
   2 I don't get satisfaction out of anything anymore.
   3 I am dissatisfied with everything.

5. I don't feel particularly guilty.
   0 I don't feel particularly guilty.
   1 I feel bad or unworthy a good part of the time.
   2 I feel quite guilty.
   3 I feel as though I am very bad or worthless.

6. I don't feel I am being punished.
   0 I don't feel I am being punished.
   1 I have a feeling that something bad may happen to me.
   2 I feel I am being punished or will be punished.
   3 I feel I deserve to be punished.

7. I don't feel disappointed in myself.
   0 I don't feel disappointed in myself.
   1 I am disappointed in myself.
   2 I am disgusted with myself.
   3 I hate myself.

8. I don't feel I am any worse than anybody else.
   0 I don't feel I am any worse than anybody else.
   1 I am critical of myself for my weaknesses or mistakes.
   2 I blame myself for everything that goes wrong.
   3 I feel I have many bad faults.
9.  
0 I don't have any thoughts of harming myself.  
1 I have thoughts of harming myself, but I would not carry them out.  
2 I have definite plans about committing suicide.  
3 I would kill myself if I could.  

10.  
0 I don't cry any more than usual.  
1 I cry more now than I used to.  
2 I cry all the time now, I can't stop it.  
3 I used to be able to cry but now I can't cry at all even though I want to.  

11.  
0 I am no more irritated now than I ever am.  
1 I get annoyed or irritated more easily than I used to.  
2 I feel irritated all the time.  
3 I don't irritated at all at the things that used to irritate me  

12.  
0 I have not lost interest in other people.  
1 I am less interested in other people now that I used to be.  
2 I have lost most of my interest in other people and have little feeling for them.  
3 I have lost all my interest in other people and don't care about them at all.  

13.  
0 I make decisions about as well as ever.  
1 I am less sure of myself now and try to put off making decisions.  
2 I can't make decisions any more without help.  
3 I can't make decisions at all any more.  

14.  
0 I don't feel I look any worse than I used to.  
1 I am worried that I am looking old or unattractive.  
2 I feel that there are permanent changes in my appearance and they make me look unattractive.  
3 I feel that I am ugly.  

15.  
0 I can work about as well as before.  
1 It takes extra effort to get started at doing something.  
2 I have to push myself very hard to do anything.  
3 I can't do any work at all.  

16.  
0 I can sleep as well as usual.  
1 I wake up more tired in the morning that I used to.  
2 I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.  
3 I wake up early every day and can't get more than 5 hours sleep.
17. I don't get any more tired than usual.
1 I get tired more easily than I used to.
2 I get tired from doing anything.
3 I get too tired to do anything.

18. My appetite is no worse than usual.
0 My appetite is not as good as it used to be.
1 My appetite is much worse now.
2 I have no appetite at all any more.

19. I haven't lost much weight, if any, lately.
0 I have lost more than 5 pounds.
1 I have lost more than 10 pounds.
2 I have lost more than 15 pounds.

20. I am no more concerned about my health than usual.
0 I am concerned about aches and pains or upset stomach or constipation or other unpleasant feelings in my body.
1 I am so concerned with how I feel or what I feel that its' hard to think of much else.
2 I am completely absorbed in what I feel.

21. I have not noticed any recent change in my interest in sex.
0 I am less interested in sex than I used to be.
1 I am much less interested in sex now.
2 I have lost interest in sex completely.
Appendix C

Mishel Uncertainty in Illness Scale-Adult Form
Mishel Uncertainty in Illness Scale – Adult Form

Instructions
Please read each statement. Take your time and think about what each statement says. Then place a “X” under the column that most closely measures how you are feeling TODAY. If you agree with a statement, then you would mark under either “Strongly Agree” or “Agree”. If you disagree with a statement, then mark under either “Strongly Disagree” or “Disagree”. If you are undecided about how you feel, then mark under “Undecided” for that statement. Please respond to every statement.

1. I don’t know what is wrong with me.

<table>
<thead>
<tr>
<th>Strongly Agree (5)</th>
<th>Agree (4)</th>
<th>Undecided (3)</th>
<th>Disagree (2)</th>
<th>Strongly Disagree (1)</th>
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2. I have a lot of questions without answers.

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<thead>
<tr>
<th>Strongly Agree (5)</th>
<th>Agree (4)</th>
<th>Undecided (3)</th>
<th>Disagree (2)</th>
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3. I am unsure if my illness is getting better or worse.

<table>
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<tr>
<th>Strongly Agree (5)</th>
<th>Agree (4)</th>
<th>Undecided (3)</th>
<th>Disagree (2)</th>
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4. It is unclear how bad my pain will be.

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<tr>
<th>Strongly Agree (5)</th>
<th>Agree (4)</th>
<th>Undecided (3)</th>
<th>Disagree (2)</th>
<th>Strongly Disagree (1)</th>
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5. The explanations they give about my condition seem hazy to me.

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<th>Strongly Agree (5)</th>
<th>Agree (4)</th>
<th>Undecided (3)</th>
<th>Disagree (2)</th>
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6. The purpose of each treatment is clear to me.

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<th>Strongly Agree (5)</th>
<th>Agree (4)</th>
<th>Undecided (3)</th>
<th>Disagree (2)</th>
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</table>
7. When I have pain, I know what this means about my condition.  
   | Strongly Agree | Agree | Undecided | Disagree | Strongly Disagree |
   | (5)            | (4)   | (3)       | (2)      | (1)             |

8. I do not know when to expect things will be done to me.  
   | Strongly Agree | Agree | Undecided | Disagree | Strongly Disagree |
   | (5)            | (4)   | (3)       | (2)      | (1)             |

9. My symptoms continue to change unpredictably.  
   | Strongly Agree | Agree | Undecided | Disagree | Strongly Disagree |
   | (5)            | (4)   | (3)       | (2)      | (1)             |

10. I understand everything explained to me.  
    | Strongly Agree | Agree | Undecided | Disagree | Strongly Disagree |
    | (5)            | (4)   | (3)       | (2)      | (1)             |

11. The doctors say things to me that could have many meanings.  
    | Strongly Agree | Agree | Undecided | Disagree | Strongly Disagree |
    | (5)            | (4)   | (3)       | (2)      | (1)             |

12. I can predict how long my illness will last.  
    | Strongly Agree | Agree | Undecided | Disagree | Strongly Disagree |
    | (5)            | (4)   | (3)       | (2)      | (1)             |

13. My treatment is too complex to figure out.  
    | Strongly Agree | Agree | Undecided | Disagree | Strongly Disagree |
    | (5)            | (4)   | (3)       | (2)      | (1)             |

14. It is difficult to know if the treatments or medications I am getting are helping.  
    | Strongly Agree | Agree | Undecided | Disagree | Strongly Disagree |
    | (5)            | (4)   | (3)       | (2)      | (1)             |
15. There are so many different types of staff; it’s unclear who is responsible for what.

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<th>Strongly Agree (5)</th>
<th>Agree (4)</th>
<th>Undecided (3)</th>
<th>Disagree (2)</th>
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16. Because of the unpredictability of my illness, I cannot plan for the future.

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<th>Strongly Agree (5)</th>
<th>Agree (4)</th>
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<th>Disagree (2)</th>
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17. The course of my illness keeps changing. I have good and bad days.

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<th>Strongly Agree (5)</th>
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<th>Undecided (3)</th>
<th>Disagree (2)</th>
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18. It’s vague to me how I will manage my care after I leave the hospital.

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<th>Strongly Agree (5)</th>
<th>Agree (4)</th>
<th>Undecided (3)</th>
<th>Disagree (2)</th>
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19. I have been given many differing opinions about what is wrong with me.

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<th>Strongly Agree (5)</th>
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20. It is not clear what is going to happen to me.

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<th>Strongly Agree (5)</th>
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<th>Undecided (3)</th>
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21. I usually know if I am going to have a good or bad day.

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<th>Strongly Agree (5)</th>
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22. The results of my tests are inconsistent.

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<th>Strongly Agree (5)</th>
<th>Agree (4)</th>
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<th>Disagree (2)</th>
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23. The effectiveness of the treatment is undetermined.

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<tr>
<th>Strongly Agree</th>
<th>Agree</th>
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<th>Disagree</th>
<th>Strongly Disagree</th>
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24. It is difficult to determine how long it will be before I can care for myself.

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<thead>
<tr>
<th>Strongly Agree</th>
<th>Agree</th>
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<th>Disagree</th>
<th>Strongly Disagree</th>
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25. I can generally predict the course of my illness.

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<th>Strongly Agree</th>
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<th>Disagree</th>
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26. Because of the treatment, what I can do and cannot do keeps changing.

<table>
<thead>
<tr>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Undecided</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>(5)</td>
<td>(4)</td>
<td>(3)</td>
<td>(2)</td>
<td>(1)</td>
</tr>
</tbody>
</table>

27. I’m certain they will not find anything else wrong with me.

<table>
<thead>
<tr>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Undecided</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>(5)</td>
<td>(4)</td>
<td>(3)</td>
<td>(2)</td>
<td>(1)</td>
</tr>
</tbody>
</table>

28. The treatment I am receiving has a known probability of success.

<table>
<thead>
<tr>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Undecided</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>(5)</td>
<td>(4)</td>
<td>(3)</td>
<td>(2)</td>
<td>(1)</td>
</tr>
</tbody>
</table>

29. They have not given me a specific diagnosis.

<table>
<thead>
<tr>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Undecided</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>(5)</td>
<td>(4)</td>
<td>(3)</td>
<td>(2)</td>
<td>(1)</td>
</tr>
</tbody>
</table>
30. My physical distress is predictable; I know when it is going to get better or worse.

<table>
<thead>
<tr>
<th>Strongly Agree (5)</th>
<th>Agree (4)</th>
<th>Undecided (3)</th>
<th>Disagree (2)</th>
<th>Strongly Disagree (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>______</td>
<td>______</td>
<td>______</td>
<td>______</td>
<td>______</td>
</tr>
</tbody>
</table>

31. I can depend on the nurses to be there when I need them.

<table>
<thead>
<tr>
<th>Strongly Agree (5)</th>
<th>Agree (4)</th>
<th>Undecided (3)</th>
<th>Disagree (2)</th>
<th>Strongly Disagree (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>______</td>
<td>______</td>
<td>______</td>
<td>______</td>
<td>______</td>
</tr>
</tbody>
</table>

32. The seriousness of my illness has been determined.

<table>
<thead>
<tr>
<th>Strongly Agree (5)</th>
<th>Agree (4)</th>
<th>Undecided (3)</th>
<th>Disagree (2)</th>
<th>Strongly Disagree (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>______</td>
<td>______</td>
<td>______</td>
<td>______</td>
<td>______</td>
</tr>
</tbody>
</table>

33. The doctors and nurses use everyday language so I can understand what they are saying.

<table>
<thead>
<tr>
<th>Strongly Agree (5)</th>
<th>Agree (4)</th>
<th>Undecided (3)</th>
<th>Disagree (2)</th>
<th>Strongly Disagree (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>______</td>
<td>______</td>
<td>______</td>
<td>______</td>
<td>______</td>
</tr>
</tbody>
</table>
Appendix D

Permission of Scale: Merle Mishel
Request Form: MUIS-Adult

I request permission to copy the Uncertainty in Illness Scale-Adult for use in my research entitled: (Still in development phase)

Does level of serotonin pre-operatively predict post-operative depression in cardiac surgical patients?

In exchange for this permission, I agree to submit to Dr. Mishel, upon completion of the study, a printout of the uncertainty data and an electronic submission or CD containing the data with the data dictionary. The data must contain information on each subject’s age, sex, education, and diagnosis, along with data on each subject’s response to each item on the scale. This data will be used to establish a normative database for clinical populations. No other use will be made of the data submitted. Credit will be given to me in reports of normative statistics that make use of the data I submitted for pooled analyses. Credit will be given to me in any reports referring to my findings.

(signature) 7/19/13

(date)

Positions and full address of Investigator
Mary Malitis MSN, CRNP
1072 Wellington Road
Tunkintown, PA 19066

EMAIL: malitisn@duq.edu
harmany@earthlink.net

Permission is hereby granted to copy the MUIS for use in the research described above.

Merle Mishel 7/19/13

Merle H. Mishel Date

Please send two signed copies of this form to: Merle H. Mishel, PhD, FAAN, School of Nursing, CB #7460 Carrington Hall, University of North Carolina, Chapel Hill, NC 27599-7460
Appendix E

IRB Approval
Consent Form
### UNIVERSITY OF PENNSYLVANIA RESEARCH SUBJECT
**COMBINED INFORMED CONSENT AND HIPAA AUTHORIZATION FORM**

<table>
<thead>
<tr>
<th>Protocol Title:</th>
<th>Exploring Variables of Post-Operative Depression in Cardiac Surgical Patients</th>
</tr>
</thead>
</table>
| Principal Investigator: | Wilson Szeto, MD  
Philadelphia Heart Institute at Penn Presbyterian Medical Center  
51 N 39th Street  
Philadelphia, PA 19104 |
| Co- Investigator: | Mary Malitas MSN, CRNP  
Philadelphia Heart Institute at Penn Presbyterian Medical Center  
51 N 39th Street  
Philadelphia, PA 19104  
PhD Candidate  
Duquesne University  
School of Nursing  
600 Forbes Avenue  
Pittsburgh, Pennsylvania  
15282  
malitasm@duq.edu |
| PhD Student Advisor: | Kathleen Sekula, PhD,  
PMHCNS, FAAN Professor,  
Duquesne University School of Nursing  
600 Forbes Avenue, 523 Fisher Hall  
Pittsburgh, Pennsylvania  
15282  
sekula@duq.edu 412-396-4865 |
| Emergency Contact: | Mary Malitas MSN, CRNP |
Why am I being asked to volunteer?

You have been invited to take part in this study because you are going to be undergoing elective cardiac surgery to treat your coronary artery disease and/or valvular heart disease. While cardiac surgery is the recognized treatment for this ischemic heart disease and/or heart valve disease, it has been associated with post-operative depressive symptomatology.

What is the purpose of this research study?
Studies have shown that patients undergoing cardiac surgical procedures may have an increase incidence of post-operative depressive symptomatology. The purpose of this study is to explore associative factors in the pre-operative phase that may influence post-operative depression symptoms.

How long will I be in the study?
Your participation in this study will last 12 weeks from your surgical date.

What are my responsibilities?
If you are enrolled in this study, you will have the following responsibilities:

- Complete pre-operative surveys
- Laboratory test (serotonin level) to be done with pre-admission testing with repeat of single laboratory test during your first post-operative visit at 4 weeks after surgery.
- Completion of follow-up questionnaires at 4 weeks and 12 weeks after surgery.
- Return follow up questionnaires in stamped addressed envelope to research team.

What am I being asked to do?
The study involves completion of questionnaires at different intervals along with an initial blood draw to be completed at time of pre-admission testing. There is a second blood draw to be performed during your first post-operative visit at approximately 4 weeks after your surgical procedure.

1. After surgical consent has been obtained, you will be asked to complete two questionnaires related to feelings of uncertainty and depressive symptomatology prior to surgery.
2. During your pre-admission testing, you will have an extra tube of blood drawn as part of the research study.
3. At 4 weeks after your surgery, you will return to the office for your post-operative visit. At that time, you will be asked to have a follow up blood test (serotonin level) drawn. This will be only one specimen and 1 teaspoon of blood will be drawn. At 4 weeks after your
surgery, follow up questionnaires will be mailed to you via USPS, a stamped addressed envelope will be provided for ease of return.

4. At 12 weeks from your surgical date, a final set of questionnaires will be mailed to you for your completion. A stamped addressed envelope will be provided for return.

What are the possible risks or discomforts?

Questionnaires
There is no risk associated with answering the questionnaires. Process of completion will be discussed with you in detail prior to answering the questionnaires. Questionnaires do not contain any identifying information. Questionnaires are by ID only.

Your Attending Physician and/or Nurse Practitioner will be notified of risk for depression in any participating patient. You will be followed by the Attending Physician and/or Nurse Practitioner if identified as being at risk for post-operative depression.

Blood Draws
Blood samples will be collected during the study. Approximately 1 teaspoon of blood will be collected during your pre-admission testing. This will not be a separate blood draw. A second blood draw will be collected at your 4 week post-operative follow up. Using a needle to remove blood from vein is called a “blood draw.” You may experience the following at the area of the needle stick when blood is drawn: This research does not pose greater than minimal risk to the participant.

• Temporary discomfort
• Bruising
• Infection (rarely)

Research related blood specimens will be handled through the University of Pennsylvania in conjunction with outside laboratory services. These specimens, which will be identifiable by number only, will be handled by personnel within the specific laboratory setting. These specimens will not be stored for future use.
You may have your specimen withdrawn at any time during the study. You may inform the PI for sample withdrawal.

The research blood results will have no impact on clinical care. Results of the research blood tests will not be documented in the patient medical record.

What if new information becomes available about the study?
During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.
What are the possible benefits of the study?
Your participation in this study might help generate knowledge that may help to establish standards of practice in order to provide guidelines for assessment, prevention, and treatment in caring for patient undergoing cardiac surgery in order to lessen the negative impact of depression during post-operative recovery.

What other choices do I have if I do not participate?
You do not have to take part in the study to receive your routine pre-operative and post-operative cardiovascular care.

Will I have to pay for anything?
All testing that are part of this research study will be provided to you free of charge. You are still responsible for any deductibles or applicable co-pays for routine office visits, and blood work that are not part of the research study.

Will I be paid for being in the study?
You will receive a $10.00 gift card at the completion of the study after the final questionnaires are returned.

When is the Study over? Can I leave the Study before it ends? This study is expected to end after all participants have completed the post-operative follow-up, and all information has been collected.

This study may also be stopped at any time by your provider or the study doctor without your consent because:

- The Primary Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The study Principal Investigator has decided to stop the study.

If you decide to participate, you are free to leave the study at any time. Withdrawal will not interfere with your future care.

Who can see or use my information? How will my personal information be protected?

We will do our best to make sure that the personal information obtained during the course of this research study will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. Please refer to the section below that explains more specifically how your personal information
will be protected.

**What personal health information is collected and used in this study and might also be disclosed?**

The following personal health information will be collected, used for research, and may be disclosed during your involvement with this research study:

- Name
- Street address
- E-mail address
- Telephone and fax numbers
- Medical record numbers
- Race or ethnic origin
- Gender, or other unique identifiers
- Dates including birth date, hospital/clinic admission or discharge dates, dates of medical events and procedures
- Medical history and ongoing medication use
- Social history
- Health status
- All information in your medical record, the results of physical exams, procedures, and tests, your health and medical history and other data collected during the study
- Information contained in your previous medical records related to your medical history and treatment
- Information about you that the study doctor may need in order to be able to monitor and report. Information may be created or collected by any provider that treats you outside of the study.

**Why is your personal contact and health information being used?**

Your personal contact information is important for the research team to contact you during the study. Your personal health information and results of tests and procedures are being collected as part of this research study.

**Who may use or disclose your personal health information? Who can see or use my information? How will my personal information be protected?**

The following individuals may use or disclose your personal health information for this research study:

- The Primary Investigator and the Co-Investigator’s study team
• Authorized members of the workforce of the UPHS and the School of Medicine, and the University of Pennsylvania support offices, who may need to access your information in the performance of their duties (For example: For research oversight and monitoring, to provide treatment, to manage accounting or billing matters).

Who, outside of UPHS and the School of Medicine, might receive your personal health information?

As part of the study, the Primary Investigator, the study team and others listed above, may disclose your personal health information, including the results of the research study tests and procedures. This information may be disclosed to those listed below:

Individuals or organizations responsible for administering the study:

• Individuals or organizations working under the direction of the Primary Investigator for the study
• Dr. Kathleen Sekula, Duquesne University, Dissertation Chair, will have access to the deidentified database only.
• That Institutional Review Board (IRB) that watches over the study
• All collaborating academic centers other than within UPHS or the School of Medicine or its associated support offices

Regulatory and safety oversight organizations

• The Office of Human Research Protections

Once your personal health information is disclosed to others outside the School of Medicine, it may no longer be covered by federal privacy protection regulations. The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any addition will be subject to University of Pennsylvania procedures developed to protect your privacy.

How long may UPHS and the School of Medicine be able to use or disclose your personal health information?

Your authorization for disclosure of your personal health information for this specific study will not expire.

The personal health information usually does not identify you personally (for example, by name, address, or social security number). Instead, the study doctor uses a code number on the study data.

The data concerning your identity will be kept only at the Penn Presbyterian Medical Center under the responsibility of Dr. Wilson Szeto and Mary Malitas MSN, CRNP.

In case of premature withdrawal from the study, any information collected on you up to the point of withdrawal will be used.

Publication of Study Results

Except as explained above, your personal health information will be kept confidential. The data
and results from this study may also be presented at meetings or in publications, but in those presentations people taking part in the study will not be identified by name.

**Will you be able to access your records?**

You have the right to look at and copy your health information. Details of study results will only be revealed the study has been completed and the results analyzed in order to preserve the validity of the research.

**Can you change your mind?**

Yes, at any time you may withdraw your approval to allow the use and disclosure of our personal health information as described here. You must do so in writing to the Primary Investigator at the address on the first page. Even if you withdraw your permission, your personal health information that was collected before we received your written request may still be used and disclosed, as necessary for the study. If you withdraw your permission to use your personal health information, you will also be withdrawn from the research study.

**What if I decide not to give permission to use and give out my health information?**

You will not be able to be in the research study.

If you sign this form, you also allow any doctor, hospital, or other medical facility that treats you after you start the study to disclose any medical information about you that relates to this study.

**Electronic Medical Records and Research Results**

What is an Electronic Medical Record?

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, results of research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any results of procedures performed as part of this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Results of research procedures performed as part of your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.

Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with
others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

**Who can I call with questions, complaints or if I’m concerned about my rights as a research subject?**

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

You may also contact Dr. James Phillips from the Duquesne University IRB if you have any questions at 1-412-396-1886.

A copy of this consent form will be given to you.

__________________________________________ Date

Name of Subject (Please Print)

__________________________________________ Date

Signature of Subject

__________________________________________ Date

Name of Person Obtaining Consent (Please Print)

__________________________________________ Date

Signature