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Walden University
2011

Abstract

Psychiatric Disorders as Potential Predictors in Medical Disease Development

By

Linda Kay Taliaferro

M.Ed., Wayne State University

B.S., Wayne State University

Dissertation Submitted in Partial Fulfillment

of the requirements for the Degree of

Doctor of Philosophy

Psychology

Walden University

November 2011

Abstract

Millions of individuals suffer disability or death from immune-based inflammatory diseases. If psychiatric disorders could be empirically linked to the prediction of immune-based inflammatory diseases, there would be a basis for promoting disease prevention measures for individuals diagnosed with one of four psychiatric disorders. Psychoneuroimmunology provided the theoretical base for understanding emotionally induced medical disease development. In this quantitative study, a parallel archival research design was used to investigate the degree to which generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder predicted the presence of atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes. There were 1,209 electronic medical records of adult patients obtained through purposive stratified sampling. A secondary data analysis was employed using descriptive cross tabulation, chi-square test of independence, and multinomial logistic regression. The findings revealed major depression recurrent was a statistically significant predictor for atherosclerosis, rheumatoid arthritis, type II diabetes and cancer. Generalized anxiety disorder was a statistically significant predictor for cancer. The results can promote positive social change by providing information that could be used to develop assessment plans that identity individuals who are at risk of developing the comorbid diseases. The prevention programs could effectively be used to minimize the subsequent development of inflammatory diseases, which in turn could decrease the onset of the medical diseases among individuals with psychiatric disorders.

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Dedication

Fear thou not; for I am with thee: be not dismayed; for I am thy God: I will strengthen thee; yes, I will help thee; yes, I will uphold thee with the right hand of my righteousness.

Isaiah 41:10

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Chapter 1

Millions of people in the United States and world-wide suffer from at least one of the inflammatory-based medical diseases of atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, or type II diabetes (Heijnen & Kavelaars, 2005; Pickup, 2003; Steptoe & Brydon, 2005; Walker, Green, Greenman, Walker, & Sharpe, 2005). Many of these individuals also have at least one of the psychiatric diagnoses of generalized anxiety disorder, posttraumatic stress disorder, major depression, recurrent, or dysthymic disorder (DSM-IV, 2000). This study investigated these psychiatric and medical comorbid conditions to determine if the psychiatric disorders predicted the presence of the medical diseases. The multidisciplinary field of psychoneuroimmunology (PNI) provides a theoretical foundation for understanding the connection between the psychiatric condition of the individual and the initiation of the acute inflammatory response. PNI serves as the basis for explaining the development of the medical diseases included in this study (Rabin, 2005). The purpose of this study was to determine if one or more of the psychiatric disorders of generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, or dysthymic disorder could be used to predict the presence one or more of the inflammatory based medical diseases of atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, or type II diabetes.

Chapter 2 will provide detail of the 138 year history of scientific and clinical documentation of the PNI psychobiological process involved in the development of atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes. This chapter, however, will provide the presentation of the problem statement,

nature of the study with the research questions, purpose of the study, theoretical framework, operational definitions, assumptions and limitations of the study, significance of the study, professional application of the results, and positive social change. This chapter will conclude with a summary of the chapter and an introduction to the remaining four chapters of the study: the literature review, methodology, data analysis, and discussion of the findings.

Problem Statement

Individuals with psychiatric and medical disease comorbidity lose 25 to 30 years of normal life expectancy (Malliori, 2010). Over 70% of patients with severe decrements in their quality of life suffer from psychiatric and medical comorbid conditions (Moussavi, 2007). Depression and anxiety affect up to 25% of the female population in the United States and up to 12% of the male population in the United States (DSM-VI). Specifically, the affective disorders included in this study were generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder. The medical diseases in the comorbid conditions investigated in this study were atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes. Prevalence studies involving cardiovascular heart disease and stroke report 71.3 million adults in the United States suffer disability or death annually (Mensah & Brown, 2007). There are 12.5 million individuals in the United States diagnosed with atherosclerosis (Pearson, 2007). Sixty-eight million individuals suffer the debilitating disease of rheumatoid arthritis (Heijnen & Kavelaars, 2005). There are 500,000 deaths annually because of cancer (University of Rochester, 2007). There are 100 million

individuals suffering with type II diabetes (Pickup & Crook, 1998). Mensah and Brown (2007) also reported that inflammatory-based diseases resulted in a healthcare cost burden that exceeds $400 billion a year for individuals and society. The rising personal and financial costs associated with the comorbid conditions indicate the need to identify additional predictors of these inflammatory based diseases for use in disease prevention assessments (Spiegel, 2003).

Psychoneuroimmunology (PNI) provides the scientific bases for including the psychiatric disorders as predictors of the medical diseases (Boscarino, 1997; Ford et al. 1998, Wells et al., 1991). PNI research has revealed that prolonged emotional distress, as with depression and anxiety, results in hormonal changes that causes a dysregulation in some cellular functions and alters immune function (Rabin, 2005). Studies using the PNI model have provided evidence showing that the immune parameters supporting the inflammatory-based disease process can be significantly altered by use of psychotherapy. However the change in the immune parameters have no effect on the disease process once the disease has been initiated (Cupal, Brewer, & Britton, 2001; Donaldson, 2000; Gruber et al., 1993; Gruber, Hall, & Hersh, 1988; Hall et al., 1996; Kraaimaat et al., 1995; Laidlaw, Booth, & Large, 1996; Luskin, 2008; Lutgendorf et al., 2000; Pawlow & Jones, 2002; Petrie et al., 1995; Sherman et al., 1997; Surwit et al., 1991; Van der Pompe et al., 1997; Witvliet et al., 2001). A detailed discussion of these studies is provided in chapter 2. However the common focus of each of the studies was to investigate the use of psychotherapy for disease amelioration or reversal. Prior to the studies by Ader and Cohen (1975) which demonstrated that the immune system can respond to classical

conditioning, the potential of psychotherapy was viewed as predominantly palliative (Spiegel, 2003). Subsequent PNI researchers have substantiated the findings by Ader and Cohen. This presents the possibility of going beyond palliative care to help individuals cope with the distress of illness, to investigating the role of psychotherapy in disease prevention. The findings of the studies investigating the effect of psychotherapy techniques with existing disease processes revealed the problem of identifying the time between the occurrence of the first diagnosis in the comorbid pair and the occurrence of the second diagnosis so that psychotherapy interventions could be utilized in prevention treatment. This is an important area of exploration. Mensah and Brown (2007) reported the problem of underuse of prevention strategies that result in less than optimal control of the risk factors in inflammatory diseases. Kiecolt-Glaser et al. (2002) reported a problem in the lack of pre-clinical information necessary to explore the efficacy of psychotherapy as a prevention treatment.

Nature of the Study

This research was predicated by PNI studies conducted by previous researchers (Batstra, Bos, & Neeleman, 2002; Boscarino, 1997; Ford et al., 1998; Kiecolt-Glaser et al., 2002). This study tested the hypothesis that a predictive relationship exists between psychiatric disorders and inflammatory based medical diseases, and that psychiatric disorders are predictors for specific medical diseases. The specific research questions for this study were:

1. For individuals with comorbid psychiatric disorder and medical disease diagnoses, what is the association between the first type of psychiatric diagnosis and the first medical diagnosis?

2. Among individuals with comorbid psychiatric and medical disease diagnoses, to what degree does the presence of a psychiatric disorder and the demographic variables (gender, race, family psychiatric history, family medical history, and chemical dependence history) significantly predict the presence of the medical disorders atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes in the comorbid pairs?

3. To what degree does the presence of a psychiatric disorder as the first diagnosis and the diagnosed psychiatric disorder predict the medical disorders for the comorbid pairs included in the study?

This study used several statistical methods to test the null hypotheses for the research questions. A descriptive cross tabulation was used to address research question 1. The chi-square test of independence was used to address research question 2, and the multinomial logistic regression was used to address research question 3.

The design of this study addressed some of the problems cited by previous researchers who used an archival research design. The researchers reported that, among the studies they reviewed, there was a broad diversity in the type of research designs selected, study inclusion criterions used, and different variables investigated in the studies, which made it difficult to generalize the findings. The broad diversity in reporting the results for the studies was also viewed as problematic in generalizing the

findings (Baumeister et al., 2005; Kiecolt-Glaser et al., 2002; Moussavi et al., 2007). Finally, the researchers reported the lack of verification of psychiatric and medical diagnoses as problematic regarding the reliability of the findings reported. The researchers reported the studies that they reviewed relied on participant self-reports, which may have confounded the findings. This study specifically addressed the methodological problems that affected the generalizability reported by previous researchers by using clinically determined diagnoses for all of the cases included in the study. This study employed a purposive stratified sampling method (Trochim, 2006). This allowed for the selection of cases with specific psychiatric disorders and specific medical diseases. The process involved accessing and reviewing patient electronic medical records using the codes from the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) for the psychiatric disorders investigated in the study and then using the diagnostic codes from the International Classification of Diseases, 9th Revision (ICD-9) for the medical diseases. An additional way in which the design of this study improved upon previous archival studies was the uniformity of clinical documentation. This uniformity was accomplished by the selection of a single healthcare system from which to draw the cases. The healthcare system has a strict clinical documentation policy to assure uniformity across the multiple hospitals in the system (HFHS Clinical Documentation Policy and Procedures, 1997-revision).

Purpose of the Study

The purpose of this study was to determine if certain psychiatric disorders predicted the presence of specific immune-based inflammatory diseases. The premise

was if psychiatric disorders could be empirically linked to the prediction of immune-based inflammatory diseases, then there would be a basis for developing and promoting disease prevention measures for individuals diagnosed with one of the four psychiatric disorders. The goal of the intervention programs would be to reduce the likelihood of the individuals developing one of the five inflammatory based medical diseases investigated in this study. The psychiatric predictor disorders in this study were generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder. The five medical diseases investigated in this study were atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes as the dependent variables. The statistical method that was used to test the prediction model was multinomial logistic regression.

This study also addressed the shortcomings of previous research by considering the influence of certain demographic and biological factors on the prediction model. The demographic variables included age, race, and gender. Several researchers (Baumeister et al., 2005; Kiecolt-Glaser et al. 2002; Moussavi et al., 2007) have suggested the importance of including such variables when studying the PNI model as it relates to comorbid psychiatric and medical conditions. The biological factors also included family history of psychiatric disorder, family history of the medical disorder, and individual history of chemical dependence. Kiecolt-Glaser et al. (2002) had suggested the importance of including chemical dependence history in studies of comorbid occurrences of psychiatric and medical conditions because of its negative effect on both mental and

physical health. Pinel (2006) recently reported the prevalence of chemical dependence among individuals suffering from comorbid conditions.

For this study, I obtained the medical and psychiatric information identified as significant in the comorbid pairing by previous PNI researchers (Kiecolt-Glaser et al., 2002; Kaye and Lightman, 2005; and Rabin, 2005). To test the hypotheses that certain psychiatric disorders predict the presence of specific immune based inflammatory diseases, this study reviewed 1,209 electronic medical records of patients treated in a multi-hospital healthcare system. The hospital system has uniform patient assessment protocols, full documentation of the medical and psychiatric diagnoses, and documented treatment histories for the patients. A purposive sampling approach was used to assure only the medical records that met the inclusion criterion were reviewed for the study. The inclusion criterion was that the records were of individuals who were 21 years of age or older, and the individuals must have at least one of the identified psychiatric disorders plus at least one of the identified medical diseases. Chapter 3 will provide greater detail of the research design.

Theoretical Framework

Psychoneuroimmunology (PNI) is an interdisciplinary field involving the scientific investigation of how emotions affect the functioning of the central nervous system. In response to prolonged emotional distress, such as depression or anxiety disorders, the hypothalamus secretes the hormone corticotrophin releasing factor (CRF). The CRF causes the increased production of the hormones epinephrine, norepinephrine, and cortisol. Over time, if the emotional distress continues, these hormonal changes cause

a dysregulation in some cellular functions and in the immune system. The hormonal changes can ultimately form the bases for the development of some medical diseases (Kaye & Lightman, 2005; Kiecolt-Glaser, 2002; Rabin, 2005). It is the interrelated action of cellular dysregulation and immune system dysregulation that results in the inflammatory response by the immune system. A review of the literature revealed anxiety and depression to be the most consistent psychiatric disorders to initiate the dysregulation process that results in the acute inflammatory response, which has been linked to the development of certain medical diseases (Kiecolt-Glaser et al., 2002; Rabin, 2005). From the broad categories of anxiety and depression, this study specifically selected the psychiatric diagnoses of generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder. The medical conditions included in this study were atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes.

In general, at the center of the stress response is the increased production of the hormones cortisol, epinephrine, and norepinephrine. These hormones contribute to the initiation of the acute inflammatory response that can eventually progress to the immune inflammatory reaction (McCance & Huether, 2002; Rabin, 2005). For instance, atherosclerosis is the result of the inflammatory response within the blood vessels and cardiovascular heart disease develops subsequent to atherosclerosis (Steptoe & Brydon, 2005). Rheumatoid arthritis results from an inflammatory response that destroys the body tissue that lines the joints. It also reflects the failure of the immune system to recognize the body's own cells (Heijnen & Kavelaars, 2005). Cancer is the failure of the immune

system to detect and destroy mutated self- cells by the inflammatory response (Walker et al., 2005). Type II diabetes is the impairment of the insulin secretion of the beta cells of the pancreas that occurs over time, initially triggered by the acute inflammatory response which was precipitated by prolonged emotional states of anxiety and/or depression (Pickup & Crook, 1997).Figure 1 presents a diagram of the PNI bases for psychiatric disorder and medical disease comorbidity. In figure 1, in the formation of psychiatric and medical disease comorbidity, the emotional experience initiates the physiological response by the endocrine system to alter hormonal output that becomes the foundation for the medical disease (Kaye & Lightman, 2005; Kiecolt-Glaser, 2002; Rabin, 2005).

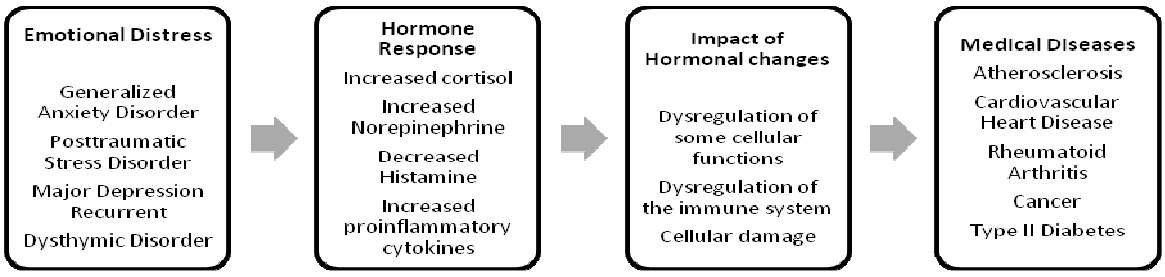

Figure 1. Pyschoneuroimmunology comorbidity model.

Seminal studies by Solomon and Moos (1963) provided the first evidence of the immune response to prolonged stress. Ader and Cohen (1975) demonstrated that the immune system can respond to classical conditioning. Experimental research designs using relaxation therapy techniques have shown the immune parameters of the

inflammatory disease processes can be significantly altered through the use of stress reduction techniques (Donaldson, 2000; Gruber, Hall, & Hersh, 1988; Gruber, Hersh, Hall, Waletzky, Kunz, & Weiss, 1993). Although these studies noted the immune function was altered, they also noted that existing medical diseases continued to progress despite the change in the inflammatory response. Findings from the studies suggested the significance of the factor of timing in the correction of the immune parameters (Ford, 1998; Kiecolt-Glaser et al., 2002). The PNI model proposed for this study presents the possibility of indentifying predictors for the diseases and an opportunity to focus on disease prevention. Chapter 2 will provide detailed discussion regarding the process of the physiological stress response initiated by emotions.

This study used the principles of PNI to investigate the degree to which certain diagnosed psychiatric disorders (such as generalized anxiety disorder, posttraumatic stress disorder, major depressive disorder, recurrent, and dysthymic disorder) predict the development of specific medical diseases (such as atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes). The statistical methods included descriptive cross tabulation, multinomial logistic regression and chi-square test for independence to test the psychiatric disorder prediction model that is based on the PNI foundation.

Operational Definitions

Adrenocorticotropic hormone (ACTH): A hormone which stimulates cortisol production from the cortex of the adrenal gland (Kaye & Lightman, 2005).

Acute inflammatory response: An initial inflammatory response that occurs to rid the body of an infectious agent or remove and repair damaged tissue without the activation of the immune system (Rabin, 2005).

Amino acids: The building blocks and break-down products of proteins (Pinel, 2003).

Antibodies: Proteins that bind specifically to antigens on the surface of invading microorganisms that promotes the destruction of the microorganism (Pinel, 2003).

Antigens: Proteins on the surface of cells that identify them as native or foreign (Pinel, 2003).

Atherosclerosis: A chronic inflammatory response to injury in the blood vessels. This disorder underlies coronary heart disease and is characterized by a process involving inflammation of the lining of blood vessels leading to the progressive accumulation of the cellular content flowing in the blood into microscopic lesions in the vessel leading to hardening of the vessels and the blockage of blood flow and heart attack (Steptoe & Brydon, 2005).

Autoimmune response: An immune response against one's own tissue resulting in tissue damage (Rabin, 2005).

Autonomic nervous system (ANS): The part of the peripheral nervous system that participates in the regulation of the internal environment of the body (Pinel, 2003).

Bioimmunoassay: The collection of blood, body fluid, or tissue to assess the presence and/or activity of components of the immune system (Dorland's Medical Dictionary, 25th Ed.; Kiecolt-Glaser et al., 2002).

Bone resorption: Loss of bone substance by physiological or pathological means (Heijnen & Kavelaars, 2005).

Cancer: Cells within the body that do not respond appropriately to chemical messages to stop growing and dividing. The uncontrolled proliferation can result in the cellular spreading from the original anatomical location to other regions and organs of the body and disrupt normal cellular processes (Walker et al., 2005).

Cardiovascular heart disease: Partial or complete blockage of the coronary arteries resulting in insufficient nutrients and oxygen reaching the heart muscle leading to damage of the heart muscle with acute chest pain or sudden death from heart failure (Steptoe & Brydon, 2005).

CD-4: Classified as 'helper T cells' because they promote immune reactions (Rabin, 2005).

Cell adhesion molecules (CAMs): Increases the adhesion of cellular debris from the blood flow to the vascular walls in the atherosclerosis process (Steptoe & Brydon, 2005).

Cognitive-behavioral therapy (CBT): A therapist guided technique of discovery of distortions in thinking that lead to error in emotional and/or behavioral responses by an individual. The end result of CBT is the reconstruction and re-building of the individual's assumptions (Fleming & Robinson, 2007).

Comorbid: The presence of additional diseases (disorders) in relation to an index disease (disorder) in one individual (Valderas et al., 2009).

Corticotrophin releasing factor (CRF): A hormone responsible for promoting the synthesis and release of ACTH. It is also has important effects on behavior and cognitive processing (Kaye & Lightman, 2005).

Cortisol: The main effector hormone of the HPA axis that has access to every cell in the body and influences many essential stress related cellular processes (Kaye & Lightman, 2005).

Cytokines: Soluble proteins released primarily from activated immune cells that serve as communication signals in cell-to-cell interactions and can influence the activity of other cells (Rabin, 2005).

Dendritic cells: Found in all tissue of the body, these cells have the capability of presenting antigens (chemical markers) of invading microorganisms to T lymphocytes in preparation for the destruction of the invading microorganism (Rabin, 2005).

Dysregulation: Disturbance or impairment of normal functioning (Rabin, 2005).

Dysthymic disorder: A chronically depressed mood that occurs for most of the day, more days than not, for at least two years (DSM-IV, 2000).

Endocrine system: The body organs/glands with the primary function of the release of hormones (Pinel, 2003).

Endothelium cells: Active tissue cells that help to maintain cardiovascular health by producing antiplatelet, anticlotting, and other factors to prevent cells from adhering to the vascular walls and forming a blockage. The cells also produce nitric oxide that maintains the flexible tone of the vascular wall (Steptoe & Brydon, 2005).

Epinephrine: A major hormone of the sympathetic nervous system with a role in the stress response to influence the liver to increase production of glucose resulting in the increase in blood sugar level, increase in breaking down body fats with increase in fatty acids in the blood which influences the pancreas to decrease production of insulin. This hormone also increases heart contractions with increased blood flow (McCance & Huether, 2002).

Ethnicity: The shared culture and lifestyle of a people (Carter et al. 1996)

Forgiveness therapy: This therapy approach does not involve reconciliation or condoning the experience. It is a process of stopping the mental rehearsal of the wrong, recognizing the emotional distress is coming from hurt thoughts, and letting go of the painful thoughts (Luskin, 2008).

Generalized anxiety disorder: This is an *a*nxiety disorder that is not precipitated by any obvious event (Pinel, 2003). It is an excessive anxiety or worry that an individual finds difficult to control (DSM-IV, 2000, Appendix D).

Glucocorticoids: Hormones derived from cholesterol that have two major functions in the stress response (1) promotes energy conservation and storage by regulating glucose and fat uptake during stress-free times (2) primes the immune system for a more rapid response to future stress once an initial stress response has occurred. Once the stress response is initiated, these hormones suppress and restrain the immune system (Kaye & Lightman, 2005)

Guided imagery and visualization: This is a psychotherapeutic technique involving use of the mind to create a sense of physical well-being and health. The

clinician uses verbal suggestions to help the patient structure the imagined place of peace and calm while exercising control over involuntary functions such as breathing (Ulmann, 2003).

Histamine: Hormone that regulates the inflammatory response by the immune system (Crouch & McClintic, 1971).

Homeostasis: The stability of an organism's constant internal environment (Pinel, 2003). All of the physiological processes necessary to sustain cell survival and function (Kaye & Lightman, 2005).

Hormones: Chemicals released by specialized cells of the endocrine system into the bloodstream that influence the activity and function of target cells and organs. The primary functions of these chemicals include reproduction, growth and development, energy storage and utilization, and maintenance of physiological equilibrium (Kaye & Lightman, 2005).

Hypothalamus-pituitary-adrenal axis (HPA Axis): The early general alarm physiological reaction to stress with the increased production and release of hormones to re-direct body systems to prepare for increased energy, defense, and healing from injury (Rabin, 2005).

Immune system: A variety of interactive cells and soluble molecules that patrol the blood and tissues to detect the presence of substances/antigens that are foreign to the body that can produce illness and destroys and removes the foreign material from the body (Rabin, 2005).

Immune-challenge: In an experimental design, the presentations of a controlled amount of a pathogen, allergen, or wound puncture to assess the immune response (Kiecolt-Glaser et al. 2002).

Immunoglobulin A (IgA): An immune molecule found in external secretions of the body and has a protective role to interfere with the ability of microorganisms to enter the external body cavities or penetrate tissue (Rabin, 2005).

Innate immune system: The immune process that is always active monitoring the body for the presence of infectious agents and destroys and removes the agents from the body (Rabin, 2005).

Macrophage: Specialized immune cells that seek out, engulf, and consume foreign microorganisms that invade the body. Macrophages also remove debris from the body (Pinel, 2003).

Major depression disorder: A depressive disorder characterized by one or more major depressive episodes without a history of manic, mixed, or hypomanic episodes that are not related to the effects of substance use, medications, or other psychiatric disorders. This disorder is associated with a high mortality rate with up to 15% of individuals with this diagnosis dying from suicide. This disorder may be preceded by dysthymic disorder (DSM-IV, 2000).

Neuroendocrinology: The study of interactions between the nervous system and the endocrine system.

Neutrophil adherence: Immune cells that bind to foreign particles in the body, such as bacteria and kill them by ingesting them (Rabin, 2005).

NK cells: A classification of immune cell that reacts to malignant cells and cells that are infected with virus to destroy those cells (Rabin, 2005).

Norepinephrine: The principle hormone/neurotransmitter of the sympathetic nervous system (Rabin, 2005). In the stress response it has the following physiological influence decreases the immune function, pupil dilation, decreased gastric secretion, dilation of blood vessels, dilation of bronchi, vasoconstriction of smooth muscle, increased blood pressure, and decrease in digestion (McCance & Huether, 2002).

Parasympathetic nervous system: Has effects opposite of the sympathetic nervous system and is associated with the autonomic nervous system at rest. There is an on-going dynamic interaction between the two systems to maintain a state of balance between alertness and rest (Rabin, 2005).

Posttraumatic stress disorder: An individual's response to a stressor that involves intense fear, helplessness, or horror. There is physiological reactivity on exposure to cues and the symptoms cause clinically significant distress or impairment (DSM-IV, 2000, Appendix D).

Pro-inflammatory cytokines: Soluble proteins that activate and mediate the inflammatory response of the immune system (Rabin, 2005).

Psychiatric and medical comorbidity: The presence of one or more index psychiatric disorders plus the relational presence of one or more medical diseases in a single individual (Valderas et al., 2009).

Psychoneuroimmunology: The study of the relation of stress, emotions, immunological dysfunction (especially autoimmunity), and disease, both physical and

mental; immunological disturbance in conjunction with mental illness (Solomon & Moos, 1964).

Psychopharmacology: The manipulation of neural activity and behavior with drugs (Pinel, 2006)

Pulsatile hormone release: The typical pattern of hormone release that occurs in large surges several times a day (Pinel, 2003).

Race: A hereditary category of a person and it involves the passing along of genes through reproduction (Carter et al. 1996)

Rheumatoid arthritis: A chronic inflammatory disease of the joints characterized by pain, decreased mobility and stiffness (Heijnen & Kavelaars, 2005).

Sympatho-adrenomedullary axis (SAM axis): Responsible for the physio-behavioral 'fight or flight' response to perceived danger i.e. cold sweat, muscle tensing, change in breathing (Rabin, 2005).

Sympathetic nervous system: Division of the autonomic nervous system with a significant role in the stress response (Rabin, 2005).

Synovium: Tissue lining of the joints (Heijnen & Kavelaars, 2005).

T-lymphocytes: Immune cells that mature in the thymus and are then excreted into the bloodstream and tissue. These cells are involved 'cell-mediated immunity' in ridding the body of foreign cells. T-cells that react against an individual's own tissue are eliminated in the thymus as are the T cells that are functionally useless (Rabin, 2005).

Type II diabetes: This disease is comprised of a heterogenous group of conditions in which the insulin secretion is not absolutely compromised (Surwit & Schneider, 1993).

Assumptions and Limitations

Assumptions of the Study

The PNI model is predicated upon several assumptions. The first is an assumption of a direct relationship between emotion and physiological processes that have been identified by the PNI model (Kaye & Lightman, 2005; Kiecolt-Glaser, 2002; Rabin, 2005). PNI research provides support for the assumption that anxiety and depression are the most prominent emotional conditions to initiate the hormonal physiological process which leads to the acute inflammatory response. The acute inflammatory response is the basis of the inflammatory immune diseases addressed in this study (Baumeister et al., 2003; Kiecolt-Glaser, 2002). There is also the assumption that comorbid psychiatric and medical conditions can occur in the absence of biological and hereditary influences (Bremner, 2002). In this study, the researcher investigated this assumption by including family history for the psychiatric and medical conditions among the independent variables.

As reported by previous researchers of psychiatric and medical disease comorbidity, there is the assumption that an archival design will provide cost effective and efficient access to a large participant sample (Baumeister, 2003; Moussavi, 2007). There is the assumption that the archival approach lacks the opportunity to gather information regarding the feelings and perspectives of the individual participants beyond what is in the existing document, as compared to other research designs, such as survey methods or qualitative data collect methods (Moussavi al., 2007).

Limitations of the Study

There were several factors related to this study that may limit the generalizability of the findings. First, the sampling was limited to a single healthcare system located in Michigan. The demographic composition of Michigan, which is located in the northeastern region of the United States, may not be representative of other regions of the country. As an example, the racial composition in Michigan is predominantly European American with African Americans as the second highest population racial group. Asian Americans comprised less than 3% of the Michigan population. Hispanic Americans comprise 4% of the population. Among the 1,209 cases reviewed, 680 were European Americans (63%), 351 were African Americans (32%), 11 were Asian Americans, and 8 were Hispanic Americans. Cumulatively, the Asian American and Hispanic American comprised less than 5% of the cases reviewed. There were thirty cases in the 'other' racial category. In determining whether or not the sample obtained for this study was representative of the demographic mix in the State of Michigan, the report by the 2008 census was used for comparison. The comparison revealed the European Americans were underrepresented in this sample. African Americans were overrepresented in the sample. Asian Americans and Hispanic Americans were underrepresented in the sample. The representativeness of the sample obtained has important implications for interpreting the findings, for generalizing conclusions, and for suggesting future research.

In addition, the use of a single healthcare entity from which sample cases were selected may have unique aspects that may not be generalizable to other healthcare facilities. There may be unique elements of how this healthcare system manages patient

care and those elements may not be in effect in other healthcare systems in the United States. The data collection and recording techniques for this facility may also differ from what other healthcare systems use.

Another factor was the study inclusion criteria which limited the cases reviewed to adults 21 years of age and older. Comorbid conditions of children and adolescents were not included in the study. The age of the individuals whose cases were reviewed was predominantly 50 years of age and over. Age may have had a confounding effect on the study because of possible age related medical conditions. Finally, the five year population cycle for this study may not have been sufficient to detect the presence of the psychiatric disorder and medical disease comorbid condition among the cases not included in the study. Previous research indicates that there may be as much as a ten years lag between the identification of a psychiatric disorder and the later manifestation of related inflammatory based medical diseases. Therefore the five year cycle of data collection from the healthcare facility may have been too short a period of time to detect the connection between a diagnosis of psychiatric disorders and inflammatory based medical diseases.

Significance of the Study

The significance of this study was to determine whether certain psychiatric disorders predict the presence of specific immune based medical diseases. The inclusion of psychiatric disorders can improve disease prevention assessment approaches. The addition of disease prevention assessment approaches has important implications in healthcare given the millions of individuals in the United States and world wide who are

diagnosed annually with psychiatric disorders that could potentially result in the development of atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes (Baumeister et al., 2007).

In addition, the design of this study directly addressed some the shortcomings the methodological issues cited by Kiecolt-Glaser et al. (2002), Baumeister et al. (2005), and Moussavi et al. (2007). These researchers reported that differences in the design of the studies that they reviewed, different styles in writing the results, and lack of verification of diagnoses were problematic in terms of generalizing the findings from the studies to other samples. The researchers also reported the need for demographic data to better understand how demographic variables impacted prediction of the progression of the medical disease. The data in this study was obtained from the electronic medical record data base of a healthcare system that has uniform information collection protocols. In addition, each case included in this study had a clearly identified psychiatric and medical diagnosis and contained pre-clinical and family history information. This study included demographic variables to address the shortcomings and methodological issues reported by previous researchers.

Professional Application of Results

The findings of this study could have immediate application by psychiatrists and physicians who diagnosis one of the identified psychiatric disorders, especially major depression recurrent or generalized anxiety disorder, in their patients. Those diagnoses should prompt additional actions such as screening for changes in the bio-immune markers for inflammatory conditions and the screening for the inflammatory based

medical disorders of atherosclerosis, cardiovascular heart disease, and cancer. The results of this study may also prompt the use of psychotherapy techniques which emphasize relaxation training for the patient as a part of the initial preventive intervention protocol. Psychotherapy and relaxation techniques would help provide patients with skills needed to help manage the psychological disorders. In turn the stress reduction techniques could help manage the immune inflammatory response which should then decrease the likelihood that the associated medical conditions would occur.

Positive Social Change

The social issue that this study addressed was the healthcare problem of psychiatric and medical disease comorbidity and the need to develop additional disease prevention assessment approaches. The health and quality of life for millions of individuals in the United States and world wide can be improved with the improvement of disease prevention assessments (Spiegel, 2003). Results from this study could be used to promote social change by contributing information regarding the relationship between the comorbid psychiatric disorders and the inflammatory based medical conditions investigated in the study. Professionals could use the information to develop assessment plans that identify individuals with psychiatric conditions that are related to the comorbid medical diseases. Professionals could then develop prevention programs that minimize the subsequent development of the inflammatory diseases. The comprehensive prevention plans could encompass periodic screening for the onset of the inflammatory diseases, education related to the prognosis of the psychiatric disorders, as well as stress management techniques to manage stress associated with the psychiatric disorders. The

overall intent of the prevention plans would be to implement preventative measures that interrupt or prevent the acute inflammatory response that precipitates the onset of the medical diseases.

Summary

This chapter provided an introduction to the study that included a presentation of the problem statement, research questions, theoretical framework of the study, operational definitions, and the assumptions and limitations of the study. This chapter concluded with a discussion of the knowledge generated by the study, the professional application of the new information, the significance of the study, and the positive social change that can occur as a result of the study. Chapter 2 will cover an in depth review of the literature related to the theoretical foundation and specific variables of this study. Chapter 3 will discuss the research design and approach, including a description of the cases included in the sample and determination of the sample size, materials used for the study, data collection procedures and the statistical methods selected to analyze the data, statement of the hypotheses, and participant protections and rights. Chapter 4 will provide a discussion the research findings. Chapter 5 will give a brief over view of the purpose of the study, the findings, the implication of the study for positive social change, recommendations for action, and recommendations for further studies.

Chapter 2: Literature Review

Introduction

Atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes affect millions of individuals throughout the United States and worldwide

(Pearson, 2007; Pickup & Crook, 1998). The intent of this research was to determine if there was a predictive relationship between those medical diseases and the psychiatric disorders of generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder. Research in the field of psychoneuroimmunology (PNI) supports the possibility that the psychiatric conditions of depression and anxiety in fact may predict onset of atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer and type II diabetes (Ford, 1998; Kiecolt-Glaser, 2002).

During the literature review, the researcher accessed peer reviewed journals and articles and academic publications as the information source for related articles. The journal articles were found at Sladen Library, which is an affiliate of Wayne State University Medical School and Henry Ford Healthcare System, EBSCO database and electronic library, and the web-based Google Scholar. The materials were downloaded electronically when journal full text was available. The selection of the medical diseases for this study was based on the published research findings that indicate a connection between the emotional state of prolonged anxiety and/or depression and the development of the inflammatory-based disease conditions of atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes (Heijnen & Kavelaars, 2005; Pickup, 2003; Steptoe & Brydon, 2005; Walker & Sharpe, 2005).

To examine literature that supports the proposed model of psychiatric conditions being predictors for certain medical conditions, this chapter presents the following sections: The Prevalence and Societal Impact of the medical conditions of atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II

diabetes; Psychiatric and Medical Comorbidity, Theoretical Foundation of Psychoneuroimmunology; Current Status of PNI Research, PNI as a Potential Mediator between Psychiatric and Medical Conditions; description of the PNI Process for the onset of Medical Disease Variables; PNI Research Using Psychotherapy; the Proposed PNI Model of this Study, Review of Research Methodologies, and Biological Variables of Possible Influence. The chapter will conclude with a summary and introduction to chapter 3 that describes the methodology used for this study.

Prevalence and Societal Impact of the Medical and Psychiatric Conditions

Statistically, prevalence studies have revealed that 12.5 million Americans are diagnosed with atherosclerosis and cardiovascular heart disease, and that number could double by the year 2050 (Pearson, 2007). Pearson also reported there is an estimated 10 year period of time between the asymptomatic stage of the diseases to the progressive damage to the blood vessel walls that may lead to heart attack or stroke. There are 550,000 people diagnosed with heart failure each year in the United States (Weisfeldt et al., 2007). In 2006 the World Congress of Cardiologists reported that 17.5 million deaths occurred worldwide in the year 2005 because of heart attack and stroke. Project Hope (2007) reported that medical science has not revealed or developed strategies for preventing cardiovascular disease, rather they have only been successful in developing strategies for making it less lethal. Heijnen and Kavelaars (2005) reported 68 million individuals world-wide suffer from the debilitating disease of rheumatoid arthritis. There are 500,000 people who die from cancer each year (University of Rochester, 2007). Pickup and Crook (1998) reported 100 million people around the world are diagnosed

with type II diabetes. In addition to the human suffering from these diseases, these medical conditions have resulted in a $400 billion a year financial burden to individuals and society through spending on healthcare and loss of productivity at jobs (Mensah & Brown, 2007). There is a pressing need for increased knowledge of the factors that are related to the development of atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes because of the heavy human burden of these diseases (Spiegel, 2003).The psychiatric conditions of anxiety and depression also have a significant impact on the perceived quality of life as well as being factors in the initiation of disease development (Baumeister et al., 2005). In this study there are two psychiatric categories; anxiety and depression. Anxiety is subdivided into the clinical diagnoses of generalized anxiety disorder and posttraumatic stress disorder. The psychiatric diagnostic category of depression is subdivided into major depression recurrent and dysthymic disorder. Generalized anxiety disorder includes the clinical features of prolonged excessive anxiety and worry. Generalized anxiety disorder affects five percent of the 307 million people living in the United States (DSM-IV, 2000). Posttraumatic stress disorder (PTSD) involves feelings of intense fear and helplessness long after a traumatic experience has occurred (DSM-IV, 2000). Bremner (2002) reported approximately 40 million individuals living in the United States suffer from PTSD.

The DSM-IV reports major depression recurrent affects 10% to 25% of the female population in the U.S. and 5% to 12% of males. Dysthymic disorder, which also involves chronic depressed mood, occurs in approximately 6% of the United States population (*DSM-IV*). Moussavi et al. (2007) predicted that by the year 2020 depression will be

second only to heart disease as the leading health burden. Moussavi and his colleagues also reported that depression is a global public health issue.

Baumeister et al. (2005) found that people suffering from psychiatric disorder and medical disease comorbidity has now become the rule rather than the exception in healthcare. These prevalence reports suggest the need for research assessing the psychological predictors of the presence of disease for the purpose of developing prevention assessment and intervention options.

Psychiatric and medical comorbidity. Comorbidity refers to the co-existence of two or more disease conditions within the same individual (Baumeister et al., 2005). This study focused on psychiatric disorder and medical disease comorbidity. In this study, the psychiatric conditions were generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder. The medical diseases were atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes. These diseases were selected because of the established PNI foundation for the development of immune based inflammatory diseases. There is also a high representation of these conditions in comorbid cases. Baumeister et al. (2005) reported anxiety and depression were the most consistent correlates associated with comorbid psychiatric and medical pairs. Moussavi and his colleagues conducted a World Health survey in which data was obtained from 245,404 adult participants from 60 countries from all regions of the world (Moussavi et al., 2007). The results revealed that depression was a comorbid condition often presented with medical diseases such as angina, arthritis, asthma, and diabetes.

In addition to depression, anxiety is prevalent in comorbid cases. In a review of 45 studies published between 1998 and 2002, Baumeister found that 70.3% of the reports were from individuals reporting anxiety in addition to depression in medical comorbid conditions. Depression and anxiety paired with medical disease were the most significant factors in their perceived diminished quality of life (Baumeister et al., 2005). Kiecolt-Glaser (1997) also found that the psychiatric disorders of generalized anxiety disorder, posttraumatic stress disorder, and major depression recurrent frequently coexisted with medical conditions such as atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes.

Findings from the aforementioned studies (Baumeister et al., 2005; Kiecolt-Glaser, 1997; Moussavi et al., 2007) suggest that there is a relationship between certain psychiatric disorders and certain medical diseases. The field of psychoneuroimmunology provides a foundation for understanding the connection between these psychiatric disorders and the medical diseases.

Theoretical Framework of Psychoneuroimmunology

Historical overview of PNI. Psychoneuroimmunology (PNI) is the multi-disciplinary, scientific investigation of the phenomenon of the emotion triggered physiological response of the immune system, via hormones released by the endocrine system, which frequently results in the development of medical disorders (Pinel, 2006). PNI studies have identified the hormones norepinephrine, epinephrine, and cortisol to be central to this process. Cortisol, in particular, has the triaging effect during times of emotional distress. In this triaging process, cortisol causes the dysregulation of certain

cellular and bodily function to give priority to physiological functions that are directly related to immediate survival needs, such as increased energy for escape. The immune system is not considered to be a priority function, and it is dysregulated. If the emotional distress is related to a real physical threat, the system returns to normal upon the resolution of the threat. If the distress is prolonged, as with the psychiatric disorders of depression and anxiety, the dysregulation is prolonged resulting in cellular damage, immune dysfunction, and the possibility of disease. The phenomenon of comorbid psychiatric and medical disease has been documented by medical science for the last 138 years.

In post Civil War America, Da Costa (1871) noted functional arrhythmia of the heart among hospitalized war veterans as a response to trauma induced anxiety. He named the disorder 'irritable heart' to describe the adaptation of physical functioning initiated by emotional stimuli. In 1915, physiologist Walter B. Cannon documented the emotions of fear and anxiety initiating a sympathetic nervous system response and adaptation to stress reflected in a change in physiological functioning. Cannon coined the term 'fight or flight response' and the term 'homeostasis'.

Selye (1936) advanced the initial work of DaCosta and Cannon by documenting the involvement of the endocrine system in the release of hormones during the condition of prolonged distress in his animal studies. Selye explored the biological functioning of a specific category of hormones central to the acute stress response called glucocorticoids. Cortisol was identified as the primary hormone related to stress in the classification of glucocorticoids. In 1963, Donald F. Klein extended Selye's work by using the principles

of psychopharmacology as a means of exploring the relationship between panic attacks and the physiological adaptation of the stress response. Klein, starting from his discovery that imipramine was effective in blocking panic attacks, went on to identify anxiety and panic disorder as distinct psychiatric conditions. He discovered that anxiety disorders have a biochemical basis. Based on the knowledge gained, Klein developed the diagnostic criteria for anxiety disorders. Those criterions remain in current use in the *DSM*. Furthering the investigation of the psychophysiology of stress, George Solomon and Rudolf Moos (1963) documented the dysregulation of the immune system as a function of the stress response. It was Solomon and Moos who coined the term 'psychoimmunology'. Later, Ader and Cohen (1975) demonstrated that the immune system could respond to classical conditioning.

Current Status of Psychoneuroimmunology

Vale and his colleagues (2001) focused on understanding the corticotrophin releasing factor (CRF), which has the central role in initiating the pituitary-adrenal response to stress. Pickup et al. (1998), Pickup (2003), and McCance and Huether (2002) give the PNI foundation for type II diabetes.

In 2002 a series of studies were published by Kiecolt-Glaser and her colleagues which explored a range of negative emotions and analyzed the relationship between negative emotions and the impact on the immune system. The main areas explored by Kiecolt-Glaser focused on the effect of anxiety and depression with regard to increased susceptibility to infectious diseases and impaired wound healing. Infectious diseases and impaired wound healing was the focus for the Kiecolt-Glaser research teams because the

immune function in these disorders were more conducive to an experimental design. Kiecolt-Glaser et al. wrote infectious pathogens could be controlled, measured by use of vaccines, and wound healing studies could be performed by use of biopsy techniques. The studies found that the immune system is compromised during times of emotional distress. Studies by other researchers related to wound healing also implicated the involvement of the inflammatory process of the immune function (Kiecolt-Glaser et al., 2002; Yang and Glaser, 2005). Recently, more attention has been placed on the acute inflammatory response of the immune system in response to prolonged anxiety and depression. Part of the acute stress response triggered by anxiety and depression is the body's increased production of proinflammatory molecules called cytokines. The purpose of the inflammatory response is to destroy infected or damaged tissue in preparation for its removal from the body (Rabin, 2005). This is the normal function of the inflammatory response. If however, this process is maintained at a heightened state for a prolonged period of time disease processes can start. The next section provides a discussion of those diseases. Some of the diseases occurring in response to the acute inflammatory response are atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes (Heijnen & Kavelaars, 2005; Pickup, 2003; Pickup & Crook, 1998; Steptoe & Brydon, 2005; Walker et al., 2005). These were the medical diseases investigated in this study. The emotional trigger for the acute inflammatory response investigated in this study were the psychiatric conditions of generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder.

PNI: A Potential Mediator between Psychiatric and Medical Conditions

The PNI process is currently believed to start with the presence of a real or imagined psychological experience of threat to the safety or emotional integrity of the individual self (Bremner, 2002). Rabin (2005) writes this psychological experience presents in the form of fear, anxiety or depression. In response to the perceived threat the hypothalamus releases the corticotrophin releasing factor (CRF), which increases activation of the stress hormone response by the endocrine system. The hypothalamus-pituitary-adrenal axis (HPA) activation leads to the secretion of adrenocorticotropic hormone (ACTH). The secretion of ACTH stimulates the adrenal cortex to secrete the hormone cortisol (McCance & Huether, 2002; Rabin, 2005).

Cortisol is a hormone that affects the functioning of the liver resulting in the increase of the blood sugar level in the blood and the breakdown of body protein in preparation for increased energy output. The catabolism of protein leads to increased amino acids in the blood. In response, the blood pressure elevates and the cardiac output increases. There is also a triaging of physiological functioning by the increased production of cortisol which suppresses the immune system, giving preference to those physiological processes necessary for immediate survival. The immunosuppression is reflected in a decrease in production of antibodies and the decrease in histamine. Histamine is a significant mediator of the inflammatory response that occurs in the disease conditions of atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes (Pickup, 1998; Rabin, 2005).

When the release of cortisol activates the HPA, the branch of the sympathetic nervous system referred to as the sympatho-adrenomedullary axis (SAM axis) is also activated. The SAM axis is responsible for increased secretion of the hormones norepinephrine and epinephrine. These hormones are responsible for the physiological response of rapid breathing, trembling, hypervigilance, and redirection of blood flow to essential organs during times of acute stress. These were the physiological changes documented by Cannon when he used the term 'fight or flight' (Cannon, 1915; Kaye & Lightman, 2005).

Figure 2 depicts the PNI model as it pertains to the relationships between variables of interest in this study. As indicated in the drawing, the model proposes that the psychiatric conditions induce the stress response, which in turn initiates the release of the stress hormones that result in the decrease in histamine. Release of the stress hormones initiates the inflammatory response of the immune system by increasing the release of proinflammatory molecules. This process then leads to the development of the medical disease condition.

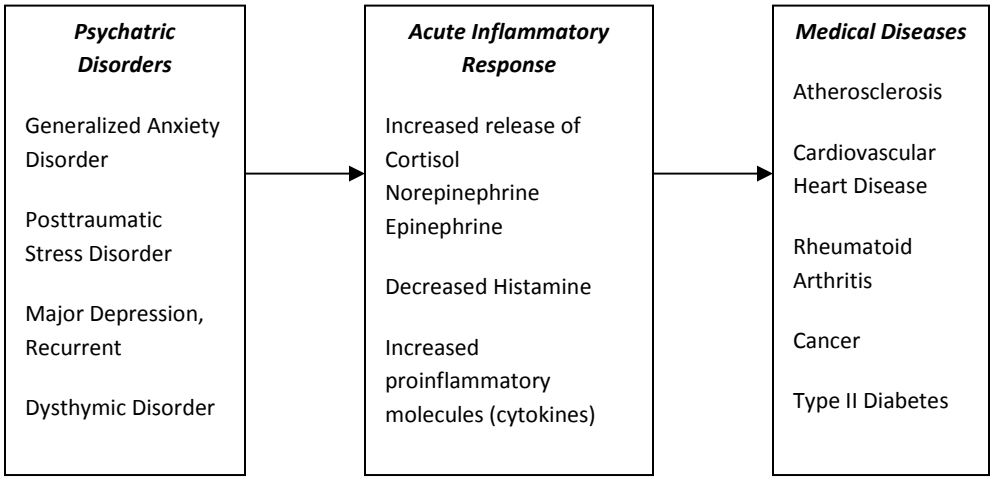

Figure 2. Diagram of the Acute Inflammatory Response:

All of the medical disease variables in the model for this study have a common etiology of being emotionally induced through the increased activation of the sympathetic nervous system, and the heightened endocrine response of increased cortisol, norepinephrine, and epinephrine which results in the dysregulation of the of the immune system (Rabin, 2005). It is theorized that the inflammatory response is related to the development of the medical diseases in the proposed study (Steptoe & Brydon, 2005). Indeed, Rabin writes that one of the reactions of the immune system's inflammatory response to anxiety or depression is the increased production of proinflammatory cytokines that further perpetuates the inflammatory response. As reported earlier, the basic function of the inflammatory response in the body is to destroy damaged, diseased, or infected cells in preparation for removal from the body (Rabin, 2005).

PNI Process for the Medical Diseases

The acute inflammatory response to prolonged psychological states of anxiety or depression is described by the PNI model as the basis of the diseases of atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes. A discussion of these processes follows:

Atherosclerosis: Atherosclerosis is an inflammatory response in the vascular system. The sympathetic nervous system triggers the endocrine system to release hormones that re-direct T-lymphocytes, monocytes, and proinflammatory cytokines to the blood vessels to initiate the wound healing process in response to the microscopic lesion injuries to the endothelium cell lining of the blood vessel walls. The lesions are caused by the shearing effect of high blood pressure. The presence of cortisol, however results in a dysfunction of the endothelial cells. The cells are designed to produce antiplatelet, anticlotting, and fibrinolytic factors to prevent cellular matter passing in the blood stream from adhering to the blood vessel walls and creating a blockage. The functional alteration of the endothelium cells by cortisol allows low-density lipoproteins (LDL) to adhere to the vessel walls and migrate into the lesion areas. When exposed to the oxygenated blood within the vascular wall, the LDL undergoes oxidation forming free radicals that further damage the vessel lining leading to reduced elasticity and hardening of the vessels. Eventually there is blockage leading to heart attack or stroke (Steptoe & Brydon, 2005).

Cardiovascular heart disease: The PNI process for the development of cardiovascular heart disease (CVD) is similar to that of atherosclerosis in that a

functional impairment of the endothelium cells lining the interior walls of the blood vessels occurs. In CVD however, it is the impairment of the endothelial cells that result in the recruitment of and adhesion of monocytes, T-lymphocytes, and platelets to the vulnerable curving areas of the vessel. Cell adhesion molecules (CAMs) mediate the adhesion process when they are up-regulated by the endothelium cells. The pro-inflammatory cytokines on the endothelium wall also attract the adhesion molecules. At the same time macrophages that have the immune function of ingesting and removing cellular debris, promote the atherosclerosis process by producing cytokines and growth factors. These factors aid in the oxidation of LDL-cholesterol and transporting those toxins through the blood vessels that further damages the arterial vessels. When an obstruction occurs in the vessel, there is a decrease in the blood flow that provides nutrients and oxygen to the heart thus resulting in cell damage. As heart muscle cells become damaged, the inflammatory response destroys the damaged cells, thus perpetuating heart damage (Steptoe & Brydon, 2005).

Rheumatoid arthritis: Rheumatoid arthritis results from the dysregulation of the immune system by the increased activation of the (HPA) axis which involves the over production of cortisol. The impaired immune system develops an autoimmune response resulting from the dysregulation of the immune system by cortisol. In this response, the host immune system reacts to its own antigens and initiates an inflammatory response that destroys the synovium cells that comprise the tissue lining the joints. With the destruction of the synovium there is eventual erosion of the joint cartilage, which results in the pain of bone rubbing against bone. Finally, bone resorption occurs, which is the

loss of bone substance. The loss of bone leads to joint deformities associated with rheumatoid arthritis (Heijnen & Kavelaars, 2005).

Cancer: Cancer results from the combination of suppression of the immune system caused by excess cortisol and the impaired ability of the immune system to detect and destroy mutations of host cells that form tumors. In this condition the inflammatory response is not effective in detecting and destroying mutated cells. The effect of the impaired immune response is compounded by the decreased production of NK cells, T-lymphocyte cells, dendritic cells, and antibodies that have anti-cancer properties (Walker et al., 2005).

Type II diabetes: Type II diabetes is a response of the innate immune system mediated by the hypothalamic-pituitary-adrenal (HPA) axis. During the stress response, proinflammatory cytokines that are released by macrophages act on the brain to release corticotrophin-releasing factor (CRF) from the hypothalamus. The CRF initiates an increased production of stress hormones, including cortisol, which suppresses the immune system. Cortisol, with norepinephrine and epinephrine influences the liver to increase insulin resistance to optimize blood sugar levels available for immediate energy output. In the chronic anxiety or depressive state, the on-going condition of hyperglycemia and dysregulation of the immune system can result in the impairment of the insulin secretion by the beta cells of the pancreas, which is the basis for the development of type II diabetes (Pickup, 2003).

Medical science is in the forefront in the treatment of these diseases once the disease process has been initiated. Studies involving psychotherapy to enhance immune

function to resist disease development, is also substantial. The next section will explore the evidence-based support for psychotherapy in lessening the effects of PNI based medical conditions.

PNI Research Using Psychotherapy

Research in PNI suggests a role for psychotherapy as a preventative or ameliorating intervention for some PNI related disease process. Kiecolt-Glaser et al. (1985) were among the first researchers to conduct studies of the effect of behavioral interventions on the immune system. They investigated the meditating effect of relaxation and guided imagery on healthy young and healthy older adults exposed to a vaccine as an immune-challenge. Kiecolt-Glaser and her team found a positive result of a 30% increase in NK cell count in response to a month of relaxation training. In a later study, Kiecolt-Glaser, Glaser, and Strain (1986) investigated the effect of relaxation training on healthy medical students. They found increases in the CD-4 cell count of the students. CD-4 is a complement component on an antibody that helps the antibody to adhere to a bacteria or other pathogen to allow the antibody to destroy it (Rabin, 2005). Subsequent archival studies by Kiecolt-Glaser (1992) regarding the association between psychiatric and medical conditions concluded there is an enhancement of the immune function with the use of psychological interventions, such as relaxation, hypnosis, self-disclosure, and cognitive-behavioral therapy.

It remained unclear, however, precisely how the above referenced enhancements to the immune function translated into discernible health improvements, such as altering the development of the disease or the severity and duration of the disease. What still had

not been explored was the use of these techniques to prevent the development of disease. Colbert (2006) presented the position that the goal of psychotherapy is to move the individual from sympathetic nervous system (SNS) dominance to parasympathetic nervous system (PNS) dominance. Figure 3 is a visual depiction of Colbert's proposition of the goals of psychotherapy with regard to emotional distress.

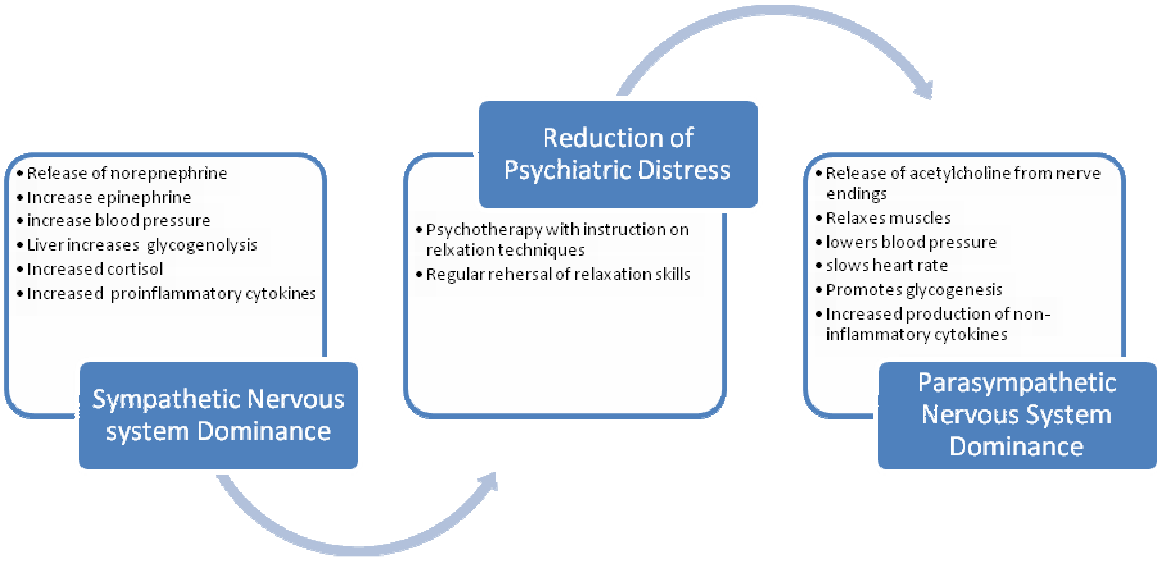

Figure 3. Diagram Depicting Colbert's Physiological Goal of Psychotherapy

PNI Studies linking Psychotherapy to Immune Function

PNI research conducted to study the immune response to psychotherapy has yielded mixed results. There have been a number of studies applying various forms of relaxation techniques, trauma disclosure, and cognitive-behavioral therapy (CBT) interventions to measure change in immune function. Some of the studies were specific to a disease processes while others were designed to assess the status of immune markers.

As an example, Kraaimaat, Brons, Geenen, and Bijlsma (1995) studied patients with rheumatoid arthritis using cognitive-behavioral therapy. The participants in the study were divided into three groups; CBT treatment, occupational therapy, and the control group comprised of patients on the wait-list. The CBT group received 10 sessions that included progressive relaxation, rational thinking, and instruction on strategies for coping with pain. The study found no therapeutic effect on the health status of the CBT group. The laboratory measures of disease activity revealed progressive deterioration actually continued during the treatment for all of the groups.

Conversely, Witvliet, Ludwig, and Vander Laas (2001) studied forgiveness therapy based on the supposition that responses that victims develop toward their offenders not only affects their cognition but also impacts their emotional and physical health. Witvliet and colleagues studied 71 participants; 35 females and 36 males. The researchers found that forgiving thoughts prompted a greater sense of control and decreased the physiological stress response as measured by electromyogram, skin conductance, blood pressure, and heart rate, all of which reflect the transition from sympathetic nervous system dominance to the parasympathetic nervous system dominance, as posited by Colbert (2007).

Petrie, Booth, Pennebaker, Davidson, and Thomas (1995) investigated trauma disclosure and its influence on the immune response. In their study forty medical students with trauma histories who also tested negative for the hepatitis B antibodies were randomly assigned to either a treatment group or control group. The hepatitis B vaccine

was used as the immune challenge. The participants in the trauma disclosure group showed significantly higher antibody levels against hepatitis B.

Sherman, Carlson, McCubbing, and Wilson (1997) investigated immune enhancement by use of progressive muscle relaxation. In this study 21 participants suffering from conditions of chronic pain alternated between relaxation exercises and rest for equal periods of time. Salivary secretion of immunoglobulin A was measured in addition to level of mood, pain, and tension before and after the exercise. Those patients receiving relaxation training had significant increases in immunoglobulin A in the saliva specimens.

Pawlow and Jones (2002) used abbreviated progressive relaxation training techniques with 46 participants in the treatment group and 15 participants in the control group. The researchers found the brief relaxation exercises led to significantly lower levels of heart rate, state anxiety, perceived stress, and salivary cortisol levels reflecting improved immune function. Also using relaxation techniques Surwit, McCaskill, Ross, and Feingloss (1991) investigated relaxation training with individuals diagnosed with Type II diabetes. In the study 38 participants were divided into two groups; group 1 received relaxation training with diabetes education and group 2 received diabetes education alone. Pre/post treatment measures were taken of the metabolic functioning of the participants. The treatment program was for eight weeks with two post treatment follow-up assessments. In general, relaxation training to significant improvement on any of the measures of glycemic control, such as glucose tolerance, glucose fasting level, or glycohemoglobin. However, participants who scored high on trait anxiety and

neuroticism on the pretest psychological assessment instruments, and showed a large initial glycemic response to epinephrine at the pre-treatment stage, showed greater improvements in glucose tolerance after relaxation training.

A number of researchers investigated the use of guided imagery on the functioning of the immune system, thus adding a cognitive component to the relaxation technique. Cupal, Brewer, and Britton (2001) explored the use of guided imagery plus relaxation techniques with 30 participants recovering from knee surgery and experiencing re-injury anxiety. The treatment group displayed greater knee strength and decrease in re-injury anxiety and pain compared to the control group. Gruber, Hall, and Hersh (1988) studied relaxation and guided imagery therapy with female cancer patients. Serum blood samples revealed that immune cell function increased. In a later study, Gruber, Hersh, Hall, Waletzky, Kunz, and Weiss (1993) conducted an 18 month study of cancer patients using guided imagery and relaxation. The results revealed an increase in NK cell activity and lymphocyte responsiveness. Donaldson (2000) used mental visualization on 20 medical students who had an infectious disease diagnosis. The researchers reported white blood cell counts were significantly increased in the treatment group. Hall, Papas, Tosi, and Olness (1996) researched the efficacy of mental imagery techniques on enhancing immune function. The research began with the hypothesis that mental imagery would augment the effect of relaxation techniques. The immune function the researchers used was neutrophil adherence. The neutrophil immune cell is necessary for the destruction of organisms, such as disease bearing bacteria that invade the body. Adherence to the foreign organism is vital for the destructive process. This study involved fifteen

participants. The researchers found the reverse of what they expected. The group that had relaxation techniques alone had a greater increase in neutrophil adherence compared to the group involved in the cognitive process of guided imagery and relaxation training.

The use of conversational psychotherapy and its effect on the immune system was explored by Van der Pompe, Dulvenvoorden, Antoni, Visser, and Heijnen (1997). In a short-term, 13 week group psychotherapy treatment with women diagnosed with breast cancer, the researchers assessed the response of the immune system. Van der Pompe et al. found lower levels of plasma cortisol among other improved immune markers in the treatment group. It was noted that the improvement was only found in individuals who already had relatively high endocrine and immune baseline levels. In another study involving the effect of cognitive-hypnotic techniques on skin reactivity to histamine, Laidlaw, Booth, and Large (1996) investigated the acute inflammatory response of the immune system. Thirty-eight participants were involved in the study. The researchers found 32 of the 38 participants had a significant decrease in weal size as a result of the therapy treatment. A weal is a skin reaction to an allergen characterized by red, raised areas on the skin. This study assessed this reaction to investigate the histamine function of the immune system. Histamine is a major hormone that modulates the production of proinflammatory cytokines. They noted that feelings of irritability, tension, and high blood pressure readings were associated with less weal size change. Those participants who were peaceful and had lower blood pressure readings had a smaller weal inflammatory response.

In another study involving the inflammatory response, Lutgendorf et al. (2000) recruited 50 participants, 28 males and 22 females who were pre-trained in relaxation using an imagery-based relaxation tape. The researchers used capsaicin as the immune challenge. Capsaicin is an active ingredient in chili peppers. Lutgendorf and his colleagues found a significantly smaller flare response among the relaxation treatment group.

Several observations were made in the review of the research involving the application of psychotherapeutic methods to assess its influence on the immune system. Psychotherapy that has a direct focus on attaining relaxation appeared most effective at affecting the immune response on a consistent basis. The influences of the immune parameters that underlie many of the medical disease processes are significantly affected. The studies also demonstrated that the immune response can be intentionally and specifically moderated by psychotherapy. The findings also demonstrated that once the disease process had been initiated, modulation of the immune system by psychotherapy had no effect on the progression of the disease. These studies indicate that the use of intervention techniques, such as psychotherapy, have been shown to have a positive impact on the immune system. In turn this improved functioning could be instrumental in lessening the likelihood that a person would develop medical diseases related to poor functioning of the immune system and the inflammatory response.

Influence of Biological and Personal Variables Related to the Inflammatory Based Medical Diseases

In addition to the psychiatric and medical diseases discussed in this chapter, previous researchers have identified personal factors such as family history of the psychiatric disorder, family history of the medical disorder, gender, and race as important to understanding the possible influence of genetic predisposition in the formation of comorbid conditions (Baumeister et al., 2005; Kiecolt-Glaser et al. 2002; Moussavi et al., 2007). Kiecolt-Glaser et al. (2002) also suggested the importance of including chemical dependence history in studies of comorbid occurrences of psychiatric and medical conditions because of its negative effect on both mental and physical health. Pinel (2006) recently reported the prevalence of chemical dependence among individuals suffering from comorbid conditions.

In considering race as a factor related to comorbid psychiatric and medical conditions, Cater, Sbrocco, and Carter (1996) clarified the distinction between race and ethnicity and the appropriate use of these terms in research. Carter and colleagues defined ethnicity as the shared culture and lifestyle of a people. Race relates to the hereditary traits of a person that involves the passing along of genes through reproduction. Carter's definition of race was used for this study. The other biological factors that were included in the present study were family history of the diagnosed psychiatric disorder and family history of the diagnosed medical disorder.

The Diagnostic and Statistical Manual of Mental Disorders (*DSM-IV*) report familial associations related to the trait of anxiety; but studies regarding the etiology of generalized anxiety disorder as an inherited predisposition are not consistent. Posttraumatic stress disorder is a condition to which a person can have a genetic predisposition for developing when exposed to trauma, but research regarding this is similarly inconclusive (Bremner, 2002). The psychiatric category of depression has strong support for a genetic link to predispositions for an individual to develop the disorder. The DSM-IV reports major depressive disorder is 1.5 to 3 times more common among first degree biological relatives. Major depression is also twice as common among adult females as males (*DSM*). The DSM-IV also reports that adult females are two to three times more likely to develop dysthymic disorder. Chemical dependence is a factor cited in all of the above psychiatric conditions as a factor to be considered when conducting a psychiatric assessment because of the direct effect of toxicity or the residual effects of drug and/or alcohol addiction on mental health functioning. The chronic toxicity from drug and alcohol addiction also has negative physiological effects that suppress the immune system (Pinel, 2006).

When viewing the diseases investigated in this study from the perspective of possible hereditary influences, Taylor and colleagues (2005) used a sequential logistic model to determine risk factors for the development of atherosclerosis and cardiovascular heart disease. The researchers found that male gender and European American descent were among the best-fit hereditary markers for prediction of disease development.

Hughes et al. (2006) explored genetic factors involved in the development of rheumatoid arthritis. Hughes and colleagues found that African Americans carry the nucleotide for rheumatoid arthritis more frequently than European Americans. Other studies focused on the relationship between family ties and the development of cancer. Schlehe and colleagues (2008) studied hereditary factors related to the development of breast and ovarian cancer in women. They found a 60% to 80% lifetime risk for the development of breast cancer and a 20% to 40% risk for the development of ovarian cancer among family members. Wolski and his colleagues (2004) investigated prostate cancer and found a 10% higher risk among male family members.

O'Rahilly, Barroso, and Wareham (2005) investigated gene variants and the development of type II diabetes. The researchers concluded there are a few gene variants that have been identified as being related but they reported more research is necessary to construct the genetic information necessary to be helpful for prevention and treatment.

Although it was beyond the scope of the present research to address the contribution of genetics to the development of psychiatric and medical comorbid conditions, it is valuable to assess the frequency of occurrence and relationship of the demographic and biological variables on the comorbid pairs that are formed. For this reason the present study used the variables of age of the first documented psychiatric diagnosis, age of the first documented medical disease diagnosis, gender, race, absence or presence of chemical dependence diagnosis, family history of a similar psychiatric diagnosis, and family history of a similar medical diagnosis as predictor variables in this study.

To investigate psychiatric predictors in medical disease comorbidity, an archival design was employed for this study. Previous researchers selecting this method have used internet searches to access medical databases, reviewed studies published in journals, or accessed medical records. The following section will provide a discussion on each of these methodological approaches.

Review of Research Methodologies

The research methodological approaches used to access information about large populations are archival research, internet medical website databases, and surveys. Archival research has contributed much to our gaining a sense of the larger scheme of the process of emotionally induced medical disorders. An example of a quantitative archival method was accomplished in a monumental study undertaken by Kiecolt-Glaser and colleagues (2002). The review included all of the PNI studies published in the journal Psychosomatic since the journal's inception in 1939 that were related to the criteria for the current study. The inclusion criterion was that the studies had to include immunoassays that measured the biochemical markers of the immune system. If the study was an in vivo study a challenge would had to have been used in the study. A challenge refers to controlled exposure to a pathogen such as a vaccine. The research articles also had to involve an immune-based disease that was diagnosed prior to the diagnosis of the medical illness. After selecting the relevant studies, Kiecolt-Glaser and her team found they had accessed 66% of all published research in the PNI field; this included what had been published in other similar journals. This study was significant because the

researchers attempted to understand the predictive relationship among the psychiatric and medical diagnoses. They found that immune function impairment covaried with the psychiatric disorders of anxiety and depression. Two major weaknesses were reported by the researchers. The first was the lack of demographic and pre-clinical information to provide clarity to the interpretation of the findings. The second limitation of the study was the broad range of research methods used among the different individual studies that were accessed (Kiecolt-Glaser et al., 2002).

Baumeister, Kalke, and Harter (2005) provided an example of a quantitative internet research method. The researchers conducted an internet-based search using the Medline website. The researchers accessed all of the English and German language literature published up to 2002 on studies involving psychiatric and medical disease comorbidity. The inclusion criterion used by Baumeister and his colleagues for including an article in their study were that the study had to be empirical in nature, the participants had to be 21 years old or older, and the participants had to have one of the six targeted medical diseases. The researchers found 481 studies, but after further screening 45 studies were accepted for the study. The authors did not discuss the number of cases required to meet statistical power in their study. In discussing the strengths and weaknesses of the methodology used, Baumeister et al. reported several factors that limited the generalizability of their findings. First that database was too small to draw conclusions about specific populations. Second, the heterogeneous methods used by the different original researchers made simple summaries of the findings very difficult, and some of the studies used the patient's self report for medical comorbidities, which led to

questionable validity of the results. In addition, when psychiatric comorbidity was assessed, some of the studies used screening instruments, which did not provide a definite psychiatric diagnosis.

Wells, Rogers, Burnam, Greenfield, and Ware (1991) utilized a parallel archival research method with a purposive sampling approach. Wells et al. accessed the clinical records of 1,152 adults in outpatient treatment programs. The researchers also included survey interviews of the participants that were conducted by trained clinicians. The focus of the study was psychiatric and medical comorbidity. The patients in their study were diagnosed with depression as the psychiatric disorder. The medical conditions included coronary artery disease, hypertension, diabetes, gastrointestinal disorder, chronic back problems, chronic lung problems, angina, and arthritis. The researchers noted difficulty with the survey component of the study because of the side-effects of the psychiatric medication with some of the patients. The researchers found that patients with clinical depression had significantly higher occurrences of hypertension and arthritis than non-depressed patients (Wells et al., 1991).

Boscarino (1997) conducted an archival study investigating the occurrence of posttraumatic stress disorder among individuals exposed to severe stress, their rate of medical problems and their use of the medical system. Boscarino reviewed the medical histories of 1,399 male Vietnam veterans who had combat exposure. A 20 year time period was used with the selection of veterans who entered the military between 1965 and 1971. An additional participant criterion was that each participant had a pay grade level of sergeant or lower. Boscarino also included an interview component and self-report

measures with his study. There were some reported difficulties with the self reporting assessments. The issue was related to the self report of symptoms and actual diagnoses of the participants in the study. Boscarino (1997) found a statistically significant link between severe emotional stress exposure that was to the presence of PTSD and medical disease.

Moussavi et al. (2007) used a mixed method survey approach in their research design. The focus of the study was the comorbidity of depression with angina, arthritis, asthma, or diabetes. The World Health Organization (WHO) sponsored the research but the organization was not involved the research design or the interpretation of the data obtained. The WHO Survey was used to collect information from 245, 404 individuals aged 21 years old or older from 60 different countries. Study participants were drawn from 26 European countries, 15 African countries, 6 from the Americas, 4 from the eastern Mediterranean, 5 from Southeast Asia, and 4 from the Pacific region. In discussing the weaknesses of the study, the researchers cited the possible problem of participants from some countries under-reporting depression because of socio-cultural factors. The researchers also reported not including questions regarding the onset and duration of illness. Despite the limitations noted by the researchers, the major finding of the study concluded that depression, in combination with any medical disease results in a greater decrement in health when compared to the medical disease alone (Moussavi, 2007).

The methodology selected for the present study was a quantitative, parallel archival design because it is the most efficient and cost effective among the options

explored (Baumeister, 2005). A purposive stratified sampling schema was used. The research problem in this study was focused on analyzing the relationship between the psychiatric and medical disease comorbid conditions. The perspective of the research posited using the psychiatric diagnosis as a predictor of the type of medical disease for the comorbid pair. The study also considered some of the biological and pre-clinical information documented for each case that could influence disease development. Being mindful of barriers and issues reported by other researchers, this study accessed and reviewed the electronic medical records of patients treated in a multi-hospital healthcare system that has uniformity in patient assessment protocols and full documentation of the medical and psychiatric diagnoses and treatment histories. The full research design for the present study will be presented in chapter three.

Summary

The literature review for this study was generated by accessing peer reviewed journals and articles and academic publications information sources. The literature reviewed provided support for the PNI model in relation to psychiatric and medical disease comorbidity. There was a gap in the literature regarding the investigation of psychiatric disorders as predictors of medical diseases. The present study investigated the psychiatric disorders of generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder as predictors of the medical diseases that result from the inflammatory response of the immune system. The medical diseases investigated in this study were atherosclerosis, cardiovascular heart disease, rheumatoid

arthritis, cancer, and type II diabetes. The research questions addressed in the present study were:

Question 1**:** For individuals with comorbid psychiatric disorder and medical disease diagnoses, what is the association between the first type of psychiatric diagnosis and the first medical diagnosis?

Question 2**:** Among individuals with comorbid psychiatric and medical disease diagnoses, to what degree does the presence of a psychiatric disorder and the demographic variables of gender, race, family psychiatric history, family medical history, and chemical dependence history significantly influence the presence of the medical disorders atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes in the comorbid pairs?

Question 3: To what degree does the presence of a psychiatric disorder as the first diagnosis and the diagnosed psychiatric disorder predict the medical disorders for the comorbid pairs included in the study?

Chapter 3: Research Method

Introduction

Chapter 2 discussed the scientific support for the psychoneuroimmunology (PNI) model as that model pertains to the current study. The PNI model was established by studies using bioimmunoassays, empirical, and experimental methods. The clinical findings of these studies revealed the dysregulation of the immune system that occurs in response to emotional conditions (Cannon, 1915; Da Costa, 1871; Kaye & Lightman, 2005; Kiecolt-Glaser, 1992; Rabin, 2005; Steptoe & Brydon, 2005; Walker et al., 2005). The purpose of this study was to determine if certain psychiatric disorders could be used to predict the presence of specific inflammatory based immune diseases. The independent predictor variables were generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder. The dependent medical disorders were atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes.

The present chapter will focus on the methodology used in the current study. The topics that will be covered in this chapter include, Research Approach, Archival Research Methods, Research Design, Sample Selection, Hypotheses and Analysis, Data Analysis, Materials and Instruments, and Participant and Record Confidentiality. The chapter will conclude with a summary.

Archival Research Methods

An archival methodological scheme was employed as the research methodology for this study. As examples of previous research of this type, Kiecolt-Glaser et al. (2002)

conducted an archival study of a single journal since the journal's inception. This involved 62 years of published studies in the area of PNI. Kiecolt-Glaser and colleagues reported methodological weakness of their study, citing broad heterogeneity in the research designs and in the interpretations by the original authors of the studies as being limiting factors of their research. The Kiecolt-Glaser study also found a lack of pre-clinical and biological information that potentially could assist in the interpretation of the data to be a limitation of their study.

Baumeister et al. (2005) conducted an archival study using an internet medical database. For the criteria specified in their project the number of cases they could accept was too small to draw conclusions about specific populations. Also, as with Keicolt-Glaser, the researchers found too broad of a difference in the methodologies used by the original researchers and the differences in reporting the findings by the original researchers was problematic. Baumeister and colleagues also questioned the validity of some of the studies because of the reliance on participant self-report for the psychiatric and/or medical diagnoses rather than having clinical documentation.

Wells, Rogers, Burnam, Greenfield, and Ware (1991) and Boscarino (1997) used a parallel archival research methodology. The focus of the study was comorbidity among depressed patients and how treatment varies across major types of clinical settings. Wells and colleagues reported problems with the survey component of their study, which required the active participation of the participants. Impaired engagement due to medication side-effects was cited.

Boscarino (1997) investigated the development of posttraumatic stress disorder and medical comorbidity among individuals with exposure to severe stress. Boscarino found a weakness of his study to be the self-report component. He reported there were issues regarding the self report of symptoms and the diagnoses in a number of the cases.

In reviewing the methodological approaches used by earlier researchers, it appeared that the quantitative archival approach had the greatest benefit for accessing a large number of cases while being cost efficient (Boscarino, 1997; Lehrer, 2002; Kiecolt-Glaser, 2002). There were several benefits of the archival design for this study. The use of electronic medical records allowed 24 hours a day access to the documents, rather than confining the researcher to the set business hours of medical record departments. This study design also eliminated the need for adequate accommodations, such as office space, at the various sites. The electronic medical records allowed the researcher access to records from a broad geographic area in the State of Michigan without having to travel to the sites. The records could be accessed from a single office site, thereby saving the cost and time associated with travel. The use of electronic medical records of a large healthcare system provided the required clinical documentation of both the psychiatric and the medical disease diagnoses. This was the information that was reported as lacking by previous researchers. In addition to uniformity in clinical documentation, these electronic medical records also contained the pre-clinical and other biological information that was identified as important to understanding possible demographic influences on psychiatric and medical disease comorbidity development (Kiecolt-Glaser et al., 2002).

This is an archival quantitative study specifically using information from medical records maintained by a multihospital healthcare system. The archival data was originally collected in accordance with the standardized documentation protocol of a single healthcare system. There were also pre-established confidentiality protections for the patients (HFHS Clinical Documentation Policy and Procedures, 1997 revision).

The archival data from a five year cycle was selected to capture the most current health status information in the records reviewed for this study. Wallis, Borgman, Mayernik, and Pepe (2008) stated that in general, the life cycle for data in the sciences is determined by each stage of a process in which information transitions from one or more persons with similar domains of knowledge and training to the next. In clinical settings the cycle may be characterized as a patient transitioning from one level of care or phase of treatment to another. Wallis et al. reported that in research, only those studies using multi-year datasets from a single location have established archival practices for maintaining current relevance of their data. The hospital system where this study was conducted met the requirements specified by Wallis.

Lyon (2003) discussed the 'scholarly knowledge cycle' with regard to secondary information. According to the article, the advent of technology and the ability to store and transfer data causes certain fields, medicine for instance, to become data rich for quantitative sciences (Lyon, 2003). Lyons wrote that the scholarly knowledge cycle extends beyond the concept of information cycles. For this to apply, Lyon wrote, a number of assumptions must be satisfied. The assumptions are a) that the integrity of the original data is maintained, b) there is a shared understanding of the concept of

provenance, c) the original dataset is adequately described using a metadata description framework based on agreed standards, d) a common ontology for the domain is understood, e) each dataset and derived data and information are uniquely identified, and f) there is an open linking technology applied to the original dataset and the derived data and information.

The archival data collected for this study was from a network of eleven major hospitals which are administrated under a single corporate body that is connected to a shared electronic medical record keeping system. All of the clinical records meeting the inclusion criterion for clinically documented psychiatric and medical disease diagnoses for this study were drawn from the January 2005 through September 2010 time period.

Study Variables

The intent of this study was to determine if certain psychiatric disorders predicted the presence of certain medical disorders. The psychiatric disorders, the biological, and the demographic factors were the independent/predictor variables. The psychiatric disorders were generalized anxiety disorder and posttraumatic stress disorder, major depression recurrent, and dysthymic disorder. The medical disorders were the dependent variables. The medical disorders were: atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II Diabetes. The biological and demographic factors were, age of the first documented psychiatric diagnosis, age of the first documented medical disease diagnosis, gender, race, absence or presence of a chemical dependence diagnosis, family history of a similar psychiatric diagnosis, and family history of a similar medical diagnosis. This study also analyzed the whether the

biological and demographic variables were related to the types of co-morbid pairs in the study.

To test the hypotheses for the research questions, data analyses consisted of descriptive cross tabulation to describe the observed frequencies of the personal and biological characteristics of cases included in the study, the chi-square tests of independence were used to analyze the patterns of the comorbid pairings, and multinomial logistic regression was used to determine the degree to which the independent variables (psychiatric disorders, biological factors, and demographic variables) predicted the type of medical disease.

Setting and Sample Selection

The source for the clinical cases in this study was the electronic medical records of adult patients treated in the Behavioral Services Division of a healthcare system comprised of a network of hospitals and clinics located in southeastern Michigan. As a member of the clinical staff this researcher had the training and security clearance to access the identified cases within the secured database website which housed the data. The initial identification of the cases was made by the designated Institutional Review Board (IRB) manager of the electronic medical records. The ICD-9 codes for the medical diseases and the DSM-IV codes for the psychiatric disorders were used to conduct the data base search of the records meeting the inclusion criterion. The specific criterion was that all of the cases must have at least one of the designated psychiatric diagnoses plus at least one of the designated medical disease diagnoses (Valderas et al., 2009). A minimum of 632 cases were required to meet the sample size recommended by Hsieh, Bloch, and

Larsen (1998). There was an increase in the sample size, as suggested by Demidenko (2008) to accommodate the possible loss of cases because of missing data. The sample size minimum was increased to 800 cases. A five year archival data population provided the source for the cases included in this study (Lyon, 2003; Wallis et al, 2008).

Achieving cultural diversity was a consideration for the cases sampled in this study. Cultural diversity was presumed in this study by selecting cases from the various hospital and clinic locations in the State of Michigan with naturally occurring population differences. The healthcare system consists of eleven major hospitals located throughout three major counties in the state, Wayne, Oakland, and Macomb. According to the 2008 state census (www.Michigan.gov), Wayne County has a population of 1,949,929 adults and represents 19.49% of the population of the state. Oakland County has a population of 1,202,174 adults and represents 12.02% of the state population. Macomb County has a population of 830,663 adult individuals representing 8.3% of the population. The total population in the counties where the health care system is the dominant healthcare provider is 3,982,766 or 39.81% of the total state population. The U.S. Census Bureau's 2008 estimate for the state of Michigan population is 10,003,422 residents. Among these residents 50.8% were female, 81.2% were European American, 14.2% were African American, 2.4% were Asian American, and 4.1% were Hispanic American. The electronic medical records for this study were drawn from this tri-county population.

A purposive stratified sampling scheme was chosen to select cases of the comorbid pairs for the study. As described by Trochim (2006), the purposive sampling approach involves accessing a particular subset of individuals through the rejection of

individuals who do not fit a particular profile. In the present study, the selection criterion of comorbidity of at least one of the psychiatric diagnoses plus at least one of the identified medical diagnoses was used. Trochim stated the stratified schema references the fact that before the sampling is done, the participants are divided into stratums or categories according to characteristics of importance to the research. An example of a stratum in the present study was the category of psychiatric disorders. From those records with psychiatric disorders, a further selection was made to identify those records that also had at least one of the identified medical diseases. The cases were selected from each of the stratums. Trochim wrote the stratified sampling method is as good or better than random sampling.

To accomplish the case selection, the electronic medical records manager at the healthcare facility identified all clinical cases meeting the inclusion criterion of having at least one of the psychiatric diagnoses plus at least one of the medical disease diagnoses by using the DSM-IV psychiatric codes and f the ICD-9 medical codes. The list of medical record numbers (MRN) for all of the identified cases were emailed to the researcher to a secured computer at the health care facility. The medical record numbers were used to access the cases within the secured system website that housed the records.

Statistical Power and Sample Size

In discussing statistical power, Burkholder (2010) emphasized the importance of the alpha level and effect size in the calculation of the sample size needed for a study. Burkholder presented a number of approaches that could be used to calculate the sample size. In order to estimate the sample size the statistical power, alpha level, and effect size

must be determined. The conventionally accepted statistical power of .80 and alpha level of .05 suggested by Burkholder (2010) was used for this study. Determining the effect size requires statistical computation. The first method presented by Burkholder was Cohen's d which requires a calculation of averages and use of a standard deviation value in the computational formula. Because the current study is categorical, and therefore non-parametric, Cohen's d could not be used.

Hsieh, Bloch, and Larsen (1998) wrote that determining sample size in logistic regression generally involves a complicated formula because of the non-linearity of this statistical test. Whittemore (1981) proposed a formula based upon the Wald's test to address this problem. Multinomial logistic regression provides for the prediction of a discrete outcome, such as group membership, from a set of variables (Demidenko, 2008). The Wald's test yields the odds ratio for the success or failure of that membership with the projection of how many exposures will need to occur to make the determination or prediction. With a re-interpretation of the term 'exposures,' Whittemore (1981) applied the formula of the Wald's test to determine sample size in epidemiological studies.

Hsieh (1989) simplified and extended the formula presented by Whittemore for the purpose of a more general use (Hsieh et al., 1998). To this end, Hsieh (1989) constructed a sample size table for multinomial logistic regression. In this table, the event proportion is equated to the number of independent variables in a study and the odds ratio is equated to the statistical power which is the odds or probability of rejecting the null hypothesis when it is false given the number of dependent variables. The intercept of the

number of independent variables in a study and the statistical power (odds ratio) for the study reveals the sample size required.

The present study used table II of the Sample Size Tables for logistic Regression developed by Hsieh. Given the present study has an alpha of .05 for a two-tailed test with P = 0 - 04 (four psychiatric diagnoses as independent variables) and odds ratio of 0 – 6 (five medical diseases as the dependent variables), and .80 statistical power, 632 medical records were required to obtain an adequate sample size.

In a review of sample size tables and statistical programs to determine sample size for logistic regression, Demidenko (2008) reports tables based on the Wald's test provide a good estimate of sample size but adjustments may be necessary given the nature of the study. To ensure adequate sample size with sufficient statistical power for this study, and adjusting for possible cases that could not be used because of missing data, an adjustment was made by the researcher to increase the minimum cases required to 800 cases for the study.

Data Analysis

Data Collection Procedure

The first step in the data collection procedure was to identify the appropriate DSM-IV codes for the psychiatric disorders and the ICD-9 codes for the medical diseases included in the study. Using these codes, the Participant Data Search Sheet (see Appendix A) was constructed. This Participant Data Search Sheet was given to the medical record staff designated by the IRB of the healthcare system who conducted a data based search of the electronic medical record system for the cases meeting the

inclusion criteria of the study. The medical record number (MRN) of each identified record was forwarded to the secured office computer of the researcher. The researcher used the MRN to access the individual records in the medical records system. The researcher accessed the demographics section and the documents section of the medical record to obtain the clinical data needed for the study. The documents included the New Patient Psychiatric Consultation and Evaluation, Patient History and Physical Examination, Intake Assessment and Evaluation. The Data Collection Sheet was used to record the clinical data that was coded using a pre-established data coding system (see Appendix B). The cases were numerically listed on the data collection sheet for later identification. The MRN was temporarily used for tracking purposes during data collection and analysis. The data collection process was a pencil and paper recording of coded data. The coded clinical and demographic data were entered onto the SPSS data file created on the home office computer of the researcher. The office computer of the researcher at the healthcare facility did not have SPSS software. The SPSS data file used by the researcher only contained encrypted data codes. The statistical analysis was completed using SPSS.

Hypotheses and Analysis

Research Question 1

Question 1. For individuals with a comorbid psychiatric disorder and medical disease diagnoses, what is the association between the first type of psychiatric diagnosis and the first medical diagnosis?

Null hypothesis 1. For individuals with comorbid psychiatric disorder and medical disease diagnoses, there is no statistically significant association between the first type of psychiatric diagnosis and the first medical diagnosis.

Alternate hypothesis 1. For individuals with comorbid psychiatric and medical diagnoses, there is a statistically significant association between the first type of psychiatric diagnosis and the first type of medical diagnosis.

The chi-square test for independence was the statistical analysis used to test the null hypothesis for the first research question. This statistic is used to identify the likelihood of a particular outcome occurring by chance by comparing observed frequencies of the variable compared to expected frequencies for the variable (Gravetter & Wallnau, 2007). This statistical procedure was appropriate for testing the null hypothesis because the researcher was interested in knowing if the presence of a given psychiatric disorder was related to the presence of a specific medical disease.

Research Question 2

Question 2. Among individuals with comorbid psychiatric and medical disease diagnoses, to what degree does the presence of a psychiatric disorder and the demographic variables (gender, race, family psychiatric history, family medical history, and chemical dependence history) significantly predict the presence of the medical disorders atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes in the comorbid pairs?

Null hypothesis 2. The psychiatric disorders (generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder) and the demographic variables (gender, race, family psychiatric history, family medical history, and chemical dependence history) are not statistically significant predictors of the presence of medical disorders.

Alternate hypothesis 2. The psychiatric disorders (generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder) and demographic variables (gender, race, family psychiatric history, family medical history, and chemical dependence history) are statistically significant predictors of the medical disorders atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes.

Multinomial logistic regression was used to test the null hypothesis for the second research question. This statistical procedure predicts the probability of an individual being grouped into one category of a variable compared to being grouped in another (Mertler & Vannatta, 2005). In this study the basis of comparison was the likelihood that a person would be diagnosed in one category of the dependent variable, medical disorder, compared to another category; therefore multinomial regression was the appropriate statistical procedure for testing the null hypothesis. Logistic regression also offers the following advantages: the assumptions of linearity, normality and homogeneity of variance are not assumed; negative values are not produced; and logistic regression can consider and analyze all types of dependent and predictor variables (Mertler & Vannatta, 2005).

Research Question 3

Question 3: To what degree does the presence of a psychiatric disorder as the first diagnosis and the diagnosed psychiatric disorder predict the medical disorders for the comorbid pairs included in the study?

Null hypothesis 3: The presence of a psychiatric disorder as the first diagnosis and the diagnosed psychiatric disorder are not statistically significant predictors of the medical disorders for the comorbid pairs included in this study.

Alternate hypothesis 3: The presence of a psychiatric disorder as the first diagnosis and the diagnosed psychiatric disorder are statistically significant predictors of the medical disorders for the comorbid pairs included in the study.

Multinomial logistic regression was the statistical procedure used to test the full model of psychiatric disorders being related to the presence of the immune based inflammatory diseases in this study. This was the appropriate statistic to use because this statistic can analyze categorical predictor variables (Peng, Lee, & Ingersoll, 2002). In interpreting the results in logistic regression the analysis included information on the overall evaluation of the logistic model, the Wald statistic for the individual predictors, and an assessment of the predictor probabilities (Peng et al., 2002).

Participant/Record Confidentiality

The medical records that were accessed were contained in a secured system of the healthcare network. A preset coding system (see Appendix B) was established so that information from the medical records could be entered on a data collection sheet using only the codes. No identifiable patient information was extracted from the secured

system. This procedure satisfied the Protected Healthcare Information (PHI) concern. Regarding the concern of patient consent, the Health and Human Services Policy for the Protection of Human Research Subjects states:

> Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publically available or if the information is recorded by the investigator in such a manner that the subjects cannot be identified, directly or through identifiers linked to the subject… there is an exemption from having to obtain a consent from the patients. (Health and Human Services Policy for the Protection of Human Research Subjects, section 46.117 [4])

The APA ethical standard 8.05 part (b) also states there is an exemption from the requirement of obtaining informed consent in the case of archival research. Approval by the Institutional Review Board (IRB) of Walden University and the Institutional Review Board of the healthcare system was not exempted. Approval to conduct the research was obtained from Walden University (IRB # 09-13-10-0358167) and Henry Ford Health System (IRB #6403).

Maintaining confidentiality of the patients' Protected Healthcare Information (PHI) is of paramount importance. The cases were viewed in the secured system of record system. The data from the cases were de-identified by use of a pre-established coding system. Only the codes were transferred to a separate data collection sheet for the use for entering the data and conducting the statistical analysis using SPSS programs. No identifiable patient information left the secured system of the hospital.

The Institutional Review Board of Walden University has published a document called The IRB Guide to Archival Research (Electronically retrieved from Walden University Research Center, December 23, 2009). The guide articulates the role of the university to protect all who have made a significant contribution to the creation of the records. It also serves to protect individuals who may potentially be impacted by the results of the research. The major sections of the archival research IRB application are: Project Information, General Description of the Proposed Research, Community Research Stakeholders and Partners, Potential Risks and Benefits, Potential Conflicts of Interest, Final Checklist and Electronic Signatures, and Data Confidentiality. The Walden University IRB does not require information regarding Data Collection Tools, Description of Research Participants, or Informed Consent for archival studies.

Summary

This chapter discussed the proposed research design, the criterion to be used for sample selection and sampling method proposed. This chapter also discussed the materials needed for the study and the statistical methods that were used to analyze the data. This chapter concluded with for the procedures used for protecting participant/medical record confidentiality as well as compliance with Walden University's Institutional Review Board and the Institutional Review Board of the healthcare system.

Chapter 4 will present the data, data analysis, and interpretation of the results of the data analyses. The chapter will discuss the hypotheses testing procedures and include descriptive tables as helpful for the discussion. Chapter 5 will provide an overview of

why the study was conducted, review the research questions, and present a summary of the findings of the analysis. Chapter 5 will conclude with a presentation of the implications for social change and recommendations for action as a result of the findings of the study.

Chapter 4: Results

Introduction

This study investigated the degree to which four psychiatric disorders predict the presence of five medical diseases. The predictor variables in the study were psychiatric disorders, demographic variables, and biological factors. The specific psychiatric disorders investigated included generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder. The demographic variables were age, race, and gender. The biological factors included in the study were family history of the psychiatric disorders, family history of the medical disorders, and individual history of chemical dependence. The medical, immune-based inflammatory diseases served as the dependent variables. The medical diseases investigated in the study were atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes.

This chapter provides a description and summary of the data collected in the study. The research method consisted of a parallel archival design (Trochim, 2006). Data were collected from electronic medical records of a large healthcare system. A purposive stratified sampling schema was used to select the cases. A two-tailed alpha level of .05 and statistical power of .80 was accepted as the criteria for judging the significance of the statistical analyses performed for this study. The Sample Size for Logistic Regression Table published by Hsieh, Bloch, and Larsen (1998) was used to determine the minimum sample size needed to meet the criteria for statistical power for the study. The table uses the number of predictors and the number of exposures or occurrences of an event to

calculate the minimum number of participants or cases needed to achieve a desired level of statistical power. Given the four psychiatric disorders as the predictor variables, the five medical diseases as the possible events, with alpha set of .05 for a two-tail distribution and, a statistical power of .80, a review of the table revealed that 632 cases would be needed for the study. Because this study involved the use of secondary data, the researcher decided to increase the sample size to a minimum of 800 medical records. The minimum number of cases was increased to accommodate the possibility of attrition of records that could not be used because of missing data.

A secondary data analysis was employed to analyze the data that were collected. Three statistical analyses were performed on the data. A descriptive cross tabulation was used to summarize the demographic characteristics of the sampled cases. A chi-square test of independence was used to test the null hypothesis for the first research question. A multinomial logistic regression was used to test the null hypotheses for the second and third research question. Results of the Wald's test, the Nagelkerke Pseudo R-square value, and the odds-likelihood ratio were used to judge the significance of results from the multinomial logistic regression. The following paragraphs present results of the descriptive data, research questions and relevant hypotheses, summary of the relevant statistical procedures, and results for each research question.

Data Collection and Screening

After gaining permission to collect data from Walden University's Institutional Review Board and the Institutional Review Board of the health care facility, the researcher accessed data from the electronic databases of the health care facility. Four

medical documents were accessed to gather data. The documents consisted of the New Patient Evaluation Psychiatric Consultation, History and Physical Evaluation, New Patient Intake and Assessment, and Patient Demographics. As a member of the clinical staff, the researcher had the appropriate training and security clearance to use the electronic medical record system. The healthcare system agreed to permit review of the cases on the secured system on the condition that no personally identifying information would be recorded from the patient records. Therefore, no information regarding patient names, social security number, home address, telephone number, or other personally identifying information was recorded on the researcher constructed data collection sheet. For tracking purposes during the data collection stage, the researcher used the assigned medical record number (MRN) for each case. The MRN was used to track the cases during the data collection and analysis phases of the research.

The first step of the data collection consisted of grouping the four psychiatric disorders and the five medical diseases into comorbid pairs. The pairs were formed by pairing the diagnostic codes from the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV; APA, 2000) for the psychiatric disorders investigated in the study with relevant medical diagnostic codes from the International Classification of Diseases, 9th Revision (ICD-9) for the medical diseases in this study. The grouping of the disorders resulted in a total of 20 comorbid pairs. This comorbid pair grouping information was then used to develop the Participant Data Search Sheet (see Appendix A) that was used as a guide for the selection of cases. Therefore cases included in the study were selected by first identifying cases in which one of the four identified

psychiatric disorders (generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, or dysthymic disorder) was the first occurring psychiatric diagnosis. The next step was to select records from that database search which also contained cases which included the ICD-9 medical codes that were used for the five medical diseases included in this study.

The next screening of the database identified the cases with which one of the medical diseases (atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, or type II diabetes) was also listed as the primary medical disease for those cases. Results from the first database search and record screening contained records which were comprised of comorbid pair cases with the four primary psychiatric and the five primary medical disease identified for each case. By convention, the health care system considers the first diagnosis listed in a case to be the primary diagnosis.

The database search used two search parameters to select cases for the study. The first parameter selected cases from the one year population cycle that spanned from January 1, 2009 to December 31, 2009. The purpose of the first search parameter was to capture the most current health status information in the medical records. The second search parameter screened for patients with birthdates which occurred before January 1, 1990. Following the groundwork established by previous researchers (Baumeister et al., 2005; Boscarino, 1997; Wells et al., 1991), this study restricted the selection of records to adult cases where the patient was 21 years of age or older. The purpose for restricting the records to those who were 21 years old or older was to avoid potential confounding of the data related to shifting between pediatric psychiatry assessments and adult psychiatry

assessments (Gregory, 2007). There are also distinct developmental and psychosocial differences between the two age categories (Santrock, 2007). The result from the first database search screened 8,133 medical records with the primary psychiatric diagnoses specified in the study. Among those records, the occurrences for 17 comorbid pairs were found. Appendix C provides a descriptive summary of the findings from the first database search. The first database search only yielded 480 cases that met the inclusion criterion. The researcher specified 800 medical records would be needed to achieve adequate statistical power for this study. Consequently an additional search was made of the database.

The second database search was conducted by expanding the population cycle to include cases from January 1, 2005 to September 30, 2010. The year 2005 was selected because it was the time in which the behavioral services division of the healthcare facility began to use the electronic medical record system. The second search produced over 40,000 potential cases. After applying the inclusion criteria for the records, the number of potential cases was reduced to 2,914 cases or approximately 14% of the originally identified cases. In an initial screening of the records selected from the database, the researcher noted that many of the cases had more than one medical diagnosis listed (multiple pairs), which resulted in an inflated count for the number of cases found. A correction was made by selecting only the first occurring medical diagnosis for each case. Once the psychiatric and medical disorders were determined, each case was then assigned to one of the comorbid pairs.

The fourth step in the data collection process was to access the actual electronic medical records in the secured system using the MRN for each of the selected cases to gain access to the record. The purpose of this step was to obtain the biological and demographic information. Shortly after the start of the review of the medical records for the demographic data it became obvious there were redundancies in the data entries. Some of the cases appeared to have more than one psychiatric disorder listed as the first diagnosis.

The researcher concluded that as patients continued seeking treatment at the facility, sometimes changes would occur in their primary psychiatric diagnosis resulting in more than one diagnosis of a psychiatric disorder. By expanding the database search to five years in the second search, the computer generated more than one case placement for some patients. The researcher halted the data collection from the chart reviews to locate and eliminate the redundant records by using the method described in the next paragraph.

To locate and eliminate multiple placements of cases, the MRNs were copied on to a blank sheet. Using the Sort & Filter function of the spreadsheet software, all of the MRNs were listed in numerical order. This listing caused all duplicate record numbers to cluster. Next, the researcher used the Microsoft select & find function to locate all of the duplicate MRN's. The researcher used the procedure of selecting the first occurring diagnosis and removing the redundant cases from the data collection sheets. This process also allowed the researcher to confirm that all of the cases were listed in the correct comorbid pair category.

After deleting the redundant cases from the data file, the final case count was 1,209. This number represented approximately 3% of the original 40,000 cases generated from the five year span specified in the second database search. The number further showed that of the 1,209 cases of the occurring comorbid pairs, 66.7% of the cases listed a psychiatric diagnoses as the first diagnosis of the comorbid pair.

Table 1 presents a summary of the demographic information of the cases included in the study. The table shows the frequency count of the number of cases with a first diagnosis of psychiatric disorder, the specified psychiatric disorder, and the medical disorders. Results showed almost 67% of the cases had a psychiatric disorder as the first disorder in the record. Dysthymic disorder, which was present in 37.5% of the records, was the most frequently occurring psychiatric disorder. Type II diabetes, which was present in 64.9% of the records was the most frequently occurring medical disorder.

Table 1

Summary descriptive statistics of whether the first diagnosis was a psychiatric diagnosis, type of psychiatric diagnoses and type of medical diagnoses

Variable	Frequency	Percent	Valid Percent	Cumulative Percent
First diagnosis psychiatric				
yes	807	66.7	**66.7**	66.7
no	402	33.3	33.3	100.0
Total	1209	100.0	100.0	
psychiatric diagnosis				
generalized anxiety disorder	266	22.0	22.0	22.0
posttraumatic stress disorder	63	5.2	5.2	27.2
major depression recurrent	427	35.3	35.3	62.5
dysthymic disorder	**453**	**37.5**	37.5	100.0
Total	1209	100.0	100.0	
medical diagnosis				
atherosclerosis	173	14.3	14.3	14.3
cardiovascular heart disease	19	1.6	1.6	15.9
rheumatoid arthritis	136	11.2	11.2	27.1
cancer	96	7.9	7.9	35.1
type II diabetes	785	**64.9**	64.9	100.0
Total	1209	100.0	100.0	

Note. The highest percent values are in boldface.

Demographic Characteristics

The case medical records were accessed from the Behavioral Services Division of a single healthcare entity comprised of a system of hospitals and outpatient clinics located in the state of Michigan. The healthcare system services a population area that has almost four million residents. The population served by the facility represents 40% of the residents in the state. Table 2 presents the acronyms that will be used to identify the

psychiatric and medical disorders. This table can be used to aid in interpreting the data presented in table 3 and throughout the chapter.

Table 2

List of Acronyms Used to Identify the Psychiatric and Medical Disorders

Acronym	Disorder/Disease
GAD	Generalized Anxiety Disorder
PTSD	Posttraumatic Stress Disorder
MDD	Major depression Recurrent
DD	Dysthymic disorders
Athero	Atherosclerosis
CVD	Cardiovascular heart disease
RA	Rheumatoid arthritis
CA	Cancer
DM	Type II diabetes

The sample for this study consisted of 1,209 cases. Table 3 presents a summary of the demographic information for the cases. The table was constructed from the results generated from the SPSS descriptive cross tabulation procedure. The results reveal that the sample contained 391 males (36%) and 689 females (64%).

Table 3 also reveals that the rates of occurrence for the specific comorbid pairings varied within the specific demographic categories. For instance, females had the highest occurrence among all of the comorbid categories for which the psychiatric disorder was the first diagnosis to occur. Females had the highest rates of occurrence for four out of five comorbid pairings related to generalized anxiety disorder; four out of five categories

for pairings related to major depression recurrent; three out of five categories of comorbid pairings related to posttraumatic stress disorder; and three out five comorbid pairings related to dysthymic disorder. Males had the highest rates of occurrence for all of the comorbid pairings related to the medical diagnosis of atherosclerosis. Males also had the highest rates of occurrence with pairings for dysthymic disorder and cardiovascular heart disease.

Table 3 provides a summary of the data regarding the race or ethnicity for the records included in the study. The table shows that among the 1,209 cases reviewed, 680 were European Americans (63%), 351 were African Americans (32%), 11 were Asian Americans, and 8 were Hispanic Americans. Cumulatively, the Asian American and Hispanic American comprised less than 5% of the cases reviewed. There were thirty cases in the 'other' racial category. In determining whether or not the sample obtained for this study was representative of the demographic mix in the State of Michigan, the report by the 2008 census was used for comparison. The comparison revealed the European Americans were underrepresented in this sample. African Americans were overrepresented in the sample. Asian Americans and Hispanic Americans were underrepresented in the sample. The representativeness of the sample obtained has important implications for interpreting the findings, for generalizing conclusions, and for suggesting future research.

The data revealed that African Americans had the highest rates of occurrence for three of the five comorbid pairings for PTSD. European Americans had the highest rates of occurrence for all of the other comorbid pairs in the study. In considering family

history and lifestyle, Table 3 reveals there was no family history of psychiatric disorder in 80% of the cases. There was no family history of the immune based inflammatory diseases central to this study in 75% of the cases. In 87% of the cases there was no history of chemical dependence. The one comorbid pair exception whereby family history had a high rate of occurrence was dysthymic disorder and rheumatoid arthritis.

Table 3

Descriptive Summary of Cases of Comorbidity Pairs and Demographic Variables

Co-morbid Pair	*n*	Gender		Race/Ethnicity					Family Psy. History[a]	Family Medical History[a]	Chem Depend. History[a]
		Male	Female	Asian Amer.	African Amer.	European Amer.	Hispanic Amer.	Other			
GAD/ Athero	20	55%	45%		25%	70%		5.0%	35%	25%	20%
GAD/ CVD	5	20%	80%		20%	80%			0%	20%	0%
GAD/ RA	29	10%	90%		28%	72%			31%	17%	17%
GAD/ CA	22	27%	73%		18%	82%			14%	41%	23%
GAD/ DM	190	40%	60%	2.1%	32%	61%	1.1%	4.2%	23%	23%	15%
PTSD/ Athero	7	71%	29%		57%	43%			0%	43%	14%
PTSD/ CVD	0	0%	0%		0%	0%			0%	0%	0%
PTSD/ RA	10	40%	60%		70%	30%			10%	0%	20%
PTSD/ CA	3	33%	67%		33%	67%			0%	33%	0%
PTSD/ DM	43	46%	54%		61%	37%	2.3%		9%	28%	7%
MDD/ Athero	107	55%	45%	.9%	20%	77%	.9%	1.9%	16%	23%	16%
MDD/ CVD	10	40%	60%		50%	50%			0%	40%	10%
MDD/ RA	39	13%	87%		23%	72%	2.6%	2.6%	15%	3%	10%
MDD/ CA	52	29%	71%		33%	64%	1.9%	1.9%	19%	21%	25%
MDD/ DM	219	28%	72%	.9%	33%	65%		.9%	16%	23%	11%
DD/ Athero	39	59%	41%	2.6%	8%	87%		2.6%	10%	26%	10%
DD/ CVD	4	75%	25%		0%	100%			0%	0%	0%
DD/RA	58	19%	81%	1.7%	31%	64%		3.4%	21%	2%	14%

DD/CA	19	16%	84%		5%	95%			11%	58%	5%
DD/DM	333	36%	64%	.6%	37%	58%	.6%	3.9%	17%	26%	11%

Note. N = 1,209 for the total sample. The percentages are of cases for which the answer was 'yes'.

One of the criteria of the study was that all individuals with cases reviewed in this study would currently be 21 years of age or older. The purpose of the age restriction to adult cases was to control for possible confounding data from pediatric psychiatric evaluations verses data obtained from adult psychiatric evaluations (Gregory, 2007). The psychosocial and developmental differences between adults and children were also a factor in selecting only one age population (Santrock, 2007). As presented in Table 4, the greatest concentration across all of the age categories in the comorbid pairs were cases of individuals who were 50 years of age and older. Table 4 also reveals high mortality rates in the comorbid pairs related to generalized anxiety disorder and cancer (50%), posttraumatic stress disorder and cancer (33.3%), major depression recurrent and atherosclerosis (30%), major depression recurrent and cancer (48.1%), and dysthymic disorder and cancer (73.7%). Although the mortality rate reflects a pattern among the comorbid pairs with European American females in the demographic data collected for this study; causation cannot be inferred.

Table 4

Frequency summary from the descriptive cross tabulation for current age in years with the comorbid pairs included in the study.

Comorbid Pairs	Age/ *Frequency*	current age in years				Total
		21 to 35	36 to 49	50 above	Deceased	
GAD/Athero	*n*	*0*	1	16	3	20
	Expected n	*.5*	2.6	15.3	1.6	20.0
	% of pairs	*.0%*	5.0%	80.0%	15.0%	100.0%
GAD/CVD	*n*	*0*	0	5	0	5
	Expected n	*.1*	.6	3.8	.4	5.0
	% of pairs	*.0%*	.0%	100.0%	.0%.	100.0%
GAD/RA	*n*	*1*	5	22	1	29
	Expected n	*.8*	3.7	22.2	2.3	29.0
	% of pairs	*3.4%*	17.2%	75.9%	3.4%	100.0%
GAD/CA	*n*	*0*	1	10	11	22
	Expected n	*.6*	2.8	16.8	1.7	22.0
	% of pairs	*.0%*	4.5%	45.5%	50.0%.	100.0%
GAD/DM	*n*	*11*	23	151	5	190
	Expected n	*5.0*	24.4	145.4	15.1	190.0
	% of pairs	*5.8%*	12.1%	79.5%	2.6%	100.0%
PTSD/Athero	*n*	*0*	0	6	1	7
	Expected n	*.2*	.9	5.4	.6	7.0
	% of pairs	*.0%*	.0%	85.7%	14.3%	100.0%
PTSD/RA	*n*	*0*	2	8	0	10
	Expected n	*.3*	1.3	7.7	.8	10.0
	% of pairs	*.0%*	20.0%	80.0%	.0%	100.0%
PTSDCA	*n*	*1*	0	1	1	3
	Expected n	*.1*	.4	2.3	.2	3.0
	% of pairs	*33.3%*	.0%	33.3%	33.3%	100.0%
PTSD/DM	*n*	*0*	12	30	1	43
	Expected n	*1.1*	5.5	32.9	3.4	43.0
	% of pairs	*.0%*	27.9%	69.8%	2.3%	100.0%
MDD/Athero	*n*	*0*	6	95	6	107
	Expected n	*2.8*	13.7	81.9	8.5	107.0
	% of pairs	*.0%*	5.6%	88.8%	5.6%	100.0%
MDD/CVD	*n*	*0*	0	7	3	10
	Expected n	*.3*	1.3	7.7	.8	10.0
	% of pairs	*.0%*	.0%	70.0%	30.0%	100.0%
MDD/RA	*n*	*1*	7	31	0	39
	Expected n	*1.0*	5.0	29.8	3.1	39.0
	% of pairs	*2.6%*	17.9%	79.5%	.0%	100.0%
MDD/CA	*n*	*1*	3	23	25	52
	Expected n	*1.4*	6.7	39.8	4.1	52.0
	% of pairs	*1.9%*	5.8%	44.2%	48.1%	100.0%
MDD/DM	*n*	*1*	24	186	8	219
	Expected n	*5.8*	28.1	167.6	17.4	219.0
	% of pairs	*.5%*	11.0%	84.9%	3.7%	100.0%
DD/Athero	*n*	*0*	1	37	1	39
	Expected n	*1.0*	5.0	29.8	3.1	39.0
	% of pairs	*.0%*	2.6%	94.9%	2.6%	100.0%
DD/CVD	*n*	*0*	0	4	0	4
	Expected n	*.1*	.5	3.1	.3	4.0
	% of pairs	*.0%*	.0%	100.0%	.0%	100.0%
DD/RA	*n*	*3*	10	43	2	58
	Expected n	*1.5*	7.4	44.4	4.6	58.0
	% of pairs	*5.2%*	17.2%	74.1%	3.4%	100.0%
DD/CA	*n*	*0*	1	4	14	19
	Expected n	*.5*	2.4	14.5	1.5	19.0
	% of pairs	*.0%*	5.3%	21.1%	73.7%	100.0%
DD/DM	*n*	*13*	59	246	14	333
	Expected n	*8.8*	42.7	254.8	26.4	333.0
	% of pairs	3.9%	17.7%	73.9%	4.2%	100.0%
	Total n	32	155	925	96	1209
	Expected n	32.0	155.0	925.0	96.0	1209.0
	% pairings	2.6%	12.8%	76.5%	7.9%	100.0%

Note. See Table 2 for acronym references

The data also revealed that in 75% of the individuals were 50 years of age or older at the time of their first psychiatric diagnosis. The data also showed that 78% of the cases were of individuals who were 50 years old or older at the time of their first medical diagnosis. Fifty percent of the cases revealed the diagnosis of the comorbid condition within one year of the first diagnosis, either psychiatric or medical.

Research Questions and Data Analysis

The purpose of this study was to determine if the diagnosis of certain psychiatric disorders was related to the subsequent onset of certain medical diseases. Three research questions were posed for this study. The results from the data analysis related to testing the null hypotheses for each question is presented below.

Research Question 1

Question 1: For individuals with comorbid psychiatric disorder and medical disease diagnoses, what is the association between the first type of psychiatric diagnosis and the first medical diagnosis?

Null hypothesis 1: For individuals with comorbid psychiatric disorder and medical disease diagnoses, there is no statistically significant association between the first type of psychiatric diagnosis and the first medical diagnosis.

Alternate hypothesis 1: For individuals with comorbid psychiatric and medical diagnoses, there is a statistically significant association between the first type of psychiatric diagnosis and the first type of medical diagnosis.

The chi-square test for independence was the statistical analysis used to test the null hypothesis for the first research question. This statistic is used to identify the likelihood of a particular outcome occurring by chance by comparing observed frequencies of the variable compared to expected frequencies for the variable (Gravetter & Wallnau, 2007). This statistical procedure was appropriate for testing the null hypothesis because the researcher was interested in knowing if the presence of a given psychiatric disorder was related to the subsequent development of medical diseases. As presented in Table 5, results of the chi-square analysis revealed that there was a statistically significant relationship between the rate of occurrence of the psychiatric condition first, and the subsequent diagnosis of the comorbid condition. The observed Pearson chi-square was X^2 (12, N = 1,209) = 99.528, p = .000. The null hypothesis was rejected because the obtained p value was less than .05. A review of the data in Table 5 revealed the rate of occurrence of cases with atherosclerosis and type II diabetes occurred at a greater rate than expected. The rates of occurrence of cases with major depression with type II diabetes also occurred at a greater rate than expected. In addition, the rates of occurrence of cases with dysthymic disorder and type II diabetes occurred at a greater rate than expected. Data from Table 5 further revealed that the greatest rate of comorbid pairing of psychiatric disorders was related to the medical diagnosis of type II diabetes. The next research question addressed the degree to which the first psychiatric diagnosis and certain demographic variables predicted the occurrence of the specified medical disorders.

Table 5

Chi-square Test of Independence for Association between the Psychiatric Diagnosis and Medical Diagnosis

		medical diagnosis					
Psychiatric Diagnosis	Count	Athero-sclerosis	Cardio-vascular heart disease	rheumatoid arthritis	cancer	type II diabetes	Total
generalized anxiety disorder	Count	20	5	29	22	**190**	266
	Expected Count	38.1	4.2	29.9	21.1	**172.7**	266.0
	% within psychiatric diagnosis	7.5%	1.9%	10.9%	8.3%	71.4%	100.0%
Post-traumatic stress disorder	Count	7	0	10	3	43	63
	Expected Count	9.0	1.0	7.1	5.0	40.9	63.0
	% within psychiatric diagnosis	11.1%	.0%	15.9%	4.8%	68.3%	100.0%
major depression recurrent	Count	**107**	10	39	**52**	219	427
	Expected Count	**61.1**	6.7	48.0	**33.9**	277.2	427.0
	% within psychiatric diagnosis	25.1%	2.3%	9.1%	12.2%	51.3%	100.0%
dysthymic disorder	Count	39	4	58	19	**333**	453
	Expected Count	64.8	7.1	51.0	36.0	**294.1**	453.0
	% within psychiatric diagnosis	8.6%	.9%	12.8%	4.2%	73.5%	100.0%
Total	Count	173	19	136	96	785	1209
	Expected Count	173.0	19.0	136.0	96.0	785.0	1209.0
	% within psychiatric diagnosis	14.3%	1.6%	11.2%	7.9%	64.9%	100.0%

Note. Psychiatric and medical pairs exceeding the expected count are boldfaced.

Research Question 2

Question 2: Among individuals with comorbid psychiatric and medical disease diagnoses, to what degree does the presence of a psychiatric disorder and the

demographic variables (gender, race, family psychiatric history, family medical history, and chemical dependence history) significantly influence the presence of the medical disorders atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes in the comorbid pairs?

Null hypothesis 2: The psychiatric disorders (generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder) and the demographic variables (gender, race, family psychiatric history, family medical history, and chemical dependence history) are not statistically significant predictors of the medical disorders.

Alternate hypothesis 2: The psychiatric disorders (generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder) and demographic variables (gender, race, family psychiatric history, family medical history, and chemical dependence history) are statistically significant predictors of the medical disorders atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes.

Multinomial logistic regression was used to test the null hypothesis for the second research question. This statistical procedure predicts the probability of an individual being grouped into one category of a variable compared to being grouped in another (Mertler & Vannatta, 2005). In this study the basis of comparison was the likelihood that a person would be diagnosed in one category of the dependent variable, medical disorder, compared to another category; therefore multinomial regression was the appropriate statistical procedure for testing the null hypothesis. Logistic regression also offers the following advantages: the assumptions of linearity, normality and homogeneity of

variance are not assumed; negative values are not produced; and logistic regression can consider and analyze all types of dependent and predictor variables (Mertler & Vannatta, 2005).

The dependent variable in the equation was the medical disorder (atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes). The independent/predictor variables in the equation were the presence of one of the psychiatric disorders, age, gender, race/ethnicity, family history of a similar psychiatric and/or medical disease diagnosis, and history of chemical dependence.

The default option in SPSS is to either use the first group or the last group of the dependent variable as the reference or comparison group (SPSS, version 15). In this study SPSS used the last variable, which was type II diabetes, as the reference group for the group comparisons. The parameter estimates for the model shows the results for each variable included in the model. Results revealed that the model had the greatest classification accuracy of 96.4% for predicting type II diabetes from the independent variables. The overall classification accuracy for this model was 65%.

Table 6

Multinomial logistic regression classification table for the medical diagnoses

Observed	Predicted Frequencies		Total	
Frequencies	Athero-sclerosis	cancer	type II diabetes	Percent Correct
atherosclerosis	18	1	154	10.4%
cardiovascular heart disease	2	0	17	.0%
rheumatoid arthritis	2	0	134	.0%
cancer	4	0	92	.0%
type II diabetes	16	1	768	97.8%
Overall Percentage	3.5%	.2%	96.4%	**65.0%**

N = 1,209. Table is adapted from the SPSS output.

Results from the omnibus table of the multinomial logistic regression revealed that the variables psychiatric diagnosis, first diagnosis psychiatric, gender, and family history of the medical diagnosis were statistically significant predictors of the type of comorbid medical diagnosis. Based upon the findings of these analyses, the null hypothesis was rejected. The chi-square results from the omnibus tests of the model coefficients revealed $X^2(52, 1{,}209) = 266.587$, $p = .000$, which was statistically significant. The Nagelkerke Pseudo R-Square provided a measure of how well the independent variables in the equation predicted the dependent variable (Gravetter & Wallnau, 2007). The Nagelkerke pseudo R-square of .224 in this analysis indicates that 22.4% of the variance in the medical disease category was accounted for by the psychiatric disorders plus the demographic and biological factors. This variance indicates a large effect size (Gravetter & Wallnau, 2007).

The results from the likelihood ratio tests, as presented in Table 8 revealed that the presence of a psychiatric disorder, the type of psychiatric disorder, gender, and history of a family member with a related medical disorder were statistically significant predictors of the type of medical disorder. Table 7 presents the legend for the acronyms used in Table 8.

Table 7

Legend for the variable names used in Table 8

psydx – psychiatric diagnosis
firstdx – first diagnosis psychiatric
cdhx – chemical dependence history
gender – gender
fammed – family history of the medical diagnosis
fampsy – family history of the psychiatric disorder
raceeth – race/ethnicity

Table 8

Psychiatric and demographic predictors for comorbidity

Effect	Model Fitting Criteria	Likelihood Ratio Tests		
	-2 Log Likelihood of Reduced Model	Chi-Square	df	Sig.
Intercept	903.385(a)	.000	0	.
psydx	1006.984	**103.600**	12	**.000**
firstdx	923.812	**20.428**	4	**.000**
cdhx	912.255	8.871	4	.064
gender	964.273	**60.888**	4	**.000**
fammed	939.002	**35.617**	4	**.000**
fampsyc	911.748	8.364	4	.079
raceeth	928.722	25.338	16	.064

a This reduced model is equivalent to the final model because omitting the effect does not increase the degrees of freedom.
b. Significant results are boldfaced

The Wald statistic was next used to determine the degree to which each of the predictor variables contributed to the regression model (Mertler & Vannatta, 2005). Regarding the occurrence of the medical disorder atherosclerosis, the results from the Wald statistics presented in Table 10 show that the type of psychiatric disorder, the presence of a psychiatric diagnosis as the first diagnosis for the comorbid pair, and gender were statistically significant predictors of atherosclerosis. The data further revealed that males with a first diagnosis of major depressive disorder were significantly more likely to have a medical diagnosis of atherosclerosis than type II diabetes.

Regarding the occurrence of cardiovascular heart disease, the data revealed that only one variable in the equation was a significant predictor. Results from the Wald statistic reveal that individuals with a first psychiatric diagnosis of major depression recurrent were significantly more likely to develop cardiovascular heart disease than type II diabetes. However it must be noted that the omnibus Wald statistic for this variable was not statistically significant. Therefore the finding for this variable may be a spurious result.

Regarding the occurrence of the medical disease rheumatoid arthritis, the results from the Wald statistics indicated that the presence of psychiatric diagnosis as the first of the comorbid pair, gender, and family medical history were significant predictors for the disease. The data further revealed that males with a psychiatric disorder, who also had a

family history of rheumatoid arthritis, were significantly more likely to have a medical diagnosis of rheumatoid arthritis than type II diabetes.

Regarding the occurrence of the medical disease cancer, the results from the Wald statistics, the presence of a psychiatric disorder for the first comorbid pair, having the psychiatric diagnosis of major depression recurrent, history of chemical dependence, and male gender were significant predictors of the disease. The result specially showed that males with the psychiatric diagnosis of major depression who had a history of chemical dependence were significantly more likely to develop cancer than type II diabetes.

Table 10 presents the results of the multinomial logistic regression analysis using the dependent and independent variables. Table 9 presents a legend for interpreting the variable names in Table 10.

Table 9
Legend for interpreting variables in Table 10

Psychiatric (**psydx**)

Generalized Anxiety Disorder =1
Posttraumatic Stress Disorder = 2
Major Depression Recurrent = 3
Dysthymic Disorder = 4

First Diagnosis Psychiatric (**firstdx**)

Yes = 1
No = 2

Chemical Dependence History (**cdhx**)

Yes = 1
No = 2

Gender (**gender**)

Male = 1
Female = 2

Race/Ethnicity (**raceeth**)

Asian American = 1
African American = 2
European American = 3
Hispanic American = 4
Other = 5

Family Medical History (**fammed**)

Yes = 1
No = 2
Unknown/Adopted = 3

Family Psychiatric History (**fampsy)**

Yes = 1
No = 2
Unknown/Adopted = 3

Table 10

Multinomial logistic regression analysis of the dependent and independent variables

Study Variables	B	Std. Error	Wald	df	Sig.	Exp(B)	95% Confidence Interval for Exp (B)	
							Lower Bound	Upper Bound
Atherosclerosis								
Intercept	-15.955	.668	569.872	1	.000			
[psydx=1]	-.181	.296	.373	1	.541	.835	.468	1.490
[psydx=2]	.189	.448	.177	1	.674	1.208	.502	2.908
[psydx=3]	1.502	.212	50.289	1	**.000**	4.490	2.965	6.800
[psydx=4]	0(b)	.	.	0	.	.	.	.
[firstdx=1]	-.405	.189	4.593	1	**.032**	.667	.460	.966
[firstdx=2]	0(b)	.	.	0	.	.	.	.
[cdhx=1]	.043	.261	.027	1	.869	1.044	.626	1.742
[cdhx=2]	0(b)	.	.	0	.	.	.	.
[gender=1]	.994	.183	29.655	1	**.000**	2.702	1.890	3.865
[raceeth=2]	13.302	.000	.	1	.	598210.048	598210.048	598210.048
[fammed=1]	.399	.665	.359	1	.549	1.490	.404	5.488
[fammed=2]	.288	.650	.197	1	.657	1.334	.373	4.773
[fampsyc=1]	-.017	.245	.005	1	.945	.983	.608	1.589
Cardiovascular Heart Disease								
Intercept	-30.156	972.761	.001	1	.975			
[psydx=1]	.833	.682	1.491	1	.222	2.300	.604	8.753
[psydx=2]	-12.543	658.875	.000	1	.985	3.57E-006	.000	.(c)
[psydx=3]	1.392	.603	5.327	1	**.021**	4.021	1.234	13.110
[firstdx=1]	-.588	.480	1.498	1	.221	.555	.217	1.424
[cdhx=1]	-.849	1.050	.654	1	.419	.428	.055	3.349
[gender=1]	.478	.482	.986	1	.321	1.613	.628	4.146
[raceeth=2]	13.120	.000	.	1	.	498810.878	498810.878	498810.878
[fammed=1]	13.104	972.761	.000	1	.989	490835.220	.000	.(c)
[fammed=2]	13.055	972.761	.000	1	.989	467573.723	.000	.(c)
[fampsyc=1]	-13.170	354.442	.001	1	.970	1.91E-006	3.79E-308	9.593E+295

(table continues)

Study Variables	B	Std. Error	Wald	df	Sig.	Exp(B)	95% Confidence Interval for Exp (B) Lower Bound/ Upper Bound	
Rheumatoid Arthritis								
Intercept	.302	1.365	.049	1	.825			
[psydx=1]	-.187	.254	.540	1	.462	.830	.504	1.365
[psydx=2]	.482	.399	1.458	1	.227	1.619	.741	3.537
[psydx=3]	-.015	.232	.004	1	.948	.985	.625	1.552
[firstdx=1]	-.721	.193	13.891	1	**.000**	.486	.333	.711
[cdhx=1]	.331	.289	1.313	1	.252	1.392	.790	2.452
[gender=1]	-1.013	.250	16.407	1	**.000**	.363	.222	.593
[raceeth=2]	-1.167	1.239	.887	1	.346	.311	.027	3.531
[fammed=1]	-1.714	.686	6.242	1	**.012**	.180	.047	.691
[fammed=2]	-.013	.576	.000	1	.982	.987	.319	3.053
[fampsyc=1]	-.013	.245	.003	1	.959	.987	.611	1.596
Cancer								
Intercept	-15.699	.814	372.285	1	.000			
[psydx=1]	.723	.330	4.795	1	**.029**	2.062	1.079	3.940
[psydx=2]	.227	.647	.124	1	.725	1.255	.354	4.458
[psydx=3]	1.388	.285	23.814	1	**.000**	4.009	2.295	7.002
[firstdx=1]	.272	.258	1.110	1	.292	1.312	.791	2.176
[cdhx=1]	.791	.299	7.014	1	**.008**	2.205	1.228	3.960
[gender=1]	-.517	.256	4.069	1	**.044**	.596	.361	.985
[raceeth=2]	12.528	.000	.	1	.	275845.043	275845.043	275845.043
[fammed=1]	.568	.790	.517	1	.472	1.765	.375	8.308
[fammed=2]	.051	.778	.004	1	.948	1.052	.229	4.835
[fampsyc=1]	-.252	.308	.669	1	.413	.777	.424	1.422

Note. Statistically significant results are in boldface.
a. Type II diabetes was the reference/comparison category

The multinomial logistic regression analysis was conducted to test null hypothesis 2 in this study. The null hypothesis stated that the psychiatric disorders and demographic variables were not statistically significant predictors of the medical diseases (atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes). The null hypothesis was rejected. The results revealed that the presence of a psychiatric disorder, the type of psychiatric disorder, gender, and history of a family

member with a related medical disease were statistically significant predictors of the type of medical disorder.

Research Question 3

Question 3: To what degree does the presence of a psychiatric disorder as the first diagnosis and the diagnosed psychiatric disorder predict the medical disorders for the comorbid pairs included in the study?

Null hypothesis 3: The presence of a psychiatric disorder as the first diagnosis and the diagnosed psychiatric disorder are not statistically significant predictors of the medical disorders for the comorbid pairs included in this study.

Alternate hypothesis 3: The presence of a psychiatric disorder as the first diagnosis and the diagnosed psychiatric disorder are statistically significant predictors of the medical disorders for the comorbid pairs included in the study.

Multinomial logistic regression was the statistical procedure used to test the full model of psychiatric disorders predictive accuracy in the development of the immune based inflammatory diseases in this study. The predictor variables were generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder. The medical diseases were atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes. The variable 'psychiatric diagnosis first' was also an independent or predictor variable. The chi-square results from the omnibus tests of the model coefficients revealed X^2 (16, 1,209) = 123. 334, p = .000 with the Nagelkerke Pseudo R-square of .110; which is a medium effect size. This finding indicates a statistically significant fit of the psychiatric disorders to the prediction model.

Further analysis also revealed that having a first diagnosis as a psychiatric disorder [X^2 (12, 1,209) = 100.133, p = .000] and the type of psychiatric disorder as the first diagnosis were [X^2 (4, 1,209) = 24.495, p = .000] were statistically significant predictors of the medical disorders. Table 11 indicates that the psychiatric diagnosis of generalized anxiety disorder was a statistically significant predictor of cancer as the medical disease. The results also showed that the psychiatric diagnosis of major depression recurrent was a statistically significant predictor for the medical diseases of atherosclerosis, rheumatoid arthritis, and cancer. The overall classification accuracy for the model was 64.9%. Based upon the findings of the analysis, the null hypothesis was rejected.

Table 11

Multinomial logistic regression of medical diagnosis with psychiatric diagnosis and first occurring diagnosis

medical diagnosis(a)		B	Std. Error	Wald	df	Sig.	Exp(B	95% Confidence Interval for Exp(B)	
								Lower Bound	Upper Bound
atherosclerosis	Intercept	-1.924	.205	87.805	1	.000			
	[FIRSTDX=1]	-.336	.184	3.326	1	.068	.715	.498	1.025
	[PSYDX=1]	-.134	.290	.214	1	.643	.874	.495	1.544
	[PSYDX=2]	.338	.442	.584	1	.445	1.402	.590	3.333
	[PSYDX=3]	**1.447**	**.207**	**48.880**	**1**	**.000**	**4.251**	**2.833**	**6.378**
cardiovascular heart disease	Intercept	-4.076	.572	50.767	1	.000			
	[FIRSTDX=1]	-.545	.477	1.310	1	.252	.580	.228	1.475
	[PSYDX=1]	.738	.679	1.184	1	.276	2.093	.554	7.911
	[PSYDX=2]	-18.364	.000	.	1	.	1.058E-08	1.058E-08	1.058E-08
	[PSYDX=3]	**1.367**	**.599**	**5.207**	**1**	**.022**	**3.923**	**1.213**	**12.694**

rheumatoid arthritis	Intercept	-1.249	.175	50.669	1	.000			
	[FIRSTDX=1]	-.832	.189	19.284	1	**.000**	.435	.300	.631
	[PSYDX=1]	-.203	.248	.671	1	.413	.816	.502	1.327
	[PSYDX=2]	.311	.383	.661	1	.416	1.365	.644	2.892
	[PSYDX=3]	.072	.227	.101	1	.751	1.075	.689	1.676
cancer	Intercept	-3.068	.304	102.178	1	.000			
	[FIRSTDX=1]	.283	.255	1.227	1	.268	1.327	.804	2.189
	[PSYDX=1]	**.729**	**.327**	**4.976**	**1**	**.026**	**2.073**	**1.092**	**3.934**
	[PSYDX=2]	.195	.642	.092	1	.762	1.215	.345	4.279
	[PSYDX=3]	**1.412**	**.282**	**25.045**	**1**	**.000**	**4.104**	**2.361**	**7.135**

a. The reference category is: type II diabetes.
b. Statistically significant results are boldfaced

The Wald statistic was used to determine the degree to which each of the predictor variables, psychiatric disorders, contributed to the regression model (Mertler & Vannatta). The default option in SPSS used the last medical disease as the reference group to be used in the comparison for the results. The reference medical disease used was type II diabetes. As shown in Table 12, the data revealed that individuals with major depression as the first occurring psychiatric diagnosis had a statistically significant greater likelihood of developing atherosclerosis, cardiovascular heart disease, and cancer than type II diabetes. The results also showed that the individuals with the psychiatric diagnosis of generalized anxiety disorder as the first occurring diagnosis in the comorbid pair were statistically significantly more likely to have a medical diagnosis of cancer than

type II diabetes. The occurrence of the medical disease of cancer was found with both generalized anxiety disorder and major depression recurrent psychiatric disorders, with either disorder occurring first. In these instances, the occurrence was statistically significant compared to the occurrence of type II diabetes.

Summary

Chapter 4 presented the findings from the statistical analyses conducted to address the question of whether the presence of psychiatric disorders was predictors of the presence of immune based inflammatory diseases. The key variables investigated in this study were the presence and type of psychiatric disorder, medical disorder, psychiatric and medical comorbidity. The demographic variables were age, race, and gender. The biological variables included in the study were family history of the psychiatric disorders, family history of the medical disorders, and individual history of chemical dependence.

The statistical methods used to test the prediction model were descriptive cross tabulation, chi-square test of independence and multinomial logistic regression. The analysis for this study found support from the data that certain psychiatric disorders predicted specific medical diseases investigated in this study.

The first research question asked if there was an association between the first type of psychiatric diagnosis and the first medical diagnosis. Results from the chi-square analysis found that generalized anxiety disorder with type II diabetes, major depression recurrent with cancer, and dysthymic disorder with type II diabetes occurred at a greater rate than expected; therefore the null hypothesis was rejected for this question.

The second research question asked if the psychiatric disorders and the demographic and biological factors combined were statistically significant predictors of the medical diseases investigated in this study. The data revealed that 66.7% of the cases included in the study were first diagnosed with a psychiatric disorder. Results also revealed that the presence of psychiatric diagnosis as the first of the comorbid pair, the type of psychiatric diagnosis, gender, and family medical history were statistically significant, therefore the null hypothesis for research question 2 was rejected. The factors of history of chemical dependence, family history of a similar psychiatric diagnosis, and race were non-significant in this analysis.

The final research question in this study inquired about the degree to which the presence of a psychiatric condition and the type of psychiatric condition predicted the presence of medical diseases included in this study. The overall classification accuracy rate for the model was 64.9%. The null hypothesis was rejected.

The observed frequencies for the biological and demographic variables revealed possible noteworthy information regarding gender, race, and the timeline between the first diagnosis and the second in the comorbid condition. Chapter 5 will provide a discussion and summary of the study. Recommendations for professional practice and future research will also be presented.

Chapter 5: Summary, Conclusion, and Recommendations

Introduction

The inflammatory based immune diseases, such as atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes are responsible for the death of millions of individuals each year in the United States and world wide (Heijnen & Kavelaars, 2005; Pickup, 2003; Steptoe & Brydon, 2005; Walker, Green, Greenman, Walker, & Sharpe, 2005). The purpose of this study was to determine if psychiatric disorders were predictors of the presence of immune based inflammatory diseases. A major premise for this study was that if one could empirically link psychiatric disorders to immune based inflammatory diseases, such as atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes, then one could have a basis for developing and promoting additional disease prevention measures for those individuals who are diagnosed with certain psychiatric disorders.

The psychiatric disorders of generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder were used as possible predictor variables for the presence of several medical diseases. This study also included demographic and biological variables as possible factors that influence the occurrence of certain diseases. The demographic variables included, age at the first documented psychiatric diagnosis, age at the first documented medical disease diagnosis, and the time between the two diagnoses. The biological variables included, gender, race, family history of a similar psychiatric disorder, family history of a similar medical diagnosis, and history of chemical dependence. The demographic variables were also included as

independent variables in the prediction model. The dependent variable was the type of medical disorder (atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes).

The PNI model, which provided the theoretical basis for this study, is founded on the study of the relationship between emotions and the response of the nervous system to emotions (Rabin, 2005). The nervous system response includes changes in the production of certain hormones, which in turn alter immune function. The major hormones in PNI are cortisol, norepinephrine, and epinephrine. During instances of prolonged experiences of emotional distress, stress related immune impairment can occur (Kiecolt-Glaser et al., 2002). This impairment of the immune function could result in the development of immune related diseases. The two most consistent emotions to trigger the immune response are anxiety and depression (Ader, 2005). From the classification system of anxiety, the present study selected the psychiatric diagnoses of generalized anxiety disorder and posttraumatic stress disorder. From the classification system of depression, the present study selected the psychiatric diagnoses of major depression recurrent and dysthymic disorder.

Previous studies in PNI have investigated the relationships between a broad range of emotional disorders and medical diseases (Baumeister et al., 2007; Boscarino, 1997; Kiecolt-Glaser et al.; 2002). This study differed from many of the previous PNI related studies that investigated the relationship between psychiatric disorders and medical diseases by maintaining the distinct psychiatric and medical disease classifications throughout all of the analyses, rather than grouping classifications into general categories.

Boscarino (1997), as an example, investigated the relationship between PTSD and medical diseases in ten medical categories (cancer, circulatory, digestive, musculoskeletal, genitourinary, endocrine-nutritional-metabolic, nervous system, skin, respiratory, and any chronic disease). Each category was comprised of several different medical diagnoses that were related to the category. In addition this study differs because the medical diseases selected for this study were confined to the inflammatory based diseases for which the PNI process has been implicated by scientific research (McCance & Huether, 2002; Rabin, 2005).

This chapter discusses the findings of the data analyses presented in chapter4 as well as an interpretation of those findings as related to the literature presented in chapter 2. The purpose of the study, limitations, practical implications, social change implications, and recommendations for future research and further action are also presented in this chapter.

Occurrence of Psychiatric Diagnosis and Medical Condition

A descriptive cross tabulation statistical analysis was conducted to determine the number of cases in this study that had a psychiatric diagnosis as the first occurring diagnosis in the comorbid pairs. The data revealed that the psychiatric diagnosis occurred first in 67% of the cases. The data also revealed dysthymic disorder to be the most frequently occurring psychiatric disorder and type II diabetes to be the most frequently occurring medical disease.

Principals from the PNI model can be used to explain the findings regarding the high number of psychiatric disorders as the first diagnosis in the comorbid pair. PNI

involves the study of how emotions affect the central nervous system (Rabin, 2005). According to the PNI model, changes in the functioning of the central nervous system in turn alter the immune system. Alterations in the immune system frequently serve as the foundation for the development of some medical diseases (McCance & Huether, 2002; Rabin, 2005). The present study was based upon the premise that psychiatric disorders may act as emotional initiators of the physiological processes that eventually lead to certain types of inflammatory based diseases. This study expanded upon that premise to investigate the predictive potential of the psychiatric disorders for the presence of specific inflammatory immune based diseases.

The PNI Model and Comorbid Pairs

In the PNI theoretical framework, the physiological response to prolonged emotional distress is the increased production of the hormones cortisol, epinephrine, and norepinephrine. These hormones contribute to the initiation of the acute inflammatory response. The physiological purpose of the inflammatory response is to destroy and remove damaged, dead, or infected cells from the body (Rabin, 2005).

The emotionally induced physiological response resulting in atherosclerosis is the inflammatory response in the blood vessel walls which leads to the progressive dysregulation of cellular function, damage, and blockage of the blood vessel (Steptoe and Brydon, 2005). The blockage of blood flow in atherosclerosis can lead to stroke or heart attack. Cardiovascular heart disease occurs when heart muscle cells die because of lack of oxygen and nutrients due to blockage in the blood vessels. The inflammatory response works to remove the damaged heart cells. This loss of heart cells results in the

development of heart disease (Steptoe & Brydon, 2005). Rheumatoid arthritis is the failure of the immune system to recognize its own cells. This dysregulation leads to the tissue destroying function of the inflammatory immune response to the body's own tissue that lines the joints (Heijnen & Kavelaars, 2005). Cancer is the failure of the immune system to detect and destroy mutated self- cells by the inflammatory response (Walker et al., 2005). Type II diabetes starts with the dysregulation of the blood glucose level in the initial stress response that progresses to the impairment of the insulin secretion of the beta cells of the pancreas by the acute inflammatory response (McCance & Huether, 2002; Pickup & Crook, 1997).

Contrary to what was expected based on prevalence studies and previous literature, the results of this study showed a consistently low number of cases in the comorbid pairs with cardiovascular heart disease. By contrast, this study found a high frequency of cases with atherosclerosis. Steptoe and Brydon (2005) posit that atherosclerosis is not only an independent medical disease, but it is also the underlying disease process that can progress to cardiovascular heart disease. The results of this study found stronger support for the PNI theory with the medical disease of atherosclerosis. There were also low case counts for posttraumatic stress disorder, with the exception of PTSD with the diseases of type II diabetes and rheumatoid arthritis. Among all of the cases included in this study, there were zero cases found for the comorbid pair of PTSD and cardiovascular heart disease. These findings also contradict what would be expected, based on the PNI research presented by Boscarino (1997) and Bremner (2002) reporting a high prevalence of PTSD. Both researchers reported a statistically significant association

between PTSD and the presence of medical disease. By contrast, the pioneering work done by Klein (1964) in his investigation of anxiety, found that anxiety disorders have an endogenous biochemical bases. The present study found a high frequency of generalized anxiety disorder and low frequency of PTSD suggesting that further research regarding a possible differential PNI response to situationally induced anxiety, as with PTSD, from endogenous anxiety, such as generalized anxiety disorder may be warranted.

Findings Related to Demographic Variables

The selection of demographic variables for this study was guided by the limitations and recommendations reported by previous PNI researchers. A concern reported by Kiecolt-Glaser et al. (2002) was related to the limited type of data available in their archival studies. After accessing almost two-thirds of the PNI studies published since 1939, Kiecolt-Glaser and colleagues reported that demographic information, such as age, gender, race, family history of the psychiatric disorder, family history of the medical disease, and individual history of chemical dependence were not documented in the journals that they accessed.

Kiecolt-Glaser et al. (2002) speculated that the demographic and biological data could contribute to the interpretation of the PNI process as related to the comorbid pairs. The present study did find distinct pattern differences in the comorbid presence of medical diseases for the demographic variables of gender, race, and age. In the present study, females with the psychiatric disorder of generalized anxiety disorder had the highest occurrence of cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes. Females with the psychiatric condition of posttraumatic stress disorder had

the highest rate of occurrence of rheumatoid arthritis, cancer, and type II diabetes. Females presenting with the diagnosis of major depression recurrent had the highest frequency of the medical diseases of cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes. Females with the psychiatric disorder of dysthymic disorder had the highest rate of occurrence of rheumatoid arthritis, cancer, and type II diabetes. All of these findings support the premise of PNI regarding the relationship between emotions, the inflammatory response, and medical diseases (Heijnen & Kavelaars, 2005; Pickup & Crook, 1998; Steptoe & Brydon, 2005; Walker et al, 2005).

Among the comorbid pairs in this study, females had the highest mortality rate for four of the comorbid pairs. The four comorbid pairs with the highest mortality rate were the psychiatric disorders of generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder, with each disorder being paired with the medical disease of cancer. The majority of the females within the high mortality rate in the previously mentioned comorbid pairs were European American. African American females had the highest rate of occurrence of posttraumatic stress disorder paired with the medical diseases of rheumatoid arthritis and type II diabetes. Hughes et al. (2006) investigated the genetic factors involved in the development of rheumatoid arthritis. Hughes and colleagues found that African Americans carry the nucleotide for rheumatoid arthritis more frequently than European Americans. In a study of three hundred thirty six middle-aged women with a history of depression and atherosclerosis, Jones, Bromberger, Sutton-Tyrrell, and Mathews (2003) found that the risk of developing vascular plaque

was twice as great in women who had a lifetime history of major depression recurrent when compared to women who had a history of single episode depression.

The male cases in this study had the highest rate of occurrence for the comorbid pairs of generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder, with each being paired with the medical disease of atherosclerosis. Males also had the highest rate of occurrence of dysthymic disorder paired with cardiovascular heart disease. These findings of male comorbidity associated with depression and heart disease are consistent with the study conducted by Ford et al (1998). In a forty year prospective observational study of more than 1000 male medical students by Ford and his colleagues (1998) at John Hopkins depression was a predictor for cardiovascular disease. The presence of major depression occurred as first condition in the 12% of the comorbid pairs and the rate of occurrence was statistically significant. Taylor and colleagues (2005) used a sequential logistic model to determine risk factors associated with the development of atherosclerosis and cardiovascular heart disease. The researchers found that male gender and being of European American descent were among the best-fit hereditary markers for the prediction of disease development. In support of the findings by Taylor (2005) this study found that atherosclerosis and cardiovascular heart disease was also most prevalent among males of European American descent. This study, however, did not find cardiovascular heart disease to be the most frequently occurring medical condition. Atherosclerosis was the medical disease that was statistically significant among the records of European American males.

Ford and his colleagues investigated major depression as the predictor of cardiovascular heart disease. They reported difficulty estimating the critical timing between the onset of the first disorder and the onset of the second disorder in the development of the comorbid condition (Ford et al., 1998). This study also included the timing between the diagnosis of the first disorder and the diagnosis of the second disorder as a predictor variable in the regression model. This study found that the timing between onset of the first disorder and onset of the second disorder occurred within one year in the majority of the cases in this study.

As previously stated, this study found a greater rate of occurrence than what was expected by chance among the categories of psychiatric disorder occurring first in the comorbid conditions, and the time between the first diagnosis and the second diagnosis. The frequency of occurrence that exceeded expectation in the categories of age, gender, race, and the pattern of comorbid pairing also contributed to the breadth of this study because of the biological and hereditary link of these variables. No inferences, however, could be drawn from the analyses conducted in this study. The following section provides a summary and discussion of the analyses that were conducted in this study.

Research Question 1

Question 1: For individuals with comorbid psychiatric disorder and medical disease diagnoses, what is the association between the first type of psychiatric diagnosis and the first medical diagnosis?

The multinomial regression analysis revealed a statistically significant relationship between the rate of occurrence of the psychiatric condition first and the

subsequent diagnosis of the comorbid condition. The data revealed the rate of occurrence of cases with atherosclerosis and type II diabetes occurred at a greater rate than expected by chance occurrence. The rates of occurrence of cases with major depression with type II diabetes also occurred at a greater rate than expected. In addition, the rates of occurrence of cases with dysthymic disorder and type II diabetes occurred at a greater rate than expected. Irwin and Cole (2005) discussed the PNI process with depression as the initiator of the inflammatory immune response. Pickup and Crook (1998) focused on this process as it related to type II diabetes. Steptoe and Brydon (2005) noted the connection between depression and atherosclerosis, with depression preceding the presence of atherosclerosis. As with the findings by the previous researchers, the findings of this study support the premise of the PNI model.

Ford et al (1998) specifically investigated prediction with the comorbid pair of major depression and cardiovascular heart disease. These researchers provided one of the few studies designed to assess psychiatric predictors for medical disease. Ford and his colleagues used major depression as the predictor and cardiovascular heart disease as the medical condition. In a forty year, prospective observational study of over one thousand male medical students at John Hopkins, it was found that depression was a statistically significant predictor for cardiovascular heart disease. In the present study, major depression recurrent was a statistically significant predictor for cardiovascular heart disease; thus supporting previous research by Ford and colleagues. The present study also found that cardiovascular heart disease occurred most frequently for males than for females.

The present study found 95 cases in the major depression and atherosclerosis comorbid pair category. Over 55% of those cases were of individuals 50 years of age or older. In the present study, major depression recurrent was a statistically significant predictor for the development of atherosclerosis.

In general, in the present study 78% of the cases reviewed were of individuals who were over fifty years of age. The present study found that 85% of the cases in the major depression recurrent and type II diabetes comorbid pair were of individuals 50 years of age or over. Surwit and Schneider (1993) reported that type II diabetes is associated with aging. In their study of depression and type II diabetes, the researchers found that approximately 15% of all Americans over the age of 65 years of age develop type II diabetes (Surwit & Schneider, 1993). In the present study, the age factor may have had a confounding effect on the results regarding the high frequency of occurrence of type II diabetes.

Research Question 2

Question 2: Among individuals with comorbid psychiatric and medical disease diagnoses, to what degree does the presence of a psychiatric disorder and the demographic variables (gender, race, family psychiatric history, family medical history, and chemical dependence history) significantly influence the presence of the medical disorders atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes in the comorbid pairs?

The null hypothesis for research question 2 was rejected. Results from the multinomial regression analysis revealed that the presence of a psychiatric disorder, the

type of psychiatric disorder, gender, and history of a family member with a related medical disorder were statistically significant predictors of the type of comorbid medical diagnosis. The presence of a psychiatric diagnosis as the first diagnosis for the comorbid pair and gender were statistically significant predictors of atherosclerosis. The data further revealed that males with a first diagnosis of major depressive disorder were significantly more likely to have a medical diagnosis of atherosclerosis than type II diabetes. The Wald statistic revealed that individuals with a first psychiatric diagnosis of major depression recurrent were significantly more likely to develop cardiovascular heart disease than type II diabetes. The data also revealed that males with a psychiatric disorder, who also had a family history of rheumatoid arthritis, were significantly more likely to have a medical diagnosis of rheumatoid arthritis than type II diabetes. The result further showed that males with the psychiatric diagnosis of major depression who had a history of chemical dependence were significantly more likely to develop cancer than type II diabetes.

Ford et al. (1998) included medical risk factors for cardiovascular disease, which included family history and chemical dependence. Their study was designed to determine if major depression was an independent risk factor for coronary artery disease. After controlling for the known medical risk factors, Ford and his colleagues found that major depression was an independent risk factor for coronary artery disease. The present study also investigated demographic and biological factors that could influence the development of the comorbid condition. While gender, race, and age were significant factors of influence, the psychiatric disorder of major depression recurrent was found to

be related to the presence of the comorbid conditions of atherosclerosis and cardiovascular heart disease.

A previous study by Surwit and Schneider (1993) investigated the relationship between stress and diabetes. The study compared diabetic patients of similar age to their non-diabetic siblings and neighbors. The results found that diabetic patients were significantly more likely to have had severe life events that lead to anxiety and depression than the control group. The stressful life events typically occurred within a three year time frame prior to the diagnosis of diabetes. The present study did not collect data related to life stressors, but PTSD was one of the psychiatric diagnoses investigated in the present study. The chi-square test of independence in Table 5 showed an association of 68.3% between PTSD and the type II diabetes revealing type II diabetes to be the most frequent pairing disease with PTSD in the present study. Again, the present study found that the presence of a psychiatric diagnosis, the type of psychiatric diagnosis plus gender, and family history of a related medical diagnosis were statistically significant predictors of the presences of certain medical disorders.

Research Question 3

Question 3: To what degree does the presence of a psychiatric disorder (generalized anxiety disorder, posttraumatic stress disorder, major depression recurrent, and dysthymic disorder) as the first diagnosis and the diagnosed psychiatric disorder predict the medical disorders (atherosclerosis, cardiovascular heart disease, rheumatoid arthritis, cancer, and type II diabetes) for the comorbid pairs included in the study?

The null hypothesis for research question 3 was rejected. Results from the multinomial regression analysis revealed that the psychiatric disorders were significant predictors of the medical diseases. The data revealed that the psychiatric disorder occurring first in the comorbid pair development was a statistically significant predictor of the presence of medical disorders. The data further revealed that individuals with major depression as the first occurring psychiatric diagnosis had a statistically significant greater likelihood of developing atherosclerosis, cardiovascular heart disease, and cancer than type II diabetes. The results also showed that the individuals with the psychiatric diagnosis of generalized anxiety disorder as the first occurring diagnosis in the comorbid pair were statistically significantly more likely to have a medical diagnosis of cancer than type II diabetes. The occurrence of the medical disease of cancer was found with both generalized anxiety disorder and major depression recurrent psychiatric disorders, with either disorder occurring first. In these instances, the occurrence was statistically significant compared to the occurrence of type II diabetes.

The findings of this study were consistent with the PNI research which has revealed a relationship between the presence of atherosclerosis, cancer, and type II diabetes with depression and or anxiety. Steptoe and Brydon (2005) present atherosclerosis as a vascular inflammatory process that leads to the development of lesions in the vascular walls. The lesions contribute to hardening of the vessels as well as blockage of blood flow through the vessel. The present study found that major depression recurrent was a statistically significant predictor for the presence of atherosclerosis, cancer, and type II diabetes. Findings from the current study also support research by

Jones et al. (2003) which also found support for the PNI model in the investigation of atherosclerosis in middle-aged women. They found that major depression recurrent resulted in a two-fold risk for the development of atherosclerosis for the 363 women included in their study. Results from the current study regarding atherosclerosis also contradict findings from Jones and colleagues which found that anxiety was not a predictor for atherosclerosis. As with the Jones et al. study, this study also found that generalized anxiety disorder and posttraumatic stress disorder were not statistically significant predictors of atherosclerosis.

The PNI model for cardiovascular heart disease as presented by Steptoe and Brydon (2005) can be used to explain the possible connection between emotional arousal states such as depression or anxiety and the presence of medical diseases. With depression and anxiety as the initiating psychiatric condition, stress associated with the conditions initiate the inflammatory process and the atherosclerotic process starts. As the vascular plaque builds blood flow is restricted or blocked. The restricted blood flow results in the restriction of oxygen and nutrients to the heart muscle. As the heart muscle cells become damaged or die the inflammatory response is initiated to remove the impaired cells. The progressive removal of the damaged heart cells is the cardiovascular heart disease process (Steptoe & Brydon, 2005). The present study found support for this PNI model, with major depression recurrent as a statistically significant psychiatric predictor of atherosclerosis. Ford et al. (1998) also found major depression to be a statistically significant predictor of cardiovascular heart disease.

Major depression recurrent and generalized anxiety disorder was statistically significant predictors for cancer in the cases in this study. Walker, Green, Greenman, Walker, and Sharp (2005) presented the PNI model for the development of cancer. They wrote that the physiological response to the prolonged psychiatric conditions of depression and anxiety could result in the impairment of the inflammatory response by the immune system. The impairment of the inflammatory response results in the failure of the immune system to recognize mutated self-cells. There is also a decrease in the production of immune system components that specifically target and rid the body of tumors, both benign and malignant (Walker et al., 2005). Jehn et al. (2006) conducted a study of 114 women who were on average 60 years of age. The researchers found that tumor status was associated with depression. In the study by John and colleagues, the level of depression was positively correlated with the progressive stage of cancer. The present study found the occurrence of major depression recurrent and generalized anxiety disorder presenting as the first diagnosis in the comorbid pair to be statistically significant predictors of the progressive stage of cancer.

Positive Social Change Implications

The social issue that this study addressed was the healthcare problem of psychiatric and medical disease comorbidity and the need to develop additional disease prevention assessment protocols. The health and quality of life for millions of individuals in the United States and world wide can be improved with the improvement of disease prevention assessments (Spiegel, 2003). The results from this study could be used to promote social change by contributing information regarding the relationship between the

comorbid psychiatric disorders and the inflammatory based medical conditions investigated in the study. Professionals could use the information to develop assessment plans that identify individuals with psychiatric conditions that are related to the comorbid medical diseases. Medical institutions could then develop prevention programs that minimize the subsequent development of the inflammatory diseases. The comprehensive prevention plans could encompass periodic screening for the onset of the inflammatory diseases, education related to the prognosis of the psychiatric disorders, as well as stress management techniques to manage stress associated with the psychiatric disorders. The overall intent of the prevention plans would be to implement preventative measures that interrupt or prevent the acute inflammatory response that precipitates the onset of the medical diseases among individuals with psychiatric disorders.

Limitations of the Study

This study may be difficult to replicate by researchers who do not have access to large healthcare facilities that use electronic medical record systems. Researchers would also need training on how to operate those systems. For this study, the researcher's ability to work within that system was invaluable for gaining medical corroboration of the diagnoses, timelines of disease onset, and the demographic and clinical histories for each case.

There were several factors related to this study that may limit the generalizability of the findings to the overall target population. First, the purposive sampling was limited to a single healthcare system located in Michigan. The demographic composition of Michigan, which is located in the northeastern region of the United States, may not be

representative of other regions of the country. As an example, the racial composition in Michigan is predominantly European American with African Americans as the second highest population racial group. Asian Americans comprised less than 3% of the Michigan population. Hispanic Americans comprise 4% of the population. Among the 1,209 cases reviewed, 680 were European Americans (63%), 351 were African Americans (32%), 11 were Asian Americans, and 8 were Hispanic Americans. Cumulatively, the Asian American and Hispanic American comprised less than 5% of the cases reviewed. There were thirty cases in the 'other' racial category. In determining whether or not the sample obtained for this study was representative of the demographic mix in the State of Michigan, the report by the 2008 census was used for comparison. The comparison revealed the European Americans were underrepresented in this sample. African Americans were overrepresented in the sample. Asian Americans and Hispanic Americans were underrepresented in the sample. The representativeness of the sample obtained has important implications for interpreting the findings, for generalizing conclusions, and for suggesting future research. In addition, the use of a single healthcare entity from which sample cases were selected may have unique aspects that may not be generalizable to other healthcare facilities.

Another factor was the study inclusion criteria which limited the cases reviewed to adults 21 years of age and older. Comorbid conditions of children and adolescents were not included in the study. The age of the individuals whose cases were reviewed was predominantly 50 years of age and over. Age may have had a confounding effect on the study because of possible age related medical conditions. Finally, the five year

population cycle for this study may not have been sufficient to detect the presence of the psychiatric disorder and medical disease comorbid condition among the cases not included in the study.

Recommendations for Action

In a study conducted by Wells, Rogers, Burnam, Greenfield, and Ware (1991) it was reported that patients with psychiatric disorders are treated in a variety of clinical settings. Those settings range from the general medicine physician to outpatient psychiatry. Therefore all healthcare sectors need to be informed of the psychiatric predictors for medical disease. Based upon the findings of this study it is recommended that patients with the diagnosis of major depression recurrent or generalized anxiety disorder to have on-going screenings for elevations in the inflammatory bio-immune markers for atherosclerosis, rheumatoid arthritis, cancer, and type II diabetes. In addition, those patients identified with these psychiatric disorders will need information regarding the possible health risk for the development of a comorbid disorder and the possible benefit of psychotherapy support.

There are several avenues available for the dissemination of the findings of this study. For the purpose of initiating a positive social change within a single healthcare organization, the healthcare system that was the research site for this study would be the first organization to approach. The organization had requested a copy of the results before the start of the study. The healthcare system also has a procedural track in place to consider innovative, evidence-based practices. This would be the appropriate venue to introduce a new disease prevention assessment approach. This researcher had the

privilege of serving on one of the committees from 2005 to 2007. The recommendations generated by the committee were implemented. In a broader spectrum, the healthcare system produces the PBS television program Minds of Medicine. This program is shown nation wide and it has won several Emmy awards for excellence. The purpose of the program is to present research conducted within the system and inform other healthcare organizations of the findings. Another means for disseminating the results could be through the American Psychological Association, of which the researcher is a member. The APA publishes over 60 journals. The APA encourages articles based on graduate research conducted by its members in an effort to encourage new researchers. Two of the journals that may be appropriate for this study are The American Psychologist and Psychological Review.

Recommendations for Further Study

A retrospective cohort longitudinal study using the medical records identified for this research, those patients identified with the psychiatric disorder who did not develop an inflammatory based disease compared to those who did develop the disease would be of benefit. It would be of interest to determine if the successful completion of psychotherapy was a statistically significant factor among either of the two groups with regard to the presence of disease. The review of psychotherapy utilization over time for patients with the psychiatric comorbidities and those who did not develop medical disease can address key treatment issues in PNI research regarding the assumption that psychotherapy will have a significant effect on medical disease prevention.

A prospective longitudinal study would be useful in further investigations of prediction in comorbidity development and analyzing psychiatric diagnoses as predictors. The present study could not provide information regarding the timing of disease onset, only the first documented disorder. A prospective study could make a contribution to this area of research.

Also in this study, the demographic characteristics of the cases reviewed suggest the need for further studies of the European American population because of the high comorbidity rate in that group. Even though the demographic mix of the sample in this study revealed this population to be underrepresented, those factors did not appear to influence the case distribution among the different comorbid pairs. In those distributions, the European Americans were dominant in the psychiatric diagnoses groups that were statistically significant predictors for the presence of disease. Those comorbid groups also had the highest mortality rates. Gender and age were also significant demographic factors. Future PNI studies should continue to include the factors of age, gender, and race to provide further information regarding these findings.

Finally, the availability of electronic medical records was an invaluable resource for this study. It is the recommendation to have more studies conducted using electronic medical records to gain documented clinical data with confirmed psychiatric and medical diagnoses.

Conclusions

This study was conducted to investigate the predictive potential for certain psychiatric disorders to predict the development of specific medical diseases. This study

accomplished identifying major depression recurrent and generalized anxiety disorder as statistically significant predictors for atherosclerosis, cancer, and type II diabetes. The observed frequencies for the biological and demographic variables revealed noteworthy information. National prevalence studies have reported high mortality rates among individuals suffering from psychiatric and medical disease comorbidity. The present study found the same occurrence of high mortality. As an example, in 14 of the 19 comorbid pairs the mortality rate ranged from 30% to 73.7% among the majority of the comorbid pairs (table 4). Based upon the findings of this study it is recommended that patients with the diagnosis of major depression recurrent or generalized anxiety disorder to have on-going screenings for elevations in the inflammatory bio-immune markers for atherosclerosis, rheumatoid arthritis, cancer, and type II diabetes. In addition, those patients with these psychiatric diagnoses will need information regarding the possible health risk for the development of a comorbid disorder and the possible benefit of psychotherapy support.

The psychiatric disorder as a predictor for medical disease model in this study offers direct, immediate application in healthcare practice. The findings of this study also offer specific direction for future research. The ultimate goal is to reduce the disability and death suffered by millions of individuals by increasing disease prevention assessment options and approaches.

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Appendix A: Data Based Search Sheet

Table 1
Participant Data Search Sheet with DSM-VI and ICD-9 Codes for the Comorbid Pairs

Comorbid Pair	DSM-IV plus ICD-9 Code
general anxiety disorder and atherosclerosis	[300.02 plus 440.9]
generalized anxiety disorder and cardiovascular heart disease	[300.02 plus 429.2]
generalized anxiety disorder and rheumatoid arthritis	[300.02 plus 714.0]
generalized anxiety disorder and cancer	[300.02 plus 199.1]
generalized anxiety disorder and type II diabetes	[300.02 plus 250.02]
posttraumatic stress disorder and atherosclerosis	[309.81 plus 440.9]
posttraumatic stress disorder and cardiovascular heart disease	[309.81 plus 429.2]
posttraumatic stress disorder and rheumatoid arthritis	[309.81 plus 714.0]
posttraumatic stress disorder and cancer	[309.81 plus 199.1]
posttraumatic stress disorder and type II diabetes	[309.81 plus 250.02]
major depression recurrent and atherosclerosis	[296.3 plus 440.9]
major depression recurrent and cardiovascular heart disease	[296.3 plus 429.2]
major depression recurrent and rheumatoid arthritis	[296.3 plus 714.0]
major depression recurrent and cancer	[296.3 plus 199.1]
major depression recurrent and type II diabetes	[296.3 plus 250.02]
dysthymic disorder and atherosclerosis	[300.4 plus 440.9]
dysthymic disorder and cardiovascular heart disease	[300.4 plus 429.2]
dysthymic disorder and rheumatoid arthritis	[300.4 plus 714.0]

dysthymic disorder and cancer [300.4 plus 199.1]

dysthymic disorder and type II diabetes [300.4 plus 250.02]

Appendix B: Coding System for Study Variables

First Diagnosis Psychiatric (**firstdx**)

Yes = 1

No = 2

Time Between Diagnoses (**timedx**)

1 to 5 Years = 1

6 to 10 years = 2

Beyond 10 years = 3

Chemical Dependence History (**cdhx**)

Yes = 1

No = 2

Family History of Psychiatric Diagnosis (**fampsyc**)

Yes = 1

No = 2

Family History of Medical Diagnosis (**fammed**)

Yes = 1

No = 2

Gender (**gender**)

Male = 1

Female = 2

Race/Ethnicity (**raceeth**)

Asian American = 1

African American = 2

European American = 3

Hispanic American = 4

Psychiatric Medical Comorbidity (**psymed**)

generalized anxiety disorder and atherosclerosis = 1

generalized anxiety disorder and cardiovascular heart disease = 2

generalized anxiety disorder and rheumatoid arthritis = 3

generalized anxiety disorder and cancer = 4

generalized anxiety disorder and Type II diabetes = 5

posttraumatic stress disorder and atherosclerosis = 6

posttraumatic stress disorder and cardiovascular heart disease = 7

posttraumatic stress disorder and rheumatoid arthritis = 8

posttraumatic stress disorder and cancer = 9

posttraumatic stress disorder and Type II diabetes = 10

major depression recurrent and atherosclerosis = 11

major depression recurrent and cardiovascular heart disease = 12

major depression recurrent and rheumatoid arthritis = 13

major depression recurrent and cancer = 14

major depression recurrent and Type II diabetes = 15

Dysthymic disorder and atherosclerosis = 16

Dysthymic disorder and cardiovascular heart disease = 17

Dysthymic disorder and rheumatoid arthritis = 18

Dysthymic disorder and cancer = 19

Dysthymic disorder and Type II diabetes = 20

Appendix C

Frequency Descriptive of Comorbid Pairs from the First Data base Search

Comorbid pair	n
Cases found for Generalized Anxiety Disorder: N = 1,458	
generalized anxiety disorder/atherosclerosis	1
generalized anxiety disorder/cardiovascular heart disease	0
generalized anxiety disorder/rheumatoid arthritis	4
generalized anxiety disorder/cancer	4
generalized anxiety disorder/type II diabetes	49
Cases found for Posttraumatic Stress Disorder: N = 263	
posttraumatic stress disorder/atherosclerosis	2
posttraumatic stress disorder/cardiovascular heart disease	0
posttraumatic stress disorder/rheumatoid arthritis	2
posttraumatic stress disorder/cancer	0
posttraumatic stress disorder/type II diabetes	11
Cases found for Major Depression Recurrent: N = 4,918	
major depression recurrent/atherosclerosis	12
major depression recurrent/cardiovascular heart disease	2
major depression recurrent/rheumatoid arthritis	36
major depression recurrent/cancer	4
major depression recurrent/type II diabetes	287
Cases Found for Dysthymic Disorder: N = 1,494	
dysthymic disorder/atherosclerosis	0

dysthymic disorder/cardiovascular heart disease	1
dysthymic disorder/rheumatoid arthritis	6
dysthymic disorder/cancer	1
dysthymic disorder/type II diabetes	61

Curriculum Vitae

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Education and Credentials

Bachelor of Science Degree in Psychology. Wayne State University

Master of Education Degree in Educational Psychology. Wayne State University

Limited Licensed Psychologist – State of Michigan

Ph.D. in Psychology – Walden University

Internationally Certified Advanced Addictions Counselor

Memberships

American Psychological Association, Student Affiliate

Psi Chi International Honor Society in Psychology

Work Experience

Orchards Children's Services - Southfield, Mi. Therapy for psychiatrically diagnosed to children in foster care, their biological parent and foster family. Court responsibilities and working with school systems on behalf of the children.

Integrity Stress Management Program – Detroit, Mi. Individual therapy to adults in a private practice facility.

Southwest Detroit Community Mental Health – Detroit, Mi. Psychotherapy for chronic mentally ill adults and dual diagnosed patients provided. Special Project: Co-therapist for the SAMI Program (Substance Abuse/Mentally Ill) with recognition received because of a significant decrease in number of patient requiring psychiatric hospitalization for a five year period of time.

Bazini Oak Clinic – Oakwood Hospital, Dearborn, Mi. Part-time general private practice under the supervision of psychiatrist, Dr. Bazini. Psychotherapy for children, adults, and families provided.

Community Care Services, CMH - Lincoln Park, Mi. Therapist in the Women's Intensive Outpatient Program for treatment of women who are chemically dependent.

Henry Ford Health System – Maplegrove Center – West Bloomfield, Mi. Inpatient Dept. Treatment of chemically dependent and dual diagnosed adults. Provide new patient evaluations and assessments, individual, group, and family therapy sessions and lectures. Special Project: Development of self-help program for anger management.