

EVALUATION OF THE VALIDITY OF CHOLESTEROL AS
A BIOMARKER FOR SUICIDE IN VETERANS

by

CHARLES REUTER

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written under the direction of

Barbara Caldwell, PhD, APN-BC

Karen D'Alonzo, PhD, RN, APNC, FAAN

and approved by

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ABSTRACT OF THE DISSERTATION

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By Charles Reuter

Dissertation Directors:

Barbara Caldwell, PhD, APN-BC

Karen D'Alonzo, PhD, RN, APNC, FAAN

Purpose: The purpose of this study was to investigate the use of total cholesterol as a biological marker for suicidality in a veteran sample.

Rationale: Previous research suggests low total cholesterol may increase the risk of suicidality in susceptible individuals by altering properties of the membranes in the brain. The low cholesterol levels appear to affect serotonin receptor exposure and cause a reduction of serotonin in the brain cells. This alters the reciprocal relationship between the serotonergic and dopaminergic systems and leads to an increase of impulsive, aggressive, self-directed aggressive behaviors, and suicidality in susceptible individuals.

Methods: Records of veterans seen at the Coatesville Veterans Affairs Medical Center for suicidality between 2009 to 2015 were reviewed. The variables identified for the study were extracted and analyzed. A total of 188 veteran records were analyzed.

Results: The cholesterol levels of veterans reporting suicide ideation or a suicide attempt were significantly lower than the group reporting neither [$F(2, 185) = 30.19, p = .000$]. There was a significant decrease in cholesterol in veterans who reported suicide ideation or a suicide attempt, when compared to an earlier visit which they were not reporting any such suicidality ($t(186) = 7.61, p < 0.05$). When attempting to define the characteristics of

veterans who reported either suicide ideation or a suicide attempt, it was clear that one group was younger, leaner, had more anxiety, sleep problems, and education than the other group.

Conclusions: There is compelling evidence that there may be a link between suicide ideation or a suicide attempt and a change in total cholesterol levels in veterans. More prospective research is needed to assess the reduction in total cholesterol levels to help clinicians identify veterans who are most at risk for suicide ideation or a suicide attempt.

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DEDICATION

To my wife Mindy and daughter Rebekah, who's love and patience I could not have done any of this without. My deepest eternal love and gratitude...

Rebekah, the world is your book. Open it up, experience it, and keep turning the page.

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CHAPTER ONE: DISCUSSION OF THE PROBLEM

The events of September 11, 2001 heralded the beginning of an onerous period of American history. Since that time, the United States has been engaged in the longest period of continuous war in its history. Although the United States has faced numerous political and economic challenges in the past, this period has tested the country's armed services in new ways previously not seen. The prolonged heightened state of military readiness that service members are pushed to maintain unfortunately creates an unmanageable level of stress for many in the ranks. The chronic stress stretches a service member's ability to cope, and degrades his / her individual readiness (Cersovsky, 2011). Too often, the end result of this unrelenting stress is depression, eventually leading to suicide.

Suicide is the 10th leading cause of death in the United States, claiming over 40,000 lives a year (Centers for Disease Control and Prevention (CDC)). The Army began officially tracking suicide rates in service members in 1980 (Bah et al., 2011), at a time when suicide rates were below the civilian rate. Since that time, suicide rates have steadily been rising while the country has been involved in two simultaneous wars (Operation Iraqi Freedom [OIF] and Operation Enduring Freedom [OEF]). In 2008, the Army suicide rate (22.2 per 100,000) surpassed the civilian rate (19 per 100,000) for the first time (Griffith, 2012a). In 2010, the National Guard suicide rate (31 per 100,000) surpassed the rates in both the Regular Army (25 per 100,000) and the Reserve component (23 per 100,000) (Griffith, 2012b). In 2011, the total Army's suicide rate of 22.9 per 100,000 (Luxton et al., 2011) was still rising, at almost double the United States civilian rate of 12.4 per 100,000 (Heron, 2013). Additionally, the last published United

States Department of Veterans Affairs (VA) Suicide Event Report identified 189.98 of all veterans per 100,000 have completed suicide between 2009 and 2012. Specifically, the VA reported a suicide rate of 44.99 per 100,000 between the ages of 18 to 29 (the largest age range of suicides) in 2005 and 56.77 per 100,000 in 2007 (Bah et al., 2011); both figures are significantly higher than the rates reported by the Army during the same time (12.7 and 16.8 per 100,000 respectively) (Black et al., 2011).

Even as the currently reported numbers by the VA are alarmingly high, the figures may in fact be lower than the true rates. As the VA stated in their last report, not all state data are included in the report, due to time constraints in analyzing the data for publication. Currently, only 21 states report suicide data to the VA. Additionally, two of the states with the largest veteran populations, California and Texas, do not report their data (Kemp & Bossarte, 2014). Furthermore, the rates may be artificially low due to classification bias on death certificates. Huguet (2014) examined death certificates and suicide mortality data from the National Violent Death Reporting System between 2003 and 2010 and cross-checked the data with Department of Defense (DoD) records. The authors reported that among the largest age group of those committing suicide (18–24 years), veterans were not specifically identified 58% of the time, indicating the reported veteran suicide rates may in fact be artificially low.

In an attempt to understand the underlying factors thought to contribute to the rise in suicide rates, much of the focus has been to identify those individuals who are most at risk. Unfortunately, much of the data are contradictory. One of the most contentious research questions is whether the number and/or length of deployments predict an increased risk for suicide. Some data suggest that the length and number of deployments

are correlated with increased risk of suicide (Friedman, 2014; Griffith, 2012; Hyman, Ireland, Frost, & Cottrell, 2012; Kline et al., 2010; Schoenbaum, Kessler, Gilman, & et al., 2014). Alternatively, other researchers have found no such correlation (Kang et al., 2015; LeardMann et al., 2013). In fact, research by LeardMann (2013) reports an inverse relationship between length of deployment and suicide risk, while Pitts et al. (2013) finds that it is not the deployment itself, but the presence of combat experience that is predictive. At particular risk are those individuals who have actively killed someone, rather than passively witnessing the event. Additionally, while Anestis et al. (2009) and Boscarino (2006) have identified Post-Traumatic Stress Disorder (PTSD) as a predictor of suicide risk, results of other studies contradict this finding (Krysinska & Lester, 2010; LeardMann et al., 2013). In addition to PTSD, Finley et al. (2015) describes a polytrauma clinical triad (PCT) comprised of PTSD, traumatic brain injury, and chronic pain, as a predictor of suicide risk. Pugh et al. (2014) describe four additional clusters beyond the PCT cluster that correlate to an increased risk of suicide including substance abuse, sleep disturbances, amputations, and chronic diseases. Additionally, there is data that indicates increasing numbers of military service members in general are increasingly being diagnosed with mental illnesses, which correlates with the increased suicide rate (Bachynski et al., 2012; Lazar, 2014; Lineberry & O'Connor, 2012; Nock et al., 2013).

Another issue confounding the increasing rates of suicide among the military is the presence of preexisting psychiatric problems in service members; these conditions may not have been identified prior to induction in the military, or were possibly exacerbated by the stresses of the military. Bachynski (2012) reported the rate of mental illness diagnosed among active duty service members had doubled between 2003 and

2008, mirroring the increasing military presence in Iraq and Afghanistan. With a vast number of service members being deployed, and an unprecedented number of service members on repeated deployments, the possibility exists that psychiatric conditions, which in ordinary situations would have been identified at the time of induction into the military, were instead overlooked. The 18-month Iraq troop surge began in 2007 and led into 2008; the period that followed saw a sharp rise in suicides and mental health diagnoses among military personnel. Lineberry (2012) explains that individuals with pre-existing psychiatric histories are normally identified before entering the military, and subsequently denied entrance. However, accurate diagnosis may not be that simple. Army Regulation (AR) 40-501 (Army, 2011a) which defines military disqualifications, lists specific mental illnesses and prior suicide attempt as grounds for disqualification for entrance into the military. The regulation that governs the Military Entrance Processing Stations (MEPS), AR 601-270 (Army, 2011b) does not address mental health other than section 8-9 of AR 601-270 which states, “The mere possibility that a psychiatric condition will arise later in military service should not be sufficient reason, in itself, for disqualification; however, such a possibility should be considered in light of other findings (such as conviction of juvenile court or adjudication of serious offenses, drug abuse history, and other background information made available to the chief medical officer) and DoD and USMEPCOM policy and guidance” (p. 15). There is nothing else mentioned in the regulations with regard to entrance into the military with any previous mental health issues. Furthermore, Nock (2013) examined 5428 records of United States Army service members and reported 58.3% of all men reviewed in the sample and 57.6% of all women reviewed in the sample had suicide ideations, and 54.9% of men and 45.9%

of women had suicide plans prior to age of enlistment. Additionally, 49.8% of men and 38.6% of women had attempted suicide prior to age of enlistment. These figures suggest that the underlying psychopathology was pre-existing, but only manifested itself with the added stressors of military service. Thus, the added burden on the military to maintain the necessary number of service members in two combat theaters, possibly allowed for individuals to enter into roles which in ordinary times, would not have been authorized.

The DoD reported in 2012 that 61% of veterans who committed suicide had accessed physical or mental health support services within the 90 days leading up to the event (Smolenski et al., 2012). During these physical and mental health support service assessments, it is common for routine blood-work to be performed. While laboratory tests are useful to diagnose specific disease states, laboratory tests may have predictive value as well. Cholesterol is one laboratory test commonly assessed on a yearly basis for active military personnel (Army, 2011a) and for veterans at Veterans Affairs Medical Centers. While the cholesterol screening is conducted primarily to identify those most at risk for cardiovascular disease, there is a growing body of research that suggests that low levels of cholesterol may predict those at higher risks for suicide (De Berardis et al., 2012).

Biomarkers are an umbrella term for biochemical, genetic, or molecular characteristics or substances used by various disciplines to explore, discover and understand a vast array of topics such as disease prediction through treatment and final outcome (Naylor, 2003). They can be substances that are measurable from human fluid, cells, or tissues; and are representative of various environmental or chemical exposures (Hulka & Wilcosky, 1988). The quintessential biomarker is neither expensive nor invasive to collect or measure, can identify clinical or treatment response phenotypes, can

identify changes in a disease, predict a disease, or confirm a diagnosis (Chiappori et al., 2015). The Army routinely tests cholesterol on every service member over 35 years old every year, and anyone under 35 years of age that may have cardiovascular risk factors (Army, 2011a). Likewise, many providers at Veterans Affairs Medical Centers routinely check a patient's cholesterol on admission. As serum cholesterol is inexpensive and routinely ordered, it is a prime biomarker to utilize for screening additional risk factors such as suicide.

Although the exact mechanism is unknown, it is posited that low levels of cholesterol (below 160 mg/dL) may cause an imbalance in serotonin and dopamine levels. Serotonergic parameters are associated with increased risk for suicide ideation and suicidal behaviors such as aggression and impulsivity (Ribeiro & Joiner, 2009). Additionally, deficiencies in the serotonergic system have been implicated in self-directed aggression (Ribeiro & Joiner, 2009). Research has shown that the serotonin and dopamine systems are closely related at a neurophysiological level. An alteration in the balance of the serotonergic system affects the balance of the dopaminergic system. While the neurotransmitter serotonin regulates emotion, behavior, and has inhibitory functions in the brain, a dysfunction of the serotonergic system has shown an increase in aggressive behaviors (Seo, Patrick, & Kennealy, 2008). There is a link between serotonin hypofunction with aggression and impulsive behavior (Seo et al., 2008; Virkkunen & Linnoila, 1993). The dopaminergic system is key to modulating aggressive behaviors and has a complementary relationship with the serotonergic system. As dopamine levels increase, the reciprocal properties of serotonin modulate aggressive behavior. When

dopamine levels increase, a deficiency or dysfunction in the serotonergic system fails to mediate the aversive actions (Seo et al., 2008).

Cholesterol levels appear to be affected by the serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) and dopamine metabolite homovanillic acid (HVA) (Gorwood, 2001). Brain-cell membrane proteins are sensitive to aqueous surroundings, are more exposed when lipid microviscosity is increased, and less exposed with higher fluidity (Engelberg, 1992). The phospholipid layer of biological membranes is a selectively permeable barrier, and loosely bound with cholesterol, so it can be interchanged with serum cholesterol. Low serum cholesterol may in-turn, lower the brain-cell-membrane cholesterol, thus lowering the lipid microviscosity, and decreasing the serotonin receptor exposure on the surface of the membrane. This results in decreased serotonin uptake from the blood and less serotonin into the brain cells (Engelberg, 1992). A reduction in cholesterol may cause an imbalance in serotonin and dopamine, which may increase depression, aggression, and self-directed aggression followed by an increase the likelihood of suicidal behavior (Mann, 2003; Zhang, 2011).

Statement of the Problem

1. Do cholesterol levels below 160 mg/dL increase the risk for either suicide ideation, or a suicide attempt (either successful or unsuccessful)?

Hypothesis: Lower cholesterol is associated with an increased risk for either suicide ideation, or a suicide attempt (either successful or unsuccessful).

2. Is cholesterol level associated with the lethality method of the suicide attempt (either successful or unsuccessful)?

Hypothesis: There is a relationship between cholesterol level and the lethality method of the suicide attempt (either successful or unsuccessful).

Secondary Aims

3. Does naturally or chemically lowered cholesterol confer a higher risk for either suicide ideation, or a suicide attempt (either successful or unsuccessful)?

Hypothesis: Suicidality is related to cholesterol medication, which chemically lowers cholesterol.

4. What is the individual change (within person change) between a non-suicidal individual's cholesterol level and a suicidal individual's level (suicide ideation or suicide attempt).

Hypothesis: There will be a significant decrease (15% expected) in total cholesterol from T1 (a non-suicidal cholesterol level) and T2 (a suicidal cholesterol level).

5. After developing a Latent Class Analysis model, how many classes are preferred, and what are the characteristics of the classes after being regressed on cholesterol?

Hypothesis: The characteristics of individuals with suicide ideation or attempting suicide will form individual classes representing various total cholesterol values.

The dependent variables are total cholesterol level, suicide attempt, and suicide ideation. The independent variables are the derived latent classes. The variables included for modeling in the latent class analysis are trauma (PTSD and TBI), substance abuse, support systems, family history of suicide, chronic pain, sleep difficulty and demographic characteristics. Cholesterol medication is a covariate in aim 3.

Definitions of Terms

The full and in-depth explanation of each defined term is described in detail with the rationale in chapter two. There are many reasons, causes, and variables that have been associated with suicide ideation, suicide attempts, and completed suicides. Many of these vary from individual to individual for a multitude of reasons. There are geographical, genetic, physiological, environmental, medical, and psychological components to consider. This study's primary aim is to explore the link between cholesterol, suicide ideation and suicide attempt (successful and unsuccessful). It is not possible in one study to explore every conceivable link or association with suicide. Thus, this study seeks to explore the main variables associated with the aims of this research as exhaustively as possible. While the original intent of the study was to also explore the association with completed suicides, when collecting the data, it became evident that the necessary variables necessary to explore that link was not available. This unfortunately excluded completed suicides from the analysis.

The largest group affected by suicide is veterans. The present study will take place at the Coatesville VAMC. To be eligible for veteran benefits and treatment at a VA facility, an individual must meet the definition of "Veteran" determined by the VA. The VA states, "For the purposes of VA health benefits and services, a person who served in the active military service and who was discharged or released under conditions other than dishonorable is a Veteran" (Veterans Affairs, 2014a).

Suicide

The term suicide originated from the Latin word *suicidium* meaning "self-murder" (Harris, 1704). Conceptually, suicide is a manifestation of the individual's desire to die

(Sadock & Sadock, 2008). The various categorizations of suicide, such as suicide ideation and suicide attempt, are discussed later. The term suicidality will refer to both suicide ideation and suicide attempt.

Operationally, suicide rates are published by the DoD in the in the Department of Defense Annual Suicide Event Report (DoDSER) (Smolenski et al., 2012). As stated in the DoDSER, suicides are determined by the Armed Forces Medical Examiner System (AFMES). As directed in DoD Directive Number 6490.14, the definition of suicide is defined by the National Center for Injury Prevention and Control, Division of Violence Prevention, Self-Directed Violence Surveillance Uniform Definitions and Recommended Data Elements (A. Carter, 2013). That definition of suicide is, “Death caused by self-directed injurious behavior with any intent to die as a result of the behavior” (Crosby, Ortega, & Melanson, 2011). This is also the definition the VA and CDC use for suicide. Although suicidal ideation and suicide attempts are not defined in the DoDSER, the CDC defines suicidal ideation as, “Thinking about, considering, or planning suicide” (CDC, 2015b). Additionally, a suicide attempt is defined as, “A non-fatal, self-directed, potentially injurious behavior with an intent to die as a result of the behavior; might not result in injury” (CDC, 2015b). For the purposes of this research, suicide ideation is defined as the desire to cause injury or harm to the self, with or without a plan, with the intent to die from the action. Additionally, for the purpose of this research, a suicide attempt is defined as the physical manifestation of the suicide ideation plan, and actions taken unsuccessfully to end the individual’s own life. Although completed suicide data was sought, the necessary variables for analysis in the study were not available. Thus, completed suicides were not available for the analysis in this study.

Lethality

Lethality is conceptually referred to in terms of the method of the intended suicidal action. The CDC has determined the rank order of suicide methods from most lethal to least lethal method. An individual choosing to end their life with a gun-shot has been determined to be the most lethal method (Vyrostek, Annest, & Ryan, 2004).

Operationally, lethality is defined as the method an individual chooses to employ in the suicide attempt. Methods will be determined from the patient care record, and based on the pilot study data, may include firearm, suffocation, cutting, jumping from height, and poisoning. An in-depth review of the CDC ranking of lethality will be discussed in chapter two, and the analysis of the method and rank order will be discussed in chapters three and four.

Cholesterol

Cholesterol is defined conceptually as a waxy, fat-like product of sterols, a lipid molecule. In eukaryotic organisms, sterols stabilize membranes composed of phospholipid bilayers. Cholesterol is invaluable to cell membrane function and structure, and required to produce hormones and water-soluble vitamins (Lamb, Kelly, Manning, & Kelly, 1998). Cholesterol is transported through the body by lipoproteins.

There are two types of lipoproteins which carry cholesterol, low-density lipoprotein (LDL) and high-density lipoprotein (HDL). Triglycerides are a type of fat that stores excess consumed energy. Total cholesterol is a calculation between LDL, HDL, and one-fifth of the triglycerides (AHA, 2015). This research focuses on total cholesterol.

Serum cholesterol is defined operationally as the laboratory value determined from a blood sample. The American Heart Association (AHA) states a total cholesterol

level under 200 mg/dL is desirable, a cholesterol level of 200 to 239 mg/dL is borderline-high, and over 240 mg/dL is very high. The AHA states the optimal score for a total cholesterol value is less than 180 mg/dL (AHA, 2014). Previous research into cholesterol and aggression indicates that a cholesterol level under 160 mg/dL puts an individual at risk. This occurs because the lipid microviscosity of the cell membrane is altered, reducing the availability of the serotonin receptors, thus triggering a cascade of events leading to a reduction of serotonin in the brain cells and ultimately suicide in susceptible individuals (Golier, Marzuk, Leon, Weiner, & Tardiff, 1995; Jacobs et al., 1992; Neaton et al., 1992; Zhang, 2011). This research is concerned with the total cholesterol level, and whether the level of 160 mg/dL identified by previous research is a significant identifier for increased risk of suicide ideation or a suicide attempt.

Depression

In the literature, depression is often reported as a significant predictor of suicidality (Hough & Lewis, 2010; Mościcki, 2001; Nock, 2011; Pfeiffer et al., 2013). The VA has identified depression as a significant cause of impaired quality of life and suicidality for veterans (US Department of Veterans Affairs). Conceptually, the guidelines the VA utilizes for identification and diagnosis of depression among veterans are based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR). The criteria has not been updated for the DSM-V. Depression is often classified according to the severity of signs and symptoms. Formal designations are Major Depressive Disorder (MDD) as well as mild, moderate, and severe depression. The VA (US Department of Veterans Affairs, 2009) follows the diagnosing criteria for MDD adapted from the DSM:

MDD diagnosis requires the presence of symptom 1, 2, or both; and at least 5 of 9 symptoms that persist for at least 2 weeks:

1. Depressed mood nearly every day for most of the day, based on self-report or observation of others
 2. Marked reduction or loss of interest or pleasure in all, or nearly all, activities for most of the day, nearly every day
 3. Significant non-dieting weight loss or weight gain (>5% change in body weight)
 4. Insomnia or hypersomnia nearly every day
 5. Psychomotor agitation or retardation nearly every day
 6. Fatigue or loss of energy nearly every day
 7. Feelings of worthlessness or excessive / inappropriate guilt nearly every day
 8. Diminished cognitive function (reduced ability to think or concentrate) nearly every day
 9. Recurrent thoughts of death and / or a suicide, suicide planning, or a suicide attempt
- (p. 13)

Depression is operationally defined by the clinician diagnosis in the health care record. All of the formal designations of depression listed earlier (MDD, mild, moderate, and severe depression and bipolar depression, as well as anxiety as it often co-exists with depression) will be grouped together as depression for the analysis. The VA depression assessment algorithm is provided in Appendix 1.

Trauma

The trauma that an individual endures is a significant contributor to suicidality. The forms of trauma identified in previous research to be included here are traumatic

brain injury (TBI) and post-traumatic stress disorder (PTSD). All trauma variables will be dichotomized as yes or no for analysis.

Traumatic Brain Injury. TBI is defined conceptually as a physical injury to the brain that can impair its functions either temporarily or permanently (Parikh, Koch, & Narayan, 2007). Operationally, TBI is defined by the diagnosis by the clinician and appearing in the health care record.

Post-Traumatic Stress Disorder. PTSD is conceptually defined as a traumatic or a perceived traumatic event that results in significant impairment to the normal functions of life (American Psychiatric Association & DSM Task Force, 2013). Operationally, the provider will determine the diagnosis of PTSD, as documented in the health care record.

Alcohol and Drug Abuse

Conceptually, alcohol and drug abuse are defined as the excess use of alcohol and drugs, which activate the reward systems of the brain. As a result, this activation reinforces the activity and can be so intense in some individuals, that the normal activities of daily living are neglected, and the drug or alcohol use becomes the primary reward sought by the individual (American Psychiatric Association & DSM Task Force, 2013). Operationally, the clinician determines and diagnoses an individual with alcohol or drug abuse and it is documented as a diagnosis in the health care record. For this study, alcohol and drug abuse will be diagnosed by the medical provider, or the mental health provider, and appear in the health care record. Additionally, the nursing admission assessment contains questions about illicit drug use and drinking patterns. The nursing assessment provides additional details beyond the diagnoses, not seen in the mental health or medical notes in regard to drug types, amounts, and frequencies. In the nursing assessment tool,

there are additional questions to determine if alcohol use has become a problem, if alcohol has negatively impacted the veteran's life, if the veteran has suffered seizures or blackouts as a result of alcohol use, and identification of the types of alcohol consumed. Once the data are collected, all illegal drug use from the sources listed above will be combined and dichotomized as yes or no for latent class analysis. Alcohol abuse will also be dichotomized from all sources listed above as yes or no for inclusion into the latent class analysis.

Support Systems

Conceptually, a support system is defined as a relationship that leads the individual to "...believe that he is cared for and loved, esteemed, and a member of a network of mutual obligations" (Cobb, 1976). Operationally, support system is determined by the interviewee's response to the interviewer asking about social support at home during the nursing admission assessment. Possible answers to the question included a possible response of none, family, friends, or military. A response other than none, indicated a positive response in the data.

Family History of Suicide

Conceptually, family history of suicide is defined as a family member with a genetic link to the individual having completed suicide (Qin, Agerbo, & Mortensen, 2002). Operationally, family history of suicide for this study is determined by the respondent answering in the affirmative to the interviewer asking about a family history of suicide during the nursing assessment interview.

Chronic Pain

Conceptually, chronic pain is any pain experienced by the individual beyond the period of time expected for healing. The pain may or may not be the result of a progressive disease, and there may or may not be an identifiable physical pathology for the pain (Flor & Turk, 2015). Operationally, chronic pain is identified in this study by the diagnosis of chronic pain in the medical record for the specific admission being reviewed. In the pilot study, chronic pain was identified as either, “Chronic Pain, Chronic Back Pain, or Chronic Neck Pain.” Other forms of chronic pain may exist in the medical record, and will be added to the data as observed.

Sleep Disturbances

Conceptually, sleep disturbances are the result of the individual not receiving the recommended seven to eight hours of sleep per night (National Institutes of Health, 2012). Sleep disturbances are commonly followed by depression, which is also associated with suicidality and is a risk factor for development of additional mental illnesses and substance abuse (American Psychiatric Association & DSM Task Force, 2013). Operationally, sleep disturbances are measured as the self-report by the respondent indicating they suffer from sleep disturbances when asked during the nursing admission assessment, or the diagnosis appearing in the diagnosis list in the medical record. The respondent reporting either difficulty getting the recommended number of hours of sleep a night, or nightmares (either related to war events or not related to war events) are asked of the respondent during the nursing assessment. If a respondent did indicate sleep disturbances, additional information was sought after in the medical record, but often not

available. This then leaves the definition of sleep disturbance open to interpretation of the respondent to determine whether or not he or she feels a sleep disturbance exists.

Delimitations

The study will be limited to veterans who have a relationship with the Coatesville VAMC between January 1, 2009 and December 31, 2015. This somewhat limits the geographical nature of the sample demographics, but not in totality. In evaluating the preliminary sample data, some veterans were transferred to Coatesville from other VAMC centers because of their specialty or previous relationships with the veteran.

Accuracy and availability of data are limited to what is accessible in the VAMC's Computerized Patient Record System (CPRS). The data in the system is entered by the medical and professional staff and is limited to their data entry. As such, data may be missing if not captured during the veteran's admission.

As stated earlier, research has shown depression to be a significant predictor of suicidality. Additionally, although Joiner (2005) does not include depression in the Interpersonal-Psychological Theory, he has previously tested the theory against depression. In the current sample, 85% of the subjects had a diagnosis of depression, eliminating the possibility of testing it against the other variables. This finding is not altogether unusual. Depression has been linked to the various other variables indicated in the current study such as low serotonin, chronic pain, and sleep disturbances (American Psychiatric Association & DSM Task Force, 2013; Cheatle, 2011; Chen, Lin, & Kao, 2015; Seo et al., 2008).

Significance of the Study

This research may produce evidence that supports the use of cholesterol as an additional screening tool for suicidality among providers. No research studies have been found that explore this approach in a military or veteran sample. While there are many factors that must be considered when evaluating a veteran for potential risk of suicide, the addition of one easy to interpret lab value can be invaluable to the clinician. This research has the potential of saving the lives of veterans suffering from emotional and psychological impairments.

Previous research has identified the variables discussed earlier to be associated with increased risk for suicidality. This research aims to examine these variables and determine if cholesterol is a valid and reliable tool for clinicians to utilize in determining an individual's overall risk for suicidality. The rates of service members and veterans completing suicide overcame the civilian rate for the first time it since was tracked in 2008 (Griffith, 2012a). These rates have continued to rise and have yet to show an indication of a plateau (Kemp & Bossarte, 2014; Smolenski et al., 2013). Identifying a common, simple to perform, non-invasive, and inexpensive test, which is both reliable and valid in helping a clinician determine if a service member is at risk for suicidality may prove to be invaluable. While great efforts by many are expended on reducing the prevalence of suicide in the military, a solution is elusive. Biomarkers offer promise in identifying those most at risk for suicide, but the cost can be prohibitive. However, both the military and VAMCs routinely for cholesterol levels on service members and veterans. Previous research has indicated that cholesterol may be a viable biomarker for suicide, but this relationship has not been researched in a veteran sample.

CHAPTER TWO: REVIEW OF THE LITERATURE

Chapter two presents a theoretical framework to guide this research study. The chapter also provides a review and synthesis of previous research of the variables identified for this study. The Interpersonal-Psychological Theory of Suicidal Behavior is discussed with the theoretical constructs of perceived burdensomeness, thwarted belongingness, and capacity for suicide. Following the discussion of the Interpersonal-Psychological Theory, a review of the empirical evidence of the variables included in this research study is discussed. The empirical evidence, theoretical components and a discussion of how cholesterol levels are related to suicide are explored. Lastly, a brief overview of research opposing the use of cholesterol as a biomarker for suicidality is provided.

Theoretical Rationale

Various conceptual frameworks exist to study suicide that can be applied to military personnel and veterans. In 2005, the Interpersonal-Psychological Theory of Suicidal Behavior was introduced (Joiner, 2005), which posits there are two mental states that, when occurring together, create a desire for suicide. Those two states are perceived burdensomeness and a sense of low belongingness. When those two states combine with a third factor, namely the capacity or the ability to commit the act, the theory proposes suicide is imminent (Joiner, 2009). While all three mental states are required to engage in suicidal behavior, a modification in one state can prevent the act of suicide (Monteith, Green, Mathew, & Pettit, 2009). According to the theory, the first two concurrent, relational propositions (thwarted belongingness and perceived burdensomeness) must occur together. When this combination occurs, it creates a desire for suicide. So while

thwarted belongingness and perceived burdensomeness are antecedents to desire, the entire theory posits that for the act of suicide to occur, a third concurrent concept must be present, and that is the capacity or capability for suicide (Joiner, 2009). A visual representation is provided in Figure 1.

Capacity

The main component of the Interpersonal-Psychological Theory is based on the principles of the Opponent-Process Theory, which proposes that repeated exposure to an affective stimulus changes over time. Instead of eliciting the original response, repeated exposure to the stimulus now elicits the opposite response (Joiner, 2009; Solomon, 1980). For example, with repeated exposure, an individual may lose the natural fear of a firearm and may actually develop an attachment for firearms over time. Among service members, it is believed that the capability and capacity for suicide is acquired over time, through repeated exposure to painful and fear-producing experiences such as fighting, combat, and weapons training (Selby et al., 2010). The theory posits an individual's experiences with painful events may not be the only factor that triggers suicidal behavior. Continued exposure to another's pain and injury, such as with military physicians who commonly treat severe combat injuries, can produce the same effect. Over time, these experiences create a higher tolerance for pain or fear and can create a sense of fearlessness for death (Joiner et al., 2009). Acquired capacity for suicide is continuous and cumulates with time. Repeated traumatic experiences and exposure to painful events will translate into greater risk (Ribeiro & Joiner, 2009). Anestis et al. (2009) theorizes that a history of childhood abuse and trauma has also been shown to create a sense of fearlessness in later life for painful experiences and death, thus compounding the risk for suicide in these individuals.

The amount and type of combat exposure and training service members engage in may increase the capacity to withstand painful and fear producing experiences. Regardless of the function they perform, many personnel in the Army commonly undergo intense combat and weapons training designed to teach soldiers how to eradicate enemies and to overcome the reservation to do so. Much of the training involves simulators that mimic real life war-time experience. Other training involves actors and is designed to reproduce a real event, including the feelings and emotions experienced in combat. The more thoroughly a service member is trained to engage in these activities, the less difficult it will be to engage in a real event when the time comes, and this may create a sense of imperviousness to the fears of death (Selby et al., 2010).

The third component of Joiner's theory links to biomarkers (Ribeiro & Joiner, 2009). Joiner and his research team have reviewed previous research on biomarkers that may correlate with suicidality. They have identified serotonin and norepinephrine as fitting with their model, both increasing self-directed aggressive behaviors (Ribeiro & Joiner, 2009). Appendix 2 presents the diagram of the Interpersonal-Psychological Theory.

Research has identified deficiencies in the serotonergic system and norepinephrine as increasing the potential for aggressive behaviors (Carballo, Akamnonu, & Oquendo, 2008; Mann, 2003). Even more importantly, deficiencies in both biochemicals have been associated with greater potential for self-directed aggression, which is an antecedent for lethal self-injury in the acquired capability component of the theory (Ribeiro & Joiner, 2009). Both the increased levels and increased frequency of aggressive behavior increase the level of acquired capability. Additionally, this

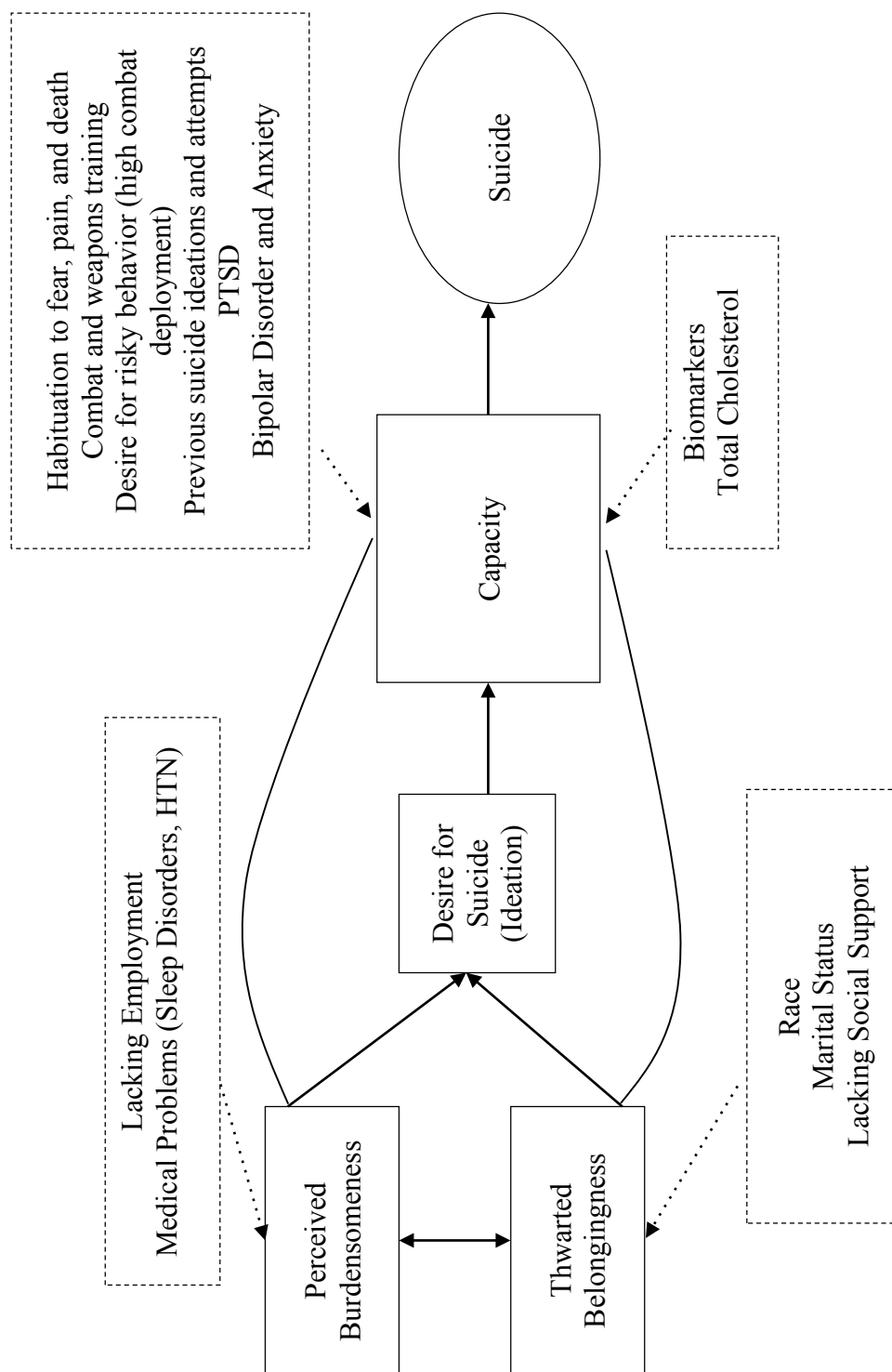


Figure 1. LCA Variables fitting the Interpersonal-Psychological Theory adapted from Joiner (2005).

Note: Applicability of various variables of the present study to the Interpersonal-Psychological Theory

component of the theory fits the stress-diathesis model for suicidal behavior as described by Mann (Mann, 2002, 2003; Mann, Waternaux, Haas, & Malone, 1999). This theory posits those who attempt suicide have a lower limit, or diathesis, for such behavior, suggesting that a relatively minor traumatic event can precipitate the suicide attempt. In this model, a low lipid level may lower the diathesis threshold and trigger the suicidal behavior.

Thwarted Belongingness

The concept of thwarted belongingness refers to the individual's sense that previously meaningful relationships have become hopelessly lost or strained and there is an inherent lack of connections to others (Anestis et al., 2009). The individual who lacks a sense of belonging has an unmet need for contact with family and friends, and feels he / she has no genuine connections to those individuals. There is a general sense of a lack of positive social interactions, and a feeling of not being cared about by others. Individuals with mental disorders or those who have been victims of childhood maltreatment have been shown to be at risk for loneliness or social isolation, which in turn creates the sense of thwarted belongingness (Van Orden et al., 2010). The sense of thwarted belongingness is especially germane to the military population, as veterans may feel family and friends have trouble connecting to them and do not understand their experiences (Selby et al., 2010). Additionally, many veterans who have fought in particularly unpopular wars such as OIF and OEF feel that their communities view them negatively and this increases the sense of thwarted belongingness (Koenen, Stellman, Stellman, & Sommer, 2003).

Burdensomeness

Perceived burdensomeness is experienced by individuals who feel they have been or are currently causing problems for others, are not able to make valuable contributions to society, or are a liability to the group's well-being (Anestis et al., 2009; Bryan, Morrow, Anestis, & Joiner, 2010). Individuals who lack employment, or are unable to obtain meaningful employment have been noted to have an increase in the sense of burdensomeness. Veterans who have been disabled or wounded in combat are at especially high risk for perceived burdensomeness. When veterans' disabilities prevent them from contributing to their families or society, and they sense they have lost a sense of purpose, the veterans may feel they are a burden (Selby et al., 2010).

In summary, the Interpersonal-Psychological Theory contains three main concepts, thwarted belongingness, perceived burdensomeness, and capacity. The concurrent, relational propositions (thwarted belongingness and perceived burdensomeness) must occur together according to the theory. When they do, the combination creates a desire for suicide. While these two concepts are relational to the desire, the entire theory posits that for the act of suicide to occur, a third concurrent relational proposition must be present, and that is the capacity or capability for suicide (Joiner, 2009). The current research focuses on the capacity, a component of the theory that pertains to biomarkers. This research aims to evaluate the hypothesis that low cholesterol affects serotonin circulation in the body and increases self-directed aggressive behaviors in susceptible individuals leading to increased risk for suicidality.

Independent and Dependent Variables

Guided by the Interpersonal-Psychological Theory of suicide and previous research, the following variables are discussed, along with evidence supporting their inclusion in this research. The dependent variables are total cholesterol level, suicide attempt, and suicide ideation. The independent variables are the derived latent classes. The variables included for modeling in the latent class analysis are trauma (PTSD and TBI), substance abuse, support systems, family history of suicide, chronic pain, sleep difficulty and demographic characteristics such as sex, education, and marital status.

Cholesterol and Suicide

The first report of an association between cholesterol and suicidality was published in 1969, in a primary prevention study to reduce unsaturated fat in diets of veterans in the Los Angeles VAMC, in order to prevent complications of atherosclerosis (Dayton, Pearce, Hashimoto, Dixon, & Tomiyasu, 1969). Researchers identified an increase in deaths unrelated to illness when cholesterol levels were lowered over 15% from individual's baseline, as compared to the control group. Although the deaths unrelated to illness included suicide, the researchers did not follow-up on this observation.

Various studies dating back to the 1970's explored the link between cholesterol and impulsivity, aggression, violence, and suicide. The earliest such study that explicitly studied the link was published by Virkkunen (1979). The author examined 274 subjects who committed various criminal offenses and found that those with personality disorders had significantly lower mean cholesterol values. Virkkunen (1983) later identified a correlation between low cholesterol levels and suicide among male homicide offenders.

In 1994, Kaplan designed an experimental study where he examined aggression, level of affiliation, and cerebrospinal fluid levels of 5-hydroxyindoleacetic acid (5-HIAA) in juvenile cynomolgus monkeys fed diets either in low-fat / low-cholesterol or high-fat / high-cholesterol. The monkeys who received the low-fat / low-cholesterol diets were more aggressive, less affiliative, and measured lower levels of 5-HIAA than their counterparts fed the opposite diet ($p < .05$) (Kaplan et al., 1994).

Zhang (2011) published a meta-analysis of previously published research identifying a correlation between cholesterol level and suicides. Of the 29 articles reviewed, 23 found that cholesterol levels were lower in those who attempted or completed suicide, three research studies found that cholesterol was higher, and three research studies found no association. The meta-analysis identified that cholesterol levels among the suicide attempts and completed suicides ranged from 147 mg/dL to 192 mg/dL ($M = 161$ mg/dL, $SD = 14.3$). The control groups had cholesterol levels which ranged from 159 mg/dL to 234 mg/dL ($M = 197$ mg/dL, $SD = 20.3$). This is consistent with other published research. Golier et al. (1995) examined 650 patients with a history of attempted suicide, and reported men with cholesterol levels below 160 mg/dL were at greater risk for suicide than those with higher levels. Atmaca et al. (2002) conducted research with 24 suicide attempters and 24 controls. The author reported mean cholesterol levels of 152.26 mg/dL (14.39) in suicidal patients, and 186.44 mg/dL (32.56) in the non-suicidal control group. Interestingly, Atmaca (2008) conducted further research, to examine cholesterol values among violent ($n = 19$) and nonviolent suicide attempters ($n = 16$), and controls ($n = 20$). The mean cholesterol values were lower

among the violent attempters ($M = 140.2$ mg/dL, $SD = 24.1$ ($p < 0.05$)), than the nonviolent attempters ($M = 164.5$ mg/dL, $SD = 28.4$ ($p < 0.01$)), and the control group ($M = 193.7$ mg/dL $SD = 27.90$ ($p < 0.001$)) respectively. In summary, previous research indicates suicidal individuals have a lower cholesterol level than non-suicidal samples, indicating a significant area for further research into suicidality.

Lipids

Lipids have several biological properties, including comprising the structural components of cell membranes and signaling. About half of the dry matter of the brain is composed of lipids, which are naturally occurring molecules. Examples of lipids are fat-soluble vitamins, sterols, fats, monoglycerides, diglycerides, triglycerides, phospholipids, and cholesterol. Lipids are found in the myelin sheath, axon, and the synaptosomal membrane. Engelberg (1992) proposes that anything that affects the balance of cerebral lipid metabolism can profoundly affect brain functioning.

Serotonin

Approximately 15% of the dry weight of the brain is composed of cholesterol. Serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) and dopamine metabolite homovanillic acid (HVA) in circulation are determined by the balance of cholesterol and polyunsaturated fatty acids. Changes in this balance may alter brain functioning and behavior by modifying cell membranes and may subsequently alter production, reuptake, and metabolism of neurotransmitters (Zhang, 2011).

Serotonin (5-hydroxytryptamine or 5-HT) is a monoamine neurotransmitter, biochemically derived from tryptophan. Serotonin is primarily found in the gastrointestinal (GI) tract and the central nervous system (CNS). Serotonin

(5-hydroxytryptamine or 5-HT) and its major metabolite 5-hydroxyindoleacetic acid (5-HIAA) are largely involved in regulating emotions and impulse control, and low levels have been linked to impulsive and aggressive behaviors (Seo et al., 2008).

Cholesterol

Previous research consistently links low levels of serotonin with impulsivity, aggression, self-directed aggression and suicide (Ribeiro et al., 2014). From a neurophysiological perspective, serotonin and dopamine work in coordination with each other, and changes in the serotonergic system can alter the balance of the dopaminergic system. Serotonin regulates emotions and behaviors and also regulates inhibitory actions such as aggression. In laboratory settings, alterations in serotonin levels have been shown to increase aggression in both animals and humans (Seo et al., 2008).

Low levels of 5-HIAA may be associated with aggression, violent suicide attempts, impulsive murders, and recidivism of murderers in humans (Seo et al., 2008). In a study of 650 psychiatric patients, Golier et al. (1995) indicated that men with cholesterol levels less than 160 mg/dL, or below the 25th percentile, were twice as likely to have made a serious suicide attempt. Low blood serotonin has been shown to increase aggression, and likewise, in susceptible individuals, can increase self-directed aggression or suicide (Golier et al., 1995; Gorwood, 2001; Kaplan et al., 1994; Neaton et al., 1992). In another study examining cholesterol and mortality rates in coronary heart disease patients, Neaton et al. (1992) reported an increased risk for suicide among subjects with cholesterol levels below 160 mg/dL.

Research indicates that the fluidity, viscosity, and functional properties of membrane dynamics are the result of membrane lipids and proteins acting in balance with

each other. When lipid microviscosity is increased, the proteins in the membrane become more exposed to aqueous surroundings. With higher fluidity, they become less exposed. The lipid microviscosity affects various functions of the membrane such as signal transmissions, transport processes, receptor binding, and protein phosphorylation. The main determinant of the microviscosity of lipid regions is the cholesterol / phospholipid molar ratio, and the main lipid components of biological membranes are cholesterol and phospholipids. As cholesterol levels increase, so does membrane lipid viscosity (Engelberg, 1992).

Heron et al. (1980) studied the synaptic membranes of mice *in vitro*. Their research found that as the microviscosity of the membrane was increased, serotonin binding was increased five-fold. Engelberg's (1992) hypothesis is that cholesterol is loosely bound in the phospholipid layer of membranes. Here, it freely exchanges with serum cholesterol. Lowering serum cholesterol, then lowers brain-cell-membrane cholesterol, lipid microviscosity, and also decreases protein serotonin receptor exposure on the membrane surface. As a result, serotonin uptake from the blood is reduced, which results in less serotonin entering the brain cells. The reciprocal relationship of serotonin and dopamine described earlier is kept in balance. Whereas serotonin normally has a modulating effect on the resulting aggressiveness seen with an increased level of dopamine, this mechanism is inhibited when cholesterol levels are low (Seo et al., 2008). The resulting decrease in receptor functioning leads to reduced suppression of impulsive, aggressive, and self-directed aggressive behavior in susceptible individuals (Zhang, 2011).

While instruments do exist to test measure the various components associated with suicidality more directly, none can be administered as routinely and simply, or are as cost effective as serum cholesterol samples. To test 5-HIAA requires a 24-hour urine specimen (Mayo Medical Laboratories, 2015b) and dopamine is measured via a blood plasma test (Mayo Medical Laboratories, 2015a). Although prices will vary by contract, the average cost for a 5-HIAA test is \$140 and a Plasma EDTA Meta for Dopamine is \$350. Research thus far has shown a strong correlation between serum cholesterol and 5-HIAA, indicating cholesterol may be an acceptable surrogate for 5-HIAA (Asellus, Nordstrom, & Jokinen, 2010; Jokinen, Nordstrom, & Nordstrom, 2010).

Previous research has established cholesterol as a reliable biomarker in making medical clinical decisions (Al-Delaimy et al., 2006; Sang-Ah et al., 2008). Furthermore, while this study sample was taken from a controlled clinical environment where subjects followed the fasting recommendations for cholesterol screening, research has also determined that non-fasting cholesterol levels are similar to fasting levels and are appropriate for clinical decisions, further expanding the possibility of cholesterol screening (Craig, Amin, Russell, & Paradise, 2000). Thus, total cholesterol may alter the microviscosity of the brain cell membrane, reducing serotonin receptor exposure. This results in less serotonin uptake, and an alteration in the balance between serotonin and dopamine, thus triggering the increased risk of suicide ideation or suicide attempt in susceptible individuals.

Suicide

The Interpersonal-Psychological Theory aims to identify those individuals who are most at risk for suicidality. To aid in understanding suicidality in the context of the proposed research, a number of concepts will be discussed.

In research, attributes and antecedents are valuable concepts needed to understand suicide. Attributes are regarded as the cause of a phenomenon (Walker & Avant, 2005). An antecedent is defined as a variable or event that precedes another variable or event (Walker & Avant, 2005). In the context of the Interpersonal-Psychological Theory, as described earlier, burdensomeness and thwarted belongingness create the desire for suicide. Once capacity has evolved, suicide is imminent (Joiner, 2009).

Joiner and his research team argue that capacity, the ability to take the necessary actions to successfully complete a suicide, is an iterative process, and habituation is a key here. As described earlier, some of the items that aid in capacity for suicide are fear producing experiences such as fighting, combat, and weapons training. As suicide becomes imminent, the individual has to be comfortable, or less fearful of the concept and the method. The beginning of the iterative process is the suicidal ideation. Habituation with the suicidal ideation leads to the suicide attempt, which if successful, is the completion or culmination of the process. In some individuals, the unsuccessful attempts are the habituation to the successful suicide completion (Joiner, 2009; Joiner, 2005; Ribeiro & Joiner, 2009; Van Orden et al., 2010). See Figure 1 for a visual representation.

Van Spijker et al. (2014) describes the attributes of suicide as repetitious and difficult to control suicidal thoughts. Additionally, repeated suicidal ideations are

associated with the emergence of suicidal behaviors and cause a reduction in the level of distress associated with suicidal thoughts. This also causes a severe impact on daily functioning. From the perspective of the Interpersonal-Psychological Theory, the attributes of suicide are an individual's sense that he/she is a burden to others, does not have a sense of belonging, and has acquired a capacity for suicide (Joiner et al., 2009). Lineberry (2012) identified attributes to suicide in the military as substance abuse and dependence and psychiatric illness. A meta-analysis identified that more than 90% of service members completing suicide had a co-existing psychiatric illness (Lineberry & O'Connor, 2012). Between 2008 and 2014, the Army and the National Institutes of Mental Health funded the Army Study to Assess Risk and Resilience in Service-members (Army STARRS). The study is the largest mental health study ever conducted with military personnel. As part of this study, Nock et al. (2013) identified key attributes to suicidality among service members. These attributes included childhood adversities (physical and sexual abuse, neglect, household dysfunction), acute stressful life events (family/romantic conflicts, divorce, infidelity, military sexual trauma), chronic stressful life events (chronic pain, illness), military related stressors (combat exposure, injury, bereavement, negative unit climate), sleep issues, PTSD, depression, and hopelessness.

The antecedent consistent with all suicides is the desire for death. Prior to the act of suicide, the desire must exist and override the desire to live (Mann, 2002; Mościcki, 2001). Chapman and Dixon-Gordon (2007) identified antecedents to suicide as intense anger within the individual, and a sense of ambivalence towards suicide. The most common psychiatric diagnosis viewed as an antecedent by Chapman and Dixon-Gordon (2007) is borderline personality disorder. Knox and Caine (2005) argue the strongest

antecedent of suicide is alcohol addiction, followed by respiratory infections and the human immunodeficiency virus (HIV). Furthermore, contrasting to Chapman, Knox describes the antecedent mental health diagnosis with the greatest link to suicide is depression. Conversely, Van Orden et al. (2010) and Nock et al. (2013) argue that depression is not an antecedent to a suicide attempt or completion, rather to suicide ideation and suicide ideation is an antecedent to suicide attempt and completion.

Other antecedent conditions that are commonly associated with suicides in the literature are childhood trauma, poor psychosocial support, lack of religious beliefs, family history or a genetic component, and low serotonin levels (Mann, 2002). Common to all suicides is the physical act of ending a life. For males in the military, the act is customarily performed with a firearm, and for females, drug overdose is the method of choice (Black, Gallaway, Bell, & Ritchie, 2011). The effect of other antecedents for suicide in veterans, such as deployments, are not conclusive. Data from research studies vary with regard to deployments and combat experience. Some research data suggest that deployments are correlated with increased risk of suicide (Friedman, 2014; Griffith, 2012; Hyman, Ireland, Frost, & Cottrell, 2012; Kline et al., 2010; Schoenbaum, Kessler, Gilman, & et al., 2014). Alternatively, other researchers have found no such correlation (Kang et al., 2015; LeardMann et al., 2013).

In summary, previous research has identified various attributes of suicide. These include repetitive and difficult to control suicidal thoughts that impact daily functioning, psychiatric illness, childhood adversities, acute stressful life events, sleep difficulty, PTSD, depression, and hopelessness. Antecedents to suicide include a desire for death which overrides the innate desire to live, intense anger, ambivalence to suicide, alcohol

addiction, HIV, childhood trauma, family history of suicide, low serotonin levels, and depression. The debate as to whether a deployment, the act of moving military personnel, equipment, and logistical support services to an area of operation outside of the contiguous United States (OCONUS) is correlated to suicidality is not clear. Six studies find a relationship between deployments and suicidality, and indicate that the repeated physical and mental stress placed on the service member degrades their psychological wellbeing. However, three studies do not find a correlation. One such example is the study by LeardMann (2013); when controlling for age and sex, and across all military branches, the author found an inverse relationship between deployments and suicidality, claiming the more time spent on deployments correlates with a reduced risk of suicidality. Across all the research studies, the variables consistently correlated with suicidality are depression and alcohol abuse.

Lethality

The method employed by an individual whom chooses the path of suicide is not without significance. The most recent DoDSER identifies the most common form of suicide completion across all branches of the military is by firearm (Table 1), followed by hanging and drug or alcohol overdose. The most common suicide attempt method across all branches of the military and the VA is drug and alcohol overdose (the VA only reports suicide attempt methods, and not completion data) (Kemp & Bossarte, 2014; Smolenski et al., 2013). The differing suicide approaches among attempts and completions can most likely be explained by lethality level of the method; the more lethal a method is, the more likely the attempt is to result in a completed suicide.

The CDC has categorized the lethality of self-harm (suicide) methods. Examining 30,622 fatal and non-fatal injuries, the CDC ranked (from most lethal to least lethal) gun shots ($n = 16,869$, 55.1% fatal), followed by suffocation (inhalation) ($n = 6,198$, 20.2% fatal), poisoning ($n = 5,191$, 17.0% fatal), other ($n = 1,109$, 3.6% fatal), fall ($n = 651$, 2.1% fatal), cut ($n = 458$, 1.5% fatal), unknown ($n = 146$, 0.5% fatal) (Vyrostek et al., 2004). Research has demonstrated a correlation between low serotonin levels and high lethality of method used in suicide attempts (Mann & Malone, 1997). Mann studied 22 patients with depression who attempted suicide. To determine lethality method, he utilized the Medical Damage Rating Scale which rates medical damage from zero equaling no damage to eight equaling death. The sample included 16 overdoses, 2 self-inflicted lacerations, 2 hanging, 1 jump from a potentially deadly height, and 1 shooting. To assess for levels of serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) among subjects in the study, a lumbar puncture was performed in the sample. Patients were also assessed for depression with the Hamilton Depression Scale, hopelessness with the Beck Hopelessness Scale, and by the number of suicide attempts. The authors did not find any correlation between lethality level and depression, previous number of suicide attempts or hopelessness. When examining 5-HIAA levels, the researchers identified one significant observation, a lower 5-HIAA level in those with a high lethality method compared to low lethality method (83.7 ± 24.2 vs. 109.7 ± 28.2 pmol/mL; $t = 2.29$, $df 20$, $p = .03$). Additionally, a high suicide planning score, assessed by the Suicide Intent Scale, was also correlated with lower 5-HIAA levels ($\chi^2 = 4.23$, $p < .04$). Mann did acknowledge the obviously small sample size, but given the difficulty of studying this specific topic, the results are still persuasive.

In summary, there is early compelling data that supports the relationship between suicidality and lethality method. The method chosen by a suicidal individual may have a biological basis that has not been fully explored. As yet, no findings have been found which link cholesterol level and lethality method, in a veteran sample, and this research aims to explore this link.

Table 1

Number and Rate of Suicide by Branch of the Military

Branch	Completion		Attempt	
	<i>N</i>	%	<i>N</i>	%
Air Force ^a				
Firearm	26	62.8	13	5.0
Hanging	9	20.9	22	8.5
Drugs / Alcohol	3	7.0	156	60.2
Army ^a				
Firearm	71	61.7	50	10.2
Hanging	34	29.6	48	9.8
Drugs / Alcohol	3	2.6	284	57.8
Marines ^a				
Firearm	30	66.7	12	5.2
Hanging	14	31.1	28	12.2
Drugs / Alcohol	0	0	127	55.5
Navy ^a				
Firearm	21	50.0	4	4.0
Hanging	15	35.7	14	13.9
Drugs / Alcohol	1	2.4	47	46.5
Veterans Administration ^b				
Poisoning			24,058	51.0
Intentional unspecified			5,425	11.5
Firearms			5,148	10.9
Sharp Object			4,842	10.3
Hanging			3,045	6.5

^aSmolenski, 2013 (most current DoDSER).

^bKemp, 2014, VA data only reports attempts. Period is between 2009-2012.

Depression

Depression is cited in the literature as a significant predictor of suicidality (Hough & Lewis, 2010; Mościcki, 2001; Nock, 2011; Pfeiffer et al., 2013). Joiner does not

include depression into the Interpersonal-Psychological Theory. Rather, he tests the theory against depression and concludes the theory is a better predictor of suicidality than depression (Joiner, 2009; Joiner et al., 2009). Joiner et al. (2009) conducted a research study with 815 participants comparing the various components of the Interpersonal-Psychological Theory to depression, family history, and suicide attempts. The study found that participants with a six month to lifetime history of depression predicted suicide ideation $F(2, 812) = 82.43, p < .05$. However, thwarted belongingness and burdensomeness predicted suicide ideation beyond depression $F(2, 810) = 17.31, p < .05$.

Although Joiner does not include depression in the theory, other researchers have demonstrated an association between hopelessness, one of the components of the theory, and depression (Cuijpers et al., 2013). Cuijpers (2013) conducted a meta-analysis of 13 research articles and 616 study participants. In a metaregression analysis, using the effect size of hopelessness as the dependent variable and the effect size of depression as independent variable, there was a significant association (slope: 0.74; 95% *CI*: 0.49–1.00; $p < 0.001$) between the two variables.

The most current DoDSER reports 55.2% of service members who completed suicide had a previous diagnosis of depression, and 70.75% of service members who attempted suicide had a previous diagnosis of depression (Smolenski et al., 2013). The rate of depression in veterans is not reported in their official suicide data report (Kemp & Bossarte, 2014), but the National Alliance of Mental Illness (NAMI) reported their research indicates 14% of all veterans suffer from depression and 95% of veterans completing suicide had a diagnosis of depression (NAMI, 2009).

However, it should be noted that not everyone with depression will experience suicidality. Depression may have neurological underpinnings, by affecting brain performance in the area of behavior regulation, at varying levels of severity. Research findings suggest that individuals with depression who complete suicide may have had dysfunction in the hypothalamic–pituitary–adrenal (HPA) axis, or abnormalities in the activity of the mitogen-activated protein (MAP) kinase, which may reduce its neurotrophic activity along with other physiological actions in the brains of those with depression and a propensity to suicidality (Mann, 2003). Beck (2008) suggests depression is correlated with a hypersensitive amygdala which is associated with a genetic polymorphism. This leads to a prejudice towards negative cognitive appraisals and a dysfunction in beliefs, which can lead to an increased risk for suicidality. There is also research examining the anterior cingulate cortex (ACC), located on the medial surface of the frontal lobe and how it relates to suicidality. The ACC monitors performance, behavior, and maintains executive control of cognition. A dysfunction in this region of the brain has been seen in patients diagnosed with depression who have attempted suicide (C. Carter et al., 1998). A research study of OEF and OIF veterans with combat experience and suicide ideation showed hyperactivity on both the ACC and prefrontal cortex (PFC) regions during self-monitoring exercises. Matthews et al. (2012) hypothesized that greater effort during self-monitoring as seen by the hyperactivity in the ACC and PFC, represents a vulnerability in the coping mechanism, which could lead to suicidality during events that require greater self-control. While there are research studies that support a neurological basis for the association between depression and suicidality,

the components of the Interpersonal-Psychological Theory may prove to be a better predictor of who is at risk for suicidal behavior.

The Anxiety and Depression Association of America (ADAA) (2015) states that while depression and anxiety are two separate disorders, they are often seen together. Previous research into behavioral risk factors has confirmed this association (ADAA, 2015; Strine et al., 2015). In this research, these two variables were associated and are discussed in chapter three in regard to conditional independence.

In summary, depression is a complex phenomenon. It is the result of, and can lead to many other forms of adverse behaviors, such as suicidality. Depression has been identified as a factor in suicidality, both in the general population and the military, but the rates are not reported by the VA. Research findings are suggestive of a neurological and physiological basis of depression. The link between a decrease in serotonin and depression is well established, and the use of selective serotonin re-uptake inhibitors to increase the amount of extracellular serotonin in the brain is among the most commonly used prescription drug treatments for depression (Chen et al., 2015; Seo et al., 2008). Research has shown that it is a variable worthy to be considered in suicidality research.

Trauma

Various forms of trauma have been implicated in suicidality. The forms of trauma identified for further analysis are TBI and PTSD. An explanation and justification of these forms of trauma follows.

Traumatic Brain Injury. TBI is a physical injury to the brain that can impair brain function, either temporarily or permanently (Parikh et al., 2007). Some common injuries are concussion, cranial fracture, cerebral contusion, or traumatic intracranial

hemorrhage (Teasdale & Engberg, 2001). Considered one of the seminal research studies examining TBI and suicide, Teasdale (2001) performed a research study consisting of 145,440 patients with traumatic brain injury, and found that patients with TBI (concussion, cranial fracture, or intracranial hemorrhage) were at significantly greater risk for suicidality than the general population. Using Cox regression analysis, the author found the hemorrhage group (hazard ratio = 1.66, 95% *CI* 1.17–2.35) had the highest rate of suicides compared to the concussion group (hazard ratio = 1.42, 95% *CI* 1.15–1.75) and the fracture group (hazard ratio = 1.50, 95% *CI* 1.06–2.13).

Brenner (2011) compared 850,472 veterans who received care at the VA for suicidality and found that veterans with TBI were 1.55 times greater (95% *CI* 1.24-1.92) to complete suicide than veterans without a history of TBI, indicating that TBI is a significant variable to consider during analysis of suicidality in veterans. The most recent DoDSEER reports 4.9% of completed suicides, and 6.1% of suicide attempts were diagnosed with TBI (Smolenski et al., 2013). Individuals affected by TBI are not identified in the VA Suicide Event Report.

Post-Traumatic Stress Disorder. The VA (2015) reports that 7 to 8% of the general population will develop PTSD during their life. PTSD occurs as the result of the individual being exposed to death (perceived or actual), or serious injury or traumatic event. The exposure may not necessarily involve the individual himself, but can include the witnessing or knowledge of a traumatic event experienced by others. The traumatic event results in intrusive symptoms that deeply and significantly affect the individual. The effects of the event can manifest themselves in symptoms which can be debilitating

and prevent normal or perceived normal functioning of the self (American Psychiatric Association & DSM Task Force, 2013).

Research has demonstrated those diagnosed with PTSD to be at increased risk for suicidality (Davidson, Hughes, Blazer, & George, 1991; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995). More recently, research findings have suggested service members and veterans with PTSD are at increased risk for suicidality (Milliken, Auchterlonie, & Hoge, 2007). Hoge et al. (2008) examined 2525 Army infantry service members after returning from a deployment to Iraq in 2008. Of the 2525 service members examined, 43.9% met DSM criteria for post-traumatic stress disorder (PTSD). In the most current release of the DoDSER, 55% of service members across all branches of the military who attempted suicide had previously been diagnosed with PTSD, and 40.5% of service members who completed suicide (Smolenski et al., 2013).

In 2011, the DoD released the Department of Defense Health Related Behaviors Survey of Active Duty Military Personnel which indicated that only five percent of all military personnel overall report PTSD symptoms, and the highest rate are in the Army and Marines at 7.2% and 7.3% respectively (Barlas, Higgins, Pflieger, & Diecker, 2013). As the incidence of PTSD in service members completing and attempted suicide reported in the DoDSER are 40.5% and 55% respectively, service members may be underreporting symptoms, indicating many they may be at greater risk for suicidality than the DoD may estimate.

Research suggests that PTSD and TBI may increase suicidality due to damage to the frontal lobe, which may increase impulsivity and lead to increased risk of suicidality (Yurgelun-Todd et al., 2011). Other research also suggests that PTSD may not exist in

isolation, but co-exists with depression as a comorbid illness. Thus, activation of the psychological pathways described earlier in depression thought to increase the risk for suicidality (Ljubicic, Peitl, Peitl, Ljubicic, & Filipovic, 2009).

In summary, various forms of trauma (TBI and PTSD) are associated with suicidality. Research has found patients suffering from TBI were at greater risk for suicidality than the general population (Teasdale & Engberg, 2001). Brenner (2011) found veterans with TBI were more likely to be at risk for suicidality than patients without TBI. The previous research cited indicates that head and psychological trauma increases the risk for suicidality and may be justified in inclusion as variables in the current research. Additionally, it may be difficult to truly compare a veteran sample to the general population due to the vast differences in experiences, such as combat and weapons training in the veteran sample which may increase the likelihood of PTSD.

Alcohol and Drug Use

Alcohol and substance abuse affect brain function and alter the dopaminergic system (Bodea & Blaess, 2015; Patriquin, Bauer, Soares, Graham, & Nielsen, 2015). The dopaminergic and serotonergic systems have a symbiotic relationship (that will be described in detail later in this chapter) that when altered, can increase aggression and self-directed aggression in susceptible individuals, which can lead to suicidality.

A meta-analysis of 43 studies and 870,967 study participants reported a strong association between substance abuse and suicide ideation OR 2.04 (95% *CI*: 1.59, 2.50; $I^2 = 88.8\%$, 16 studies); suicide attempt OR 2.49 (95% *CI*: 2.00, 2.98; $I^2 = 94.3\%$, 24 studies) and suicide completion OR 1.49 (95% *CI*: 0.97, 2.00; $I^2 = 82.7\%$, 7 studies) (Poorolajal, Haghtalab, Farhadi, & Darvishi, 2015). Research studies have also

demonstrated a correlation between suicidality and alcohol abuse (Preuss et al., 2015). Preuss (2015) conducted research with 293 alcohol-dependent (AD) patients and 499 controls from Germany, and 180 AD patients and 402 controls from Poland. The Genetics of Alcoholism interview tool was used to gather information on criminal behaviors, alcohol related violence, and alcohol dependent characteristics. In the German sample, 16.2 % of AD patients with no history of criminal activity, 21.9% of AD patients with a history of non-violent criminal activity, and 40.9% of AD patients with a history of violent criminal activity had a suicide attempt history ($\chi^2 = 8.4, p < .05$). In the Polish sample, 27.3% of AD patients with no history of criminal activity, 26.1% of AD patients with a history of non-violent criminal activity, and 45.2% of AD patients with a history of violent criminal activity had a suicide attempt history ($\chi^2 = 6.22, p < .05$).

Additionally, a retrospective research study of 45,741 veterans of OIF and OEF between 2010 and 2014 found alcohol use was strongly correlated with suicidality (Maguen et al., 2015). In the study, 75.3% of veterans admitted having suicidal thoughts, 12.5% admitted having a plan, 9.5% had a prior attempt, and 4.3% had both suicidal thoughts and a plan. There is also evidence that substance abuse in the presence of other conditions such as PTSD exacerbates the risk for suicidality. Finley et al. (2015) examined 5653 veterans of OEF and OIF between 2009 and 2011 who were admitted into the VA system for suicidal behavior. The research identified that while veterans with the diagnosis of PTSD ($OR = 2.3$; 95% $CI = 2.0, 2.6$) or a suicide attempt ($OR = 2.0$; 95% $CI = 1.4, 2.9$) were at increased risk for suicide ideation, the addition of substance abuse significantly increased the risk for suicide ideation ($OR = 4.7$; 95% $CI = 3.9, 5.6$) or a suicide attempt ($OR = 4.3$; 95% $CI = 2.7, 6.7$). Likewise, a veteran was at increased risk

for suicide ideation, with the diagnosis of depression ($OR = 2.8$; 95% $CI = 2.4, 3.4$) or a suicide attempt ($OR = 2.5$; 95% $CI = 1.7, 3.9$), but again, the addition of substance abuse significantly increased the risk for suicide ideation ($OR = 6.8$; 95% $CI = 5.4, 8.4$) or a suicide attempt ($OR = 6.8$; 95% $CI = 4.2, 11.1$).

The DoDSER reports 21.2% of completed suicides had a history of substance abuse and 29.0% of service members attempting suicide had a history of substance abuse. Additionally, 38.4% of service members used alcohol during the suicide event and 34% during the attempt (although this finding does not necessarily indicate a history of abuse) (Smolenski et al., 2013).

In summary, alcohol and substance abuse have been shown to be associated with suicidality. Alcohol and substance abuse affect brain function and can lead to aggression and suicidality. Across all the studies, suicidality was associated with alcohol or substance abuse. This association was also identified in a veteran sample. Research indicates alcohol and substance abuse are variables to include in this research.

Support Systems

Germaine to the Interpersonal-Psychological Theory is the discussion of support systems. The capacity component of the theory that includes biological markers fits the stress-diathesis model for suicidal behavior as described by Mann (Mann, 2002, 2003; Mann et al., 1999). As Mann (2003) describes the factors influencing suicidality in the model and factors pertinent to treatment, he discusses support systems. Mann describes support systems as a cornerstone for treatment of suicidality. Additionally, Kleiman and Liu (2013) analyzed data from the 2007 Adult Psychiatric Morbidity Survey containing a 7,461 participants. The analysis identified that perceived social support is associated with

a decrease in suicidality ($OR = 0.68, p < .001$). Social support is an important factor in suicidality, and the presence of a strong support system may decrease the likelihood of a suicide event.

In summary, the capacity component of the Interpersonal-Psychological Theory is similar to the stress-diatheses model for suicidal behavior. Research has indicated that the lack of sufficient support systems may increase the risk of suicidality. Conversely, the presence of a reliable support system can aid in the treatment of someone who is being treated for suicidality, and increase the likelihood of a successful recovery.

Family History of Suicide

Familial suicidal behavior has been documented as a significant predictor of both suicide attempts (Johnson, Brent, Bridge, & Connolly, 1998; Murphy & Wetzel, 1982; Shafii, Carrigan, Whittinghill, & Derrick, 1985) and completed suicides (Brent et al., 1994; Cheng, Chen, Chen, & Jenkins, 2000; Gould, Fisher, Parides, Flory, & Shaffer, 1996). Two meta-analyses found that those attempting or completing suicide, with a family history of either attempted or completing suicide, were correlated with greater mental illness diagnoses (Geulayov, Gunnell, Holmen, & Metcalfe, 2012; Victor & Klonsky, 2014). Geulayov (2012) specifically identified that children with parents who completed suicide were at increased risk for affective disorders. Qin et al. (2002) reported that a family history of suicide and mental illness increased suicide risk both significantly and independently ($OR\ 2.58$ [95% $CI\ 1.84–3.61$] and 1.31 [1.19–1.45], respectively). Previous research suggests familial history of suicide may be a significant predictor of identifying those at risk for suicidality.

In summary, an individual who has either attempted or completed suicide is more likely to have a genetic family link to someone who has either attempted or completed suicide. Research suggests this link may be by way of familial history of mental illness.

Chronic Pain

Chronic pain has long been associated with suicidality (Cheatle, 2011). Hooley (2014) frames the link by way of the Interpersonal-Psychological Theory. Suicide can be seen as an escape from unbearable physical and / or emotional pain. Chronic pain may also increase the capacity for suicide by increasing the fearlessness for death as described by Joiner (2005). Additionally, Hooley (2014) posits chronic pain can also lead to the hopelessness that Joiner identified as a component of the theory, thus creating a desire for death and dissolving the natural fear of death.

Wilson et al. (2013) also sought to understand the connection between suicidality and chronic pain in terms of the Interpersonal-Psychological Theory. Wilson studied 303 patients in a chronic pain rehabilitation center. Chronic pain was correlated to both distress in personal relations and a sense of burdensomeness on others and significantly predicted suicide ideation ($\beta = 0.12, p = .037$) and ($\beta = 0.25, p < .001$) respectively. For some, suicide may be the only way to end the constant suffering from their pain (Fishbain, 1999). Additionally, Kanzler et al. (2012) studied chronic pain in a military sample and found that chronic pain was associated with perceived burdensomeness and was the strongest predictor of suicide ideation, surpassing previously reported strong indicators of suicide ideation such as depression and pain severity.

In summary, chronic pain has been linked with suicidal behavior. Research suggests that chronic pain may increase the capacity for suicidal behavior by increasing

the fearlessness of death, and can also increase the feelings of hopelessness. Additionally, chronic pain has been shown to be associated with the sense of burdensomeness, further justifying the applicability of the Interpersonal-Psychological Theory.

Sleep Disturbances

The National Institutes of Health (NIH) (2012) recommend that adults receive seven to eight hours of sleep a night. Disturbances in sleep and the circadian rhythm that prevent the full recommended amount of sleep have been known to increase risks for many health concerns, including problems with brain cognition (Kohyama, 2014). Many of the variables listed earlier, such as trauma and PTSD, which have been shown to increase risks for suicidality have been shown to also result in sleep disturbances (Caldwell & Redeker, 2005). Additionally, inadequate sleep has also been shown to increase the risk of suicidality, independent of comorbid mental health disorders in the general population (Goodwin & Marusic, 2008).

The DoD Health Related Behaviors Survey of Active Duty Military Personnel report that 59.1% of all active military personnel are not receiving the recommended amount of sleep each night (Barlas et al., 2013). The DoDSER estimates that 12.2% of service members completing suicide and 12.5% of individuals who have attempted suicide have a diagnosed sleep disorder (Smolenski et al., 2013). This information is not available in the VA report, indicating it is an area requiring further research.

In summary, the DSM indicates that sleep disturbances are common among individuals suffering from chronic pain, which was previously discussed (American Psychiatric Association & DSM Task Force, 2013). If each risk factor independently

raises the risk for suicidality, the two together may theoretically elevate the risk exponentially.

Cholesterol Opposition

Conversely, the evidence in support of cholesterol as a biomarker for suicidality is far from conclusive, suggesting the need for further research. There is documented evidence of a link among cholesterol levels, depression, and suicidal behavior. However, various psychological conditions, treatments, and medications may impact other factors which influence cholesterol levels such as exercise and eating habits (Zhang, 2011). A study by D'Ambrosio et al. (2012) examined 220 patients diagnosed with bipolar disorder and found no statistically significant correlation between cholesterol and suicidality. Although D'Ambrosio's research study findings were not statistically significant, the research study found a ten-point difference between violent suicide attempters ($M = 186.5$ mg/dL SD 45.0) and non-violent suicide attempters ($M = 195.9$ mg/dL, $SD = 42.5$).

Researchers studying Spanish suicide attempters found that cholesterol levels were significantly lower in attempters than non-attempters (Diaz-Sastre et al., 2007; Perez-Rodriguez et al., 2008). However, when the same research group attempted to replicate the study in the United States, they found no association (de Leon et al., 2011). Their research suggests there may be differences between sexes, age, body mass index (BMI), or metabolic syndrome, that warrant further research. A replication study also failed to find an association between cholesterol and suicidality (Persons, Coryell, & Fiedorowicz, 2012).

In two additional studies examining bipolar patients, researchers did not find a correlation between suicidality and cholesterol (Almeida-Montes et al., 2000; Tsai, Kuo, Chen, & Lee, 2002). Similarly, no such association was reported in a study of affective disorder patients (Huang, 2001). However, no research found thus far has explored the link in a veteran sample.

Conclusion

As the rate of suicide in veterans show no signs of decline, every tool available must be used to its fullest potential. Biomarkers offer promise in identifying those at risk for suicide, but can be cost prohibitive. A recently published study shows promise for the use of amino acids as a biomarker for suicide (Szabo et al., 2014). Cholesterol is already a common test utilized by the DoD and VAMCs, incurring no additional cost. Research into cholesterol as a biomarker for suicide offers promise as the currently available research indicates that a cholesterol level below 160 mg/dL may help identify those most at risk. However, no research has been found thus far that tests the hypothesis in a veteran sample. While cholesterol testing is not offered as a definitive and conclusive test to evaluate someone for suicide potential, research thus far does show promise for its use as an effective screening tool to assist providers in identifying those most at risk. Additionally, this research further expands previous published research by incorporating variables from a sample with a military background not previously seen.

CHAPTER THREE: METHODS

Chapter three presents the research design for the study, and includes the research setting, sampling method, data collection process, and data analysis. To examine the relationship between total cholesterol levels and either suicide ideation or a suicide attempt, a retrospective review of data for veterans who were admitted to the Coatesville VAMC for either a suicide ideation or a suicide attempt were collected for analysis.

Description of Research Setting

There are 151 VA medical centers throughout the United States. The Coatesville Veterans Affairs Medical Center (VAMC) is primarily a psychiatric hospital, located in Pennsylvania and serves over 12,000 veterans a year (Pomorski, 2013). The staff includes 1335 full-time employees, 352 nursing staff, 37 physicians, 31 psychologists, and 53 social workers (Pomorski, 2012, 2013). The facility provides both inpatient and outpatient services. There are 452 inpatient beds, comprised of four medical units, 50 psychiatry beds, 169 community living center beds, and 229 domiciliary beds. In 2013, these beds cared for a total of 2,684 inpatients and residents (80 hospice, 113 medical, 668 psychiatric, 897 substance abuse, 216 post-traumatic stress disorder, 216 homeless veterans, and 494 community living center). Data are available for more recent years, but the reports do not discuss the specifics as in-depth as the 2013 report.

Data collection consisted of a retrospective chart review at the Coatesville VAMC from January 2009 through December 2015. Veterans were selected from cases in the VAMC Suicide Prevention Hotline database. This database was created and maintained by the Coatesville VAMC. Entry into the system is the result of a completed suicide, a suicide attempt, or an active suicide ideation with evidence of a plan (such as a suicide

note or evidence of preparation, such as stock piling medications). All of the veterans entered into the database resulted in an admission to the hospital or a completed suicide. In the case of a completed suicide, the veteran was previously a patient at Coatesville VAMC, and thus has records in their local database.

Sample

The sample data collection was conducted retrospectively from the data stored in the electronic computer charts at the Coatesville VAMC. To be eligible for veteran benefits and treatment at VA facility, an individual must meet the definition of “Veteran” determined by the VA. The VA states, “For the purposes of VA health benefits and services, a person who served in the active military service and who was discharged or released under conditions other than dishonorable is a Veteran” (Veterans Affairs, 2014b).

Sample size for the study was determined using G*Power Statistical Power Analysis for Mac (Faul, Erdfelder, Buchner, & Lang, 2009). In the calculation, α was set to a standard error of .05. To determine the effect size, a pilot study was performed and determined an effect size of .55 for individuals who were admitted for a suicide attempt. The power ($1-\beta$) was set to .95. The sample size calculation was determined to be 90 participants.

Once the veteran data were provided, the medical were was retrieved from the VAMC CPRS system for the analysis. The sample demographics encompassed subjects between 18 and 70 years of age. The majority of the veterans selected were White, but the sample also included some Blacks, and Hispanics. Additionally, the majority of the sample was males.

Aims

This research seeks to help identify veterans at risk for suicide. The number and rate of suicides in the military and veterans continue to rise in drastically substantial numbers (Smolenski et al., 2013). Based on previously published research and exploratory research for this research study, the following research questions and hypothesis are presented:

Among Veterans:

1. Do cholesterol levels below 160 mg/dL increase the risk for either suicide ideation, or a suicide attempt (either successful or unsuccessful)?

Hypothesis: Lower cholesterol is associated with an increased risk for either suicide ideation, or a suicide attempt (either successful or unsuccessful).

2. Is cholesterol level associated with the lethality method of the suicide attempt (either successful or unsuccessful)?

Hypothesis: There is a relationship between cholesterol level and the lethality method of the suicide attempt (either successful or unsuccessful).

Secondary Aims

3. Does naturally or chemically lowered cholesterol confer a higher risk for either suicide ideation, or a suicide attempt (either successful or unsuccessful)?

Hypothesis: Suicidality is related to cholesterol medication, which chemically lowers cholesterol.

4. What is the individual change (within person change) between a non-suicidal individual's cholesterol level and a suicidal individual's level (suicide ideation or suicide attempt).

Hypothesis: There will be a significant decrease (15% expected) in total cholesterol from T1 (a non-suicidal cholesterol level) and T2 (a suicidal cholesterol level).

5. After developing a Latent Class Analysis model, how many classes are preferred, and what are the characteristics of the classes after being regressed on cholesterol?

Hypothesis: The characteristics of individuals with suicide ideation or attempting suicide will form individual classes representing various total cholesterol values.

The dependent variables are total cholesterol level, suicide attempt (either successful $n = 1$ or unsuccessful $n = 79$), and suicide ideation ($n = 56$). The independent variables are the derived latent classes. The variables included for modeling in the latent class analysis are trauma (PTSD and TBI), substance abuse, support systems, family history of suicide, chronic pain, sleep difficulty and demographics of the sample. Cholesterol medication is a covariate in aim 3.

Descriptive Statistical Analysis

Descriptive statistics include frequencies for the categorical data, means, standard deviations and range of values for the continuous variables and are reported to provide the reader a sense of the background of the sample. These variables include the continuous variables of age, years in the military, and total cholesterol level. Dichotomous variables in the dataset included race, marital status, employment status, anxiety, depression, bipolar disorder, PTSD, a history of substance abuse, a family history for suicide, a history of impulsiveness (which is seen with serotonin hypofunction), sleep problems, alcohol use, military branch, reporting a lack of social support, and reporting a positive relationship with either children, parents, or family.

Assessment of Statistical Testing Assumptions

Some of the veterans included in the retrospective analysis had multiple visits to the VA for varying reasons. Repeated measures taken from the same individual poses a risk for violation of the assumption of independence for ANOVA and Chi-square tests as well as the latent class conditional independence criteria. A sub-analysis of the repeated measure cases was derived from finding those documented cases that were noted as not having a primary diagnosis for a suicide attempt or suicide ideation diagnosis, and having an occurrence date prior to the admission date for the suicide ideation or attempt event (hypothesis 4). These cases were then tested for individual change (within person change) between a non-suicidal individual's cholesterol level and a suicidal individual's level (suicide ideation, suicide attempt). Multiple observation cases that were noted to have a significant correlation, only the first ideation / attempt admission observation, was retained for analysis. Additionally, the correlations found to be non-significant, by [a small correlation (≤ 0.2)] at least a p -value of .10 or greater, were retained for the bivariate and latent class analyses.

Bivariate Statistical Analysis

Bivariate analytical methods of Analysis of Variance and Chi-square tests were used to test hypotheses 1 and 3. Hypothesis 1 tested if cholesterol levels below 160 mg/dL increase the risk for suicide ideation or attempt. Low cholesterol is expected to increase the likelihood of suicide attempts (either unsuccessful or successful) or suicidal ideation. Further, a decrease of total cholesterol of 15% may increase the likelihood of a suicide attempt (Dayton et al., 1969).

Hypothesis 3, posits suicidality is significantly related to cholesterol medication, which chemically lowers cholesterol. The taking of cholesterol medications was dichotomized to yes or no. The unadjusted odds ratio was obtained. The computations for the chi-square statistic were performed, and statistical significance was determined at the 0.5 level.

Analysis of Variance (ANOVA)

One-way ANOVA is a statistical method to determine if there is a significant difference between independent groups (Field, 2007). The analysis used the primary suicidality visit which caused the subject to appear in the Suicide Prevention Coordinator's database as to avoid violating the assumption of independence for ANOVA. The independent variable for aim 2 was the lethality method. The dependent variable was the cholesterol level. The Centers for Disease Control and Prevention (CDC) has determined the lethality of self-harm (suicide) methods. This ranking was used as ordinal (categorical) data. The categories, ranked in order of most lethal to least lethal are: 1) gunshot; 2) suffocation (inhalation); 3) fall; 4) unknown; 5) other; 6) poisoning (Vyrostek et al., 2004). Analysis then determined if there was a correlation between the cholesterol level and lethality of the chosen method of suicide (either in the form of ideation or attempt).

Repeated Measures Analysis of Variance (RANOVA) is useful to measure the individual or within person change as opposed to the change between various groups. In RANOVA, the independent variable has categories, or related groups at a specific point in time (Field, 2007). The independent variable for aim 4 was either a successful or

unsuccessful suicide attempt or suicide ideation, and the dependent variables were time one (T1) and time two (T2) cholesterol levels.

Latent Class Analysis

Latent class modeling is a statistical method for finding subtypes of related cases (latent classes) from observed categorical and/or continuous variables by using the observed values of variables for each individual (Nylund, Asparouhov, & Muthén, 2007). The probability of membership in each class is estimated by the prevalence of each latent class, and Bayes' theorem is used to estimate *a posteriori* probability of class membership. Based on the *a posteriori* probability, assignment of the case to the latent class with the highest *a posteriori* probability was performed.

Criterion of Conditional Independence

Often some variables are related or dependent. Examples include items on related symptoms, multiple indicators, or repetitions over time of the same measured item. Such items are termed “conditionally dependent” or “locally dependent” because they are associated within latent classes. If this dependence is not accounted for, model fit indices will be too high. Conditional independence may be an inappropriate assumption in some applications. For example, one may have two very similar symptom items, such that responses on them are often always associated (e.g. depression and anxiety). For this and certain related situations, extensions of the latent class model exist that apply robust parameters (Uebersax, 2000).

Assessment of Model Fit

The assessment of model fit compares the observed cross-classification frequencies to the expected frequencies predicted by the model. The difference is

assessed with a likelihood ratio (LR) Chi-square statistic. Unlike traditional statistics where one looks for exception (that is, $p \leq 0.05$), a model with values exceeding the critical value is considered a non-plausible model. Conversely, a non-significant Chi-square statistic indicates a plausible model. Parsimony indices are also used as measures of model fit. Common parsimony indices include:

Akaike Information Criterion (AIC):

$AIC = -2\ln(L) + 2p$ where $\ln(L)$ is the log-likelihood, and p is the number of estimated model parameters; and

Bayesian Information Criterion (BIC):

$BIC = -2\ln(L) + p*\ln(N)$ where N is the total number of observations.

For these indices, smaller values correspond to more parsimonious models. In comparing different models for the same data, models with lower values on these indices are considered a better fit.

Entropy:

An entropy estimate for these models is calculated and is defined based on a range of $[0, 1]$, with values near one indicating high certainty in classification and values near zero indicating low certainty. This result indicates high likelihood of classification based on the revised posterior probabilities. Unless the classification is very good (high entropy), the biased estimates and biased standard errors for the relationships of class membership with other variables is possible (Masyn, Henderson, & Greenbaum, 2010).

Number of Latent Classes

Nylund et al. (2007) suggests starting with two latent classes and assess the initial model fit using the AIC and BIC indices. When using two or more latent classes, the

Lo-Mendell-Rubenstein likelihood ratio test is used to compare the estimated model with the model using one fewer classes. A low p -value indicates that the estimated model is preferable to the alternative model (Muthén & Muthén, 2004). Background knowledge of the model and the population can also help guide the researcher in considering how many classes there may likely be and if there are too few or too many latent classes.

Sample Size Considerations

Published information regarding sample size and latent class analysis is varied. A study by Reaven and Miller (1979) used a sample of 145 to test for diabetes grouping noting strong classifications into three groups termed normal, chemical diabetes, and overt diabetes. Other studies have used from sample sizes as small as 76 (Acosta et al., 2008; Bailey, Moran, Pederson, & Bento, 2007; Pears, Kim, & Fisher, 2008) to thousands of observations (Weich et al., 2011). While the consideration that, "...more is better" in the case of LCA, it is planned that a parsimonious model will be assessed to conserve the sample size used on these analyses.

Discrete and continuous time survival analyses are often limited by the lack of analysis of heterogeneity within the data. There is a downward bias in survival analysis, as individuals more likely to experience the event will do so earlier, those with predisposing factors against experiencing the event become fewer over time, hence the downward trajectory (Masyn et al., 2010). Whether or not a subset of individuals within a sample is more likely to experience the event than another individual is important, and LCA may help to determine this.

By incorporating latent class analysis using observed variables to identify underlying factors, differing trajectories for event occurrence may be identified and in

this analysis, may be useful to assess the hypothesis that cholesterol levels are lower in those cases that attempt suicide (either successful or unsuccessful) or have suicidal ideation compared to cholesterol levels of patients at a time when they were not admitted for a successful suicidal attempt or ideation.

Latent class analysis and multi-level models for analyzing longitudinal data do not depend on meeting measurement, or necessarily, independence assumptions. The instrument measures can be nominal or ordinal, as well as continuous. There is also no assumption of linearity, or equal spacing within the measurement scale as in Structural Equation Modeling (SEM) (Uebersax, 2000).

Latent class analysis involves using an estimation maximization (EM) algorithm estimating a regression model under the assumption that the regression coefficients differ across unobserved (latent) segments, yielding improved predictions (Nylund et al., 2007; Uebersax, 2000). Regression using latent class analysis allows the indicator variables to vary by latent class, thus allowing individuals with similar responses to be grouped together.

The proposed analysis will assess key dichotomous and continuous variables to derive the optimal number of latent classes that, based on these data in this sample population is hypothesized to be two classes. The derived latent class variable will be regressed on the cholesterol continuous variable to assess for differences in cholesterol levels as part of the latent class assignment. It is hypothesized that there are no significant differences in cholesterol levels between the latent class groups.

CHAPTER FOUR: ANALYSIS OF THE DATA

The purpose of the study was to determine if a cholesterol level is an effective and reliable variable to determine risk for suicidality in veterans. Data were collected on veterans who were treated at the Coatesville VAMC for either suicide ideation, or a suicide attempt (either successful or unsuccessful) and were listed in the Suicide Prevention Coordinator's database. Once those veterans were identified, other visits were searched for and collected on the same veteran. Information collected included demographic data, cholesterol levels, information relating to the suicide ideation or suicide attempt, military data, medical data, psychiatric data, and historical family data. These data were obtained from the nursing admission assessment, mental health notes, and medical notes in CPRS.

Statistical Description of the Variables

Data were electronically collected through the VAMC Virtual Private Network (VPN) and entered into the Statistical Package for the Social Sciences (SPSS). Data analyses were performed in SPSS v23, Mplus v7, and Statistical Analysis Software (SAS) v9.4 as necessary for each statistical method. A codebook, raw data, clean data, copies of outputs and syntax were maintained on encrypted computers and servers on the VA network and the Rutgers University network. The patient list obtained from the Suicide Prevention Coordinators remained in electronic form on the VAMC secured and encrypted network in the user folder set up by the VAMC. The list was only accessible either on site at Coatesville, or through their VPN system on a computer that meets their security requirements, and requires authentication with a Common Access Card (CAC), CAC reader and personal identification number (PIN). No veteran identifiable

information was obtained or recorded in the dataset. The data collection process yielded a total of 190 observations from 129 unique veterans. Data were entered in SPSS and frequencies were computed to identify any unusual data entries. Cholesterol levels were assessed using the VA's own lab mean of 175 mg/dL and standard deviation (SD) values of 30 mg/Dl. One case with a greater than 3 SD variation was removed from the analysis resulting in a final case number of 188 observations for 128 unique veterans. Errors noted by unusual data entries outside the expected values (i.e. 3 in a dichotomous element) were reviewed with the original data in the system and corrected as much as possible. If the value was noted to be incorrectly entered in the record, the value was removed from the dataset. The descriptive statistics for the overall sample are summarized in Tables 2, 3, 4, and 5.

Table 2

Descriptive statistics for the overall sample – Continuous variables (N=188)

Variable	Sample		Range	
	Mean	SD	Min	Max
Age (years)	46.98	13.39	22	79
BMI	29.02	5.62	18.7	64.6
Years in the military	3.92	2.95	1	20
Total Cholesterol	180.20	38.0	108	290

Table 3

Cholesterol Levels

	N	M	SD	Min	Max
Group Cholesterol	188	180.20	38.0	108	290
Non-suicidal	52	210.10	35.5	120	290
Attempt / Ideation	136	168.76	32.4	108	275
Ideation Only	56	173.64	34.0	108	275
Attempt Only	80	165.35	30.2	110	250

Table 4

Demographics – Categorical (dichotomous variables) (N=188)

Variable	Sample	
	Frequency	%
Gender (Male)	170	90.4
Single (not married)	155	82.4
Education		
HS / GED	154	81.9
Assoc. degree	17	9.0
Bachelor degree	11	5.9
Master degree	1	0.5
Doctorate degree	2	1.1
Missing	3	1.6
Employed (No)	126	67.0
Race		
White	141	75
Black	46	24.5
Hispanic	1	0.5
Military Branch		
Army	94	50.0
Air Force	17	9.0
Navy	50	26.6
Marines	25	13.3
Missing	2	1.1
Living Quarters		
Homeless	65	34.6
Apartment	45	23.9
House	48	25.5
Missing	30	16.0

Table 5

Health Related Demographics – Categorical (dichotomous variables) (N=188)

Variable	Sample	
	Frequency	%
Current Smoker	111	59.0
Diagnoses		
Depression	159	84.6
Pain (chronic, back, neck)	15	8.0
Anxiety	25	13.3
PTSD	74	60.6
TBI	10	5.3
Bipolar	27	14.4
Hypertension	32	17.0
Substance Abuse	53	28.2
Hyperlipidemia	32	17.0
Cholesterol Meds	40	21.3
Family Hx of Suicide	53	28.2
Impulsive Hx	70	37.2
Sleep Problems	103	54.8
Lack of Social Support	67	35.6
Positive Relationship with either Children, Parents, or Family	60	31.9

Assessment for Statistical Testing Assumptions

As described above, 52 of the 188 observations were documented from multiple visit types from the same individuals. This posed a risk for violation of the assumption of independence for ANOVA as well as latent class analysis. A sub-analysis of the repeated measures cases was derived from finding those documented cases that were noted as not an attempt or ideation diagnosis having an occurrence date prior to the target admission date for suicide ideation or attempt. The results of these analysis showed that twelve cases comprised the 52 repeated visits and showed that the time to the target admission varied widely between 4 months to 151 months (see table 6) and the correlation between these visits was not significant

($r = 0.33$, $p = 0.29$). This rigorous and transparent process to identify the variation in these time-to-target admissions provides sufficient evidence to use all 188 observations for parametric testing and the latent class analysis.

Descriptive Statistical Analysis

Descriptive statistics were computed for variables to provide a meaningful constellation of the sample. These variables include the continuous variables of age, years in the military, and total cholesterol level. Dichotomous variables in the dataset include being Caucasian or not, married or single, being employed, reporting depression, reporting anxiety, a history of Post traumatic Distress Disorder, a diagnosis for being bipolar, a history of substance abuse, a family history for suicide, a history of impulsiveness, sleep problems, alcohol use, whether or not the individual was deployed, whether or not the individual was in the Army branch of the military, and reporting a lack of social support, and reporting a positive relationship with either children, parents, or family.

Suicide

Suicide ideations and suicide attempts were computed. The suicidal sample included 56 (29.8%) veterans with suicide ideation and 80 (42.6%) with a suicide attempt. Some veterans may have multiple visits as described above with the assessment of assumptions for ANOVA and LCA. Of the veterans who had multiple visits, 13 (6.9%) also were treated as an in-patient for drug treatment (see Table 7).

Lethality

The methods of the suicide attempts were computed. Of the veterans who attempted suicide, 10 (5.3%) were by firearm, 50 (26.6%) were by drug overdose,

4 (2.1%) were by hanging, 4 (2.1%) were by jumping, and 8 (4.3%) were by cutting. The unsuccessful attempts by firearm included veterans who had a misfire (malfunction of a loaded firearm to fire), placing an unloaded firearm to the head and pulling the trigger, or placing a loading firearm to the head and not pulling the trigger. None of the attempts resulted in an injury from the firearm.

Cholesterol

The cholesterol levels were computed for the overall value as well as, non-suicidal, suicide ideation, suicide attempt, and ideation and attempt combined. See table 3. The overall sample mean value was 180.20 mg/dL ($SD = 38.0$) with a range of 108 mg/dL to 290 mg/dL. The mean suicidality group value was 168.76 mg/dL ($SD = 32.4$) with a range of 108 mg/dL to 275 mg/dL. The mean non-suicidal group value was 210.10 mg/dL ($SD = 35.5$) with a range of 120 mg/dL to 290 mg/dL. In the latent class analysis, total cholesterol was regressed on the two class and three class models. There were no significant differences in latent class models or in the latent classes themselves in either the 2-class or 3-class models.

Depression

Veteran medical and mental health records were reviewed for a diagnosis of depression. Of the 188 observations for analysis, 159 (84.6%) of the veterans had a diagnosis of depression (see Table 5). Due to the large number of observations with the diagnosis of depression, analysis of the variable was not possible. The variable was tested in the LCA models, but was ultimately excluded as the presence in the models produced lower entropy, thus decreased classification probability in the model results.

Trauma

The two forms of trauma: TBI and PTSD were computed (see Table 5). Of the 188 observations, 10 (5.3%) had a diagnosis of TBI and 74 (60.6%) had a diagnosis of PTSD. Although it may be difficult to compare a veteran sample to the general population due to the vast differences in experiences, such as combat and weapons training in the veteran sample which may increase the likelihood of PTSD, it may help to put it in perspective. Approximately 7 to 8% of the general population will develop PTSD during their lifetime (Veterans Affairs, 2015).

Alcohol and Drug Abuse

The rates of alcohol and drug abuse were computed and grouped as substance abuse for analysis. Of the 188 observations, 53 (28.2%) reported a history of substance abuse (see Table 4). The NIH reported in June 2015 that 8.0% of the general population suffer from substance abuse (National Institute on Drug Abuse, 2015).

Support Systems

The prevalence of support systems was computed in the sample. Of the 188 observations, 67 (35.6%) reported a lack of a support system (see Table 5). This information is obtained from the nursing admission assessment. There is no definition or guidance in the assessment as to what constitutes a support system, except asking the interviewee for either family, friends, or military. No record reviewed indicated anyone sought out clarification. The determination here is that a support system may have a variety of meanings to each individual. However, ultimately, the interviewee is determining whether or not he or she feels they have support in their life.

Family History of Suicide

A family history of suicide was extracted from the records and computed. Of the 188 observations, 53 (28.2%) of the sample indicated a family history of suicide (see Table 5). The admission assessment does not ask for a family history of attempted suicide. A 2002 study found that individuals with a family history of suicide had an increased risk for completing suicide by two to three times.

Chronic Pain

Veterans diagnosed with either chronic pain, chronic back pain, or chronic neck pain were combined for the analysis. Of the 188 observations, 15 (8.0%) of veterans were diagnosed with chronic pain (see Table 5).

Sleep Disturbances

Veterans who reported sleep disturbances were computed. Sleep disturbances are determined by the interviewee when asked by the interviewer. Of the 188 observations, 103 (54.8%) of veterans reported sleep disturbances (see Table 5).

Hypotheses

Bivariate analytical methods of Analysis of Variance and Chi-square tests were used to test hypotheses 1 and 3. One-way ANOVA was used to test hypothesis 2. Hypothesis 4 was tested with RANOVA. Latent Class Analysis tested hypothesis 5.

Hypothesis 1

Hypothesis 1 was derived from the theoretical position that a cholesterol level may increase the risk for either suicide ideation or suicide attempts in susceptible veterans. Among the total sample ($n = 188$), there was a statistically significant difference between the group neither reporting suicidal ideation nor a suicide attempt

($M = 210.10$, $SD = 35.5$), and the group reporting either suicide ideation or a suicide attempt ($M = 168.76$, $SD = 32.4$), $t(186) = 7.61$, $p < .05$, 95% $CI [30.62, 52.04]$.

Furthermore, Cohen's d effect size value ($d = 1.22$) suggests a high practical significance.

One-way ANOVA tested the group reporting neither suicide ideation nor suicide attempt ($n = 52$) the suicide ideation group ($n = 56$) and the suicide attempt group ($n = 80$). There was a significant effect of cholesterol at the $p < .05$ level for the three groups [$F(2, 185) = 30.19$, $p = .000$].

Post hoc comparisons using the Bonferroni test indicated that the mean cholesterol level for the non-suicidal group ($M = 210.10$, $SD = 35.53$, $p = .000$) differed significantly from the suicide ideation group ($M = 173.64$, $SD = 35.08$, $p = .000$, 95% $CI [21.00, 51.90]$) and the suicide attempt group ($M = 165.35$, $SD = 30.17$, $p = .000$, 95% $CI [30.46, 59.04]$). However, the suicide ideation and suicide attempt groups did not significantly differ from each other ($p = .46$). Hypothesis 1 is supported.

Hypothesis 2

Hypothesis 2 was derived from the theoretical position that a cholesterol level may be related to the lethality method of the suicide attempt in veterans. Among the suicide attempt group ($n = 79$), there was a statistically significant difference between the lethality groups: gun-shot ($n = 10$), over dose ($n = 49$), hanging ($n = 4$), jumping ($n = 4$), and cutting ($n = 8$) at the $p < .05$ level [$F(4, 70) = 2.51$, $p = .049$].

Post hoc comparisons using the Bonferroni and Tukey tests indicated that the mean cholesterol level for the various lethality groups did not differ significantly.

Hypothesis 2 is not supported.

Hypothesis 3

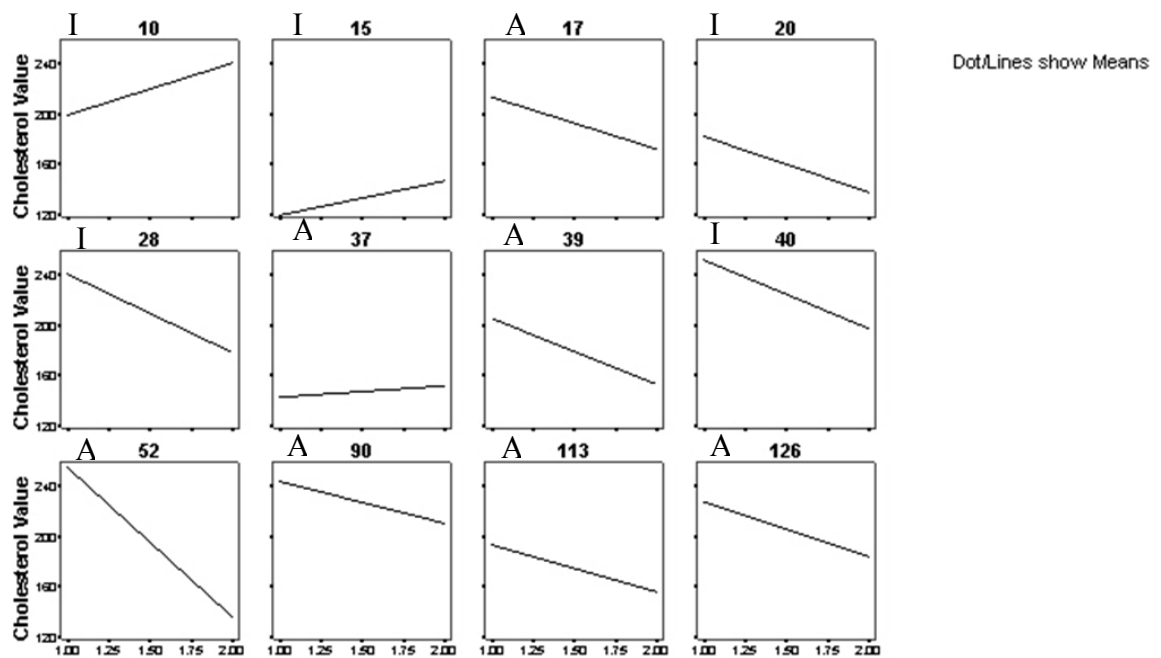
Hypothesis 3 was derived from the theoretical position that cholesterol medication may increase the likelihood of suicide ideation or suicide attempt. There were 148 veterans not on cholesterol medications in the sample. Of the 148 veterans, 41 reported neither suicide ideation or suicide attempt, 46 reported suicide ideation, and 61 reported a suicide attempt. There were 40 veterans on cholesterol medications in the sample. Of the 40 veterans, 11 reported neither suicide ideation or suicide attempt, 10 reported suicide ideation, and 19 reported a suicide attempt. There is no indication that cholesterol medication increases the risk for either suicide ideation or suicide attempt, $\chi^2(2, N = 188) = 0.68, p = .71$. Hypothesis 3 is not supported.

Hypothesis 4

Hypothesis 4 was derived from the theoretical position that there will be a significant decrease (15% expected) in total cholesterol from T1 (a non-suicidal cholesterol level) and T2 (a suicidal cholesterol level). The repeated measures analysis showed some compelling results relative to cholesterol change in the initial visit and target admissions. As seen in Figure 3 and Table 6, the mean in nine of the twelve cases showed a decrease of at least one standard deviation in cholesterol between the initial visit and the ideation / attempt admission. There were seven cases with the subsequent admission diagnosis for suicide attempt and five admitted for suicidal ideation. As seen in Table 6, suicidal ideation cases had mean cholesterol levels that varied from increasing, decreasing or staying relatively constant, whereas all of the suicide attempt cases showed mean total cholesterol decreases between the initial test and subsequent admission. See also Table 6 and Figure 3.

As a group, the non-ideation / non-attempt group ($n = 52$) had a mean cholesterol level of 210.10 mg/dL (35.5) compared to the ideation/attempt group ($n = 136$) having a mean cholesterol level of 168.76 mg/dL. This was statistically significant ($t_{(186)} = 7.61, p < 0.05$). Hypothesis 4 is supported.

Figure 2



I = Suicide Ideation

A = Suicide Attempt (successful or unsuccessful)

Table 6

Repeated Measures Analysis (n = 12)

Case ID	Time (months)	T1	T2	Change chol units	Greater than 1 SD change	Suicidal Ideation or Attempt
52	151	260	130	-130	Yes	Attempt
40	19	250	200	-50	Yes	Ideation
39	50	210	150	-60	Yes	Attempt
37	29	130	150	+20	No	Attempt
28	17	240	180	-60	Yes	Ideation
20	22	180	130	-50	Yes	Ideation
17	18	210	170	-40	Yes	Attempt
15	11	120	150	+30	Yes	Ideation
10	12	200	240	+40	Yes	Ideation
90	5	250	210	-40	Yes	Attempt
113	144	190	150	-40	Yes	Attempt
126	16	230	180	-50	Yes	Attempt
<i>Mean</i>	41.12	205.83	170			
<i>SD</i>	48.77	43.49	32.15			

Hypothesis 5

Hypothesis 5 was derived from the theoretical position that the characteristics of individuals with suicide ideation or attempting suicide will form individual classes representing various total cholesterol values. All models were run using the same variables for consistency of the results. A review of the entropy statistics and fit statistics to assess the contribution of each variable was completed. The remaining variables that provided the most parsimonious model for the analysis included all noted in Table 7. The review of the three class to two class models showed the two class model to have a better fit indices (BIC) and slightly lower entropy (0.924) compared to the three-class model (0.950).

Table 7

<i>Differences between Suicidal Ideation and Suicide Attempt Groups</i>				
	Ideation	Attempt	χ^2 or F	p
Caucasian Yes		X	3.48	0.06
Army Vet Yes	X		3.56	0.06
Pain (chronic, back, neck) Yes		X	5.86	<0.05
Opiates Yes		X	6.78	<0.05
Nightmares r/t war	X		3.12	0.07
Cholesterol Value	173.64 (35.08)	165.35 (30.17)	2.17	0.143
Age	48.75 (14.10)	46.41 (13.31)	1.018	0.315
BMI	29.73 (7.22)	28.263 (4.66)	2.063	0.153
Years in Military	3.64 (2.45)	4.18 (3.38)	0.969	0.327

Three Class LCA Compared to Two Class LCA Fit indices and Continuous Variable Comparison.

The third latent class consisted of the three eldest cases (mean age = 71.1) in the sample and had a mean BMI (34) that was higher, and had mean years in the military that was much higher when compared to the other two classes (18.8 years, compared 4 years in class one and 3.2 years in class two). Class one had the lowest mean age, BMI and years in the military; and remained the same in both models. Class two had a lower mean age (55 years) and BMI (30) than class three, but higher than class one. In summary, although the three class model has somewhat better fit indices, the LRT test for the three class to two class model was not significant, indicating to accept the simpler model as well as the fact that the two class model had more free parameters indicating a better model. Also, given that the third latent class only had three very different cases when compared to the other two classes, the face validity of the three class model is not supported. As seen in Table 8, the two class model had $n = 69$ in class one and $n = 119$ cases in class two.

Entropy of the two-class model was .924, compared to .950 with the three-class model, with entropy being defined on a range of [0, 1]. The values near one indicating high certainty in classification and values near zero indicating low certainty. This result indicates high good likelihood of classification based on the revised posterior probabilities. Unless the classification is very good (high entropy), biased estimates and biased standard errors for the relationships of class membership with other variables is possible (Masyn et al., 2010).

Latent Class Analysis for Continuous Variables and Revised Posterior Probabilities for Dichotomous Variables for The Two-Class Model.

Tables 8 and 9 as well as Figure 4, together show the differences between the two latent classes in the analysis. As stated, total cholesterol was not statistically significantly different when regressed by class. However, latent class one was on average, younger and leaner compared to cases in latent class two. There was no statistical difference in years in the military between the two classes (Table 8). The revised probabilities for the dichotomous variables are shown in Table 9, and graphically in Figure 4. As a result of entry of the 17 variables into the model, a revealing constellation of characteristics emerge. Latent class one were more likely to be employed, white, have post high school education, from the Army military branch, have a diagnoses documentation for PTSD, sleep difficulty, and war nightmares (Figure 4). Furthermore, this class was more likely to have a current suicide attempt than latent class two. The second class on average was 14 years older, heavier, was diagnosed with hyperlipidemia, and hypertension, as well as reporting a lack of a social support system. This class also had a higher probability of a

previous suicide attempt and a higher probability of previous suicidal ideation.

Hypothesis 5 is supported.

Table 8

Two Class to Three Class Estimates of Model Fit

	2-class model	3-class model
Loglikelihood	-3604.32	-3547.57
AIC	7310.12	7247.14
BIC	7475.70	7493.11
Entropy	0.924	0.95
Lo-Mendell-Rubin Adj. Test	$p = .0004$	$p = 0.06$
Number of Free Parameters	51	76

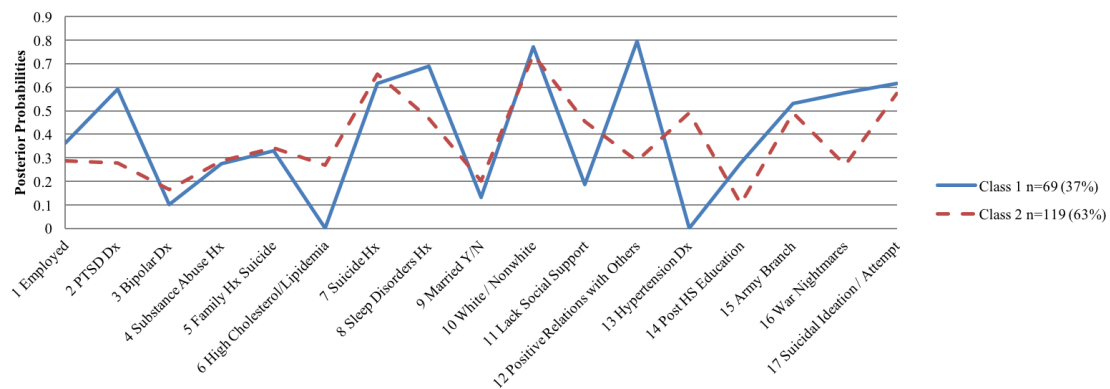
Table 9

Statistically Significant Latent Class Classification Differences

	Class 1 (n = 69)	Class 2 (n = 119)	T _(df)	p
Age	33.11 (6.16)	55.64 (6.16)	-24.97 ₍₁₈₅₎	<0.05
BMI	27.02 (4.91)	30.18 (5.92)	-3.25 ₍₁₈₅₎	<0.05
Years in Military	4.02 (2.16)	3.87 (3.37)	0.43 ₍₁₈₃₎	0.67

Table 10

Figure 3. Latent Class Analysis Revised Posterior Probabilities for Class Membership



Revised Probabilities for the Dichotomous Variables

	Class 1 (n = 69) (37%)	Class 2 (n = 119) (63%)
1 Employed	0.364	0.288
2 PTSD Dx	0.592	0.278
3 Bipolar Dx	0.103	0.167
4 Substance Abuse Hx	0.274	0.286
5 Family Hx of Suicide	0.329	0.343
6 High Cholesterol / Hyperlipidemia	0	0.269
7 Suicide Hx	0.617	0.656
8 Sleep Disorder Hx	0.689	0.466
9 Married Y / N	0.132	0.201
10 White / Non-White	0.771	0.738
11 Lack Social Support	0.187	0.455
12 Positive Relationships w/ Others	0.796	0.288
13 Hypertension Dx	0	0.492
14 Post HS Education	0.278	0.105
15 Army Branch	0.530	0.492
16 War Nightmares	0.575	0.269
17 Suicidal Ideations / Attempt	0.617	0.572

Additional or Ancillary Findings and Analysis of Same

The original goal of the research was to assess total cholesterol levels for those who completed suicides. Unfortunately, the data were not available. Although the list provided by the Suicide Prevention Coordinators included completed suicides, there was no retrievable data in the system for those veterans. In one case, a veteran who was being treated at Coatesville for substance abuse indicated suicide ideation. Upon completing the substance abuse treatment, the veteran denied any further suicidal ideations. The veteran was found the next day by family in his motel room following a successful suicide. His cholesterol level was tested prior to discharge and was 152 mg/dL. Although one case alone does not represent a significant finding, this case is compelling.

Interestingly, previous civilian and military research has cited marriage as a protective measure to suicidality (Hoyer & Lund, 1993; Nock et al., 2013; US Department of Veterans Affairs, 2013). That was not the case in this sample $\chi^2(1, N = 188) = 0.83, p = .36$.

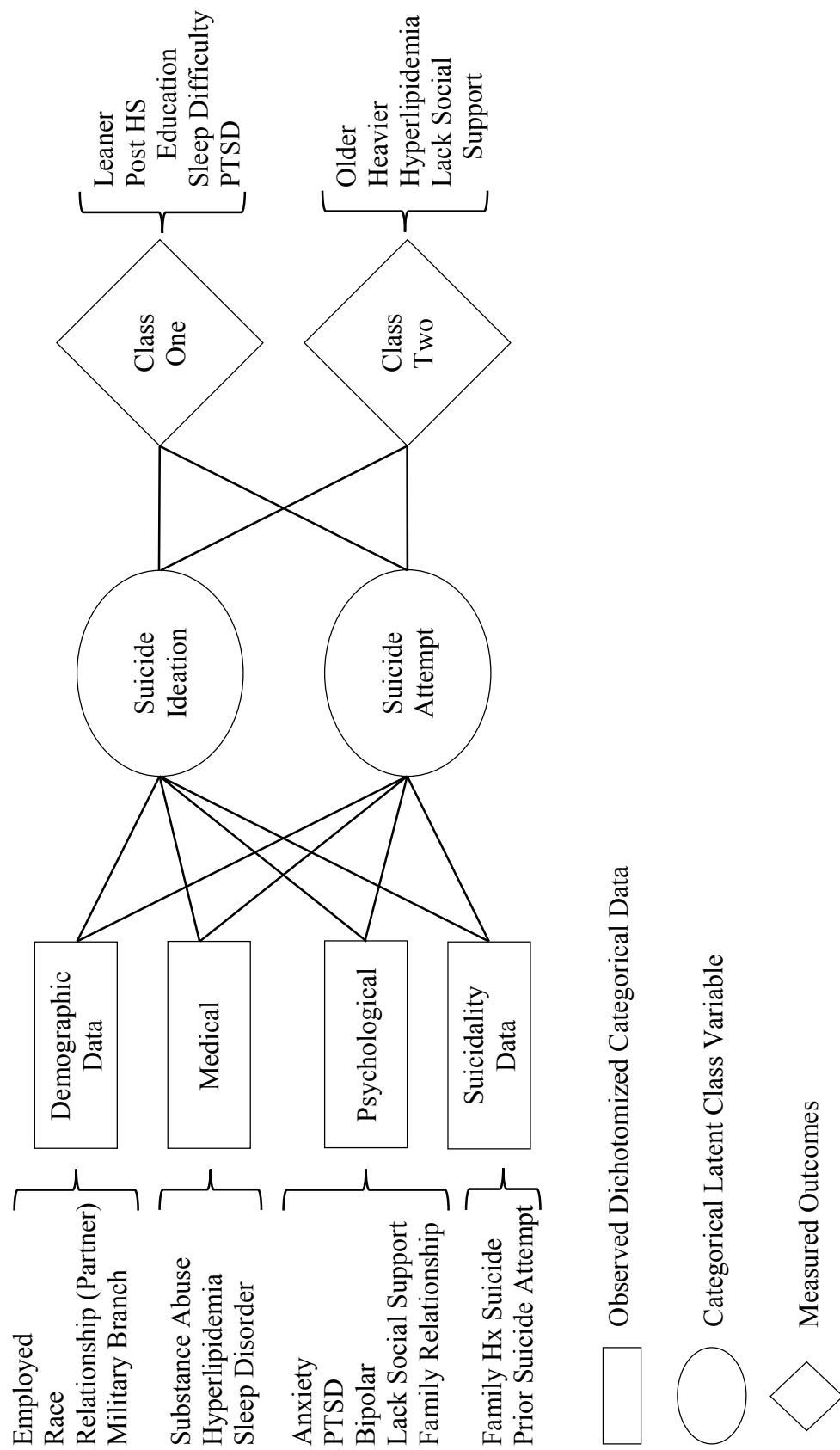


Figure 4. Adaptation of a General Latent Class Analytical Model (adapted from Nylund, 2007)

CHAPTER FIVE: DISCUSSION OF THE FINDINGS

The purpose of this study was to determine if total cholesterol levels are a valid and reliable indicator of suicidality risk in veterans. This chapter includes an interpretation of the findings of the hypothesized relationships based on the theoretical propositions of the Interpersonal-Psychological Theory of Suicide (Joiner, 2005; Joiner et al., 2009).

Findings for each Hypothesis

Lower Total Cholesterol Predicts Suicide Risk

The mean total cholesterol of the entire sample's ($n = 188$) was 180.30 mg/dL ($SD = 38.0$). The suicide ideation group ($n = 56$) had a mean total cholesterol of 173.64 mg/dL ($SD = 34.0$) and the suicide attempt group ($n = 80$) had a mean of 165.35 mg/dL ($SD = 30.2$). The mean cholesterol of the suicidality group was 168.76 mg/dL ($SD = 32.4$). The total range for the entire sample was 108 mg/dL to 290 mg/dL, which is a fairly large range. The body mass index (BMI) for the group ranged from 18.7 to 64.6 with a mean of 29.0 ($SD = 5.62$) and a median of 27.9. The CDC indicates that a BMI below 18.5 is underweight, between 18.5 and 24.9 is healthy, and over 30.0 is obese (CDC, 2015a). While the BMI for the sample as a whole was overweight, it was bordering on obesity.

There was a statistically significant difference between veterans reporting neither suicidal ideation nor a suicide attempt, and veterans reporting either suicide ideation or a suicide attempt ($M = 168.76$, $SD = 32.4$), $t(186) = 7.61$, $p < .05$, 95% CI [30.62, 52.04]. The statistical analysis revealed that in this sample, there was a statistically significant difference in total cholesterol levels between the group reporting neither suicidal ideation

nor a suicide attempt ($M = 210.10$, $SD = 35.53$, $p = .000$) and the group reporting suicide ideation ($M = 173.64$, $SD = 35.08$, $p = .000$, 95% CI [21.00, 51.90]), the group reporting suicide attempt ($M = 165.35$, $SD = 30.17$, $p = .000$, 95% CI [30.46, 59.04]), and the ideation and attempt group combined ($M = 168.76$, $SD = 32.4$), $t(186) = 7.61$, $p < .05$, 95% CI [30.62, 52.04]. The results indicate that total cholesterol may play a factor in suicidality worthy of further research. The Interpersonal-Psychological Theory discusses the three components of suicide, a sense of burdensomeness, thwarted belongingness, and the capacity for the act. Furthermore, the theory indicates that all three components are necessary for an individual to desire to end their life, and an alteration in one component can prevent the act from occurring. The capacity for suicide is a multifaceted component, with many variables contained in it. Whether an alteration in cholesterol level is sufficient to completely alter the capacity component of the theory is not clear, and further research is needed.

Total Cholesterol Level and Lethality of Method

It was hypothesized that total cholesterol levels may be related to the chosen method of the suicide attempt. The analysis indicated a statistically significant difference between each method of attempt, but the post hoc analysis failed to find a significant difference. Tukey post hoc comparison is usually the preferred method with larger samples, and Bonferroni with smaller. Both post hoc methods were attempted in the analysis, and both failed to show significant results. This most likely is related to the small size in each individual method, and a larger sample size may produce different results.

There may also be a flaw in the overall hypothesis. As described earlier, the Interpersonal-Psychological Theory states that an individual must be comfortable with the chosen method of suicide. While an attempt is a failed result, a successful attempt culminates in death. Thus, someone attempting suicide with a firearm, the most lethal method, would most likely result in a completed suicide, and not an attempt, which was not able to be measured here. The gun shot attempts identified were the result of a misfire, placing an unloaded firearm to the head and pulling the trigger, or placing a loading firearm to the head and not pulling the trigger. While the hypothesis is not supported, a larger sample size, or a sample that includes completed suicides may provide different results.

Suicidality and Cholesterol Medication

Hypothesis 3 aimed to determine if there was a significant difference between veterans who were suicidal and on cholesterol lowering medications and those who were not on cholesterol lowering medications. The analysis found no significant difference. However, the results could possibly have been confounded by the lack of cholesterol lowering medications in veterans who, if not for contraindications to cholesterol lowering medications, should have been prescribed cholesterol lowering medication. For example, a contraindication of cholesterol medication is alcohol drinking in excess. Of the total sample, 64 (34.0%) were diagnosed with alcohol dependence, 73 (38.8%) reported using alcohol, and 21 (11.2%) reported alcohol has become a problem for them. The need for cholesterol medications is usually determined by a number of factors, but in regard to cholesterol levels, the LDL is most commonly assessed. While the LDL was not collected for this dataset, 58 (30.8%) of the sample had a total cholesterol over 200 mg/dL, the

level the AHA considers high (AHA, 2014). In these veterans, 33 (56.9%) had a diagnosis of alcohol dependence. While the hypothesis was not supported here, further research with a larger sample size, and in a sample without alcohol use as a confounder may provide different results.

Within Person Change from Time One to Time Two

Hypothesis 4 theorized that veterans who were seen in the VA for a reason unrelated to suicidality and had their cholesterol tested, and then seen again at a later date for either suicide ideation or a suicide attempt, would have a significant reduction in total cholesterol level. The sample size ($n = 12$) was small, thus not eliminating the possibility the findings did not occur by chance. Nevertheless, the results are intriguing. Nine of twelve veterans in this analysis had a statistically significant reduction of one standard deviation in their total cholesterol level from a cholesterol test unrelated to a suicidality event, to a later test for either suicide ideation or a suicide attempt. In the small sample, the hypothesis is supported and yields credence to further testing in a larger sample.

Latent Characteristics

The goal of hypothesis 5 was to determine the characteristics of the sample reporting either suicide ideation or a suicide attempt, and statistically group them together based on their common latent characteristics. The analysis found that there were ultimately two classes in the sample, although an attempt to broaden it to three was made. The first class was younger, better educated, leaner, had more anxiety and sleep difficulty, and more likely to have a current suicide attempt than the second class. The second class on average was 14 years older, heavier, was diagnosed with hyperlipidemia,

and felt they did not have a support system, had a family history of suicides, and had previous suicide ideations and attempts.

The results are interesting as they portrayed characteristics of the sample which varied greatly in terms of age, educational background, and physical attributes. Thus, these results will help to focus future research and narrow in on a more specific sample for closer analysis.

Additional or Ancillary Findings

An interesting finding in the analysis was that while previous research in both military and civilian samples view marriage as a protective factor, that was not seen in this sample. There was no evidence that marriage would protect from suicidality in this study.

In summary, hypothesis testing supported hypothesis 1, 4, and 5. The findings suggest a complex relationship between cholesterol and suicidality. A reduction in total cholesterol may alter the microviscosity of the brain cell membrane thus reducing the serotonin receptor exposure. As discussed earlier, this may cause an imbalance in the complementary relationship between serotonin and dopamine leading to an increase risk for suicidality. As the total cholesterol level falls, so does the serotonin level. This suggests that total cholesterol may be a valid proxy for serotonin, although not on a one to one basis, the exact levels will require further research.

This research does not aim to suggest a cause and effect relationship between total cholesterol and suicidality. The aims here are to present the data, analysis, and identify a relationship worthy of further research. Furthermore, to give clinicians pause to consider the variables in making their clinical decisions when presented with someone who

presents with a suicide ideation or a suicide attempt, and low total cholesterol. Not everyone with low cholesterol will contemplate suicide. However, a veteran who has a low total cholesterol, feels he or she is a burden to others, does not feel he or she is making valuable contributions to society, and reports a desire to end their own life is in desperate need of immediate intervention. There is also evidence supporting the applicability of the Interpersonal-Psychological Theory of Suicide in a veteran sample, and the premise that an alteration in one of the three components of the theory may be able to prevent the escalation of events from suicide ideation, to suicide attempt, to suicide completion. Furthermore, there is support in the data to warrant and justify continuing research exploring the link between cholesterol and suicidality.

CHAPTER SIX: SUMMARY, CONCLUSIONS, IMPLICATIONS, RECOMMENDATIONS

Summary

The aim of this research was to examine the relationship between total cholesterol levels in veterans and suicidality. It was hypothesized that lower total cholesterol levels may help identify who is at risk for suicidality. Additionally, this research sought to determine if total cholesterol levels were related to the method of the suicide attempt, if cholesterol medications altered the risk for suicidality, what was the individual (within person) change between a non-suicidal cholesterol level and a suicidal cholesterol level, and to determine the latent classes and characteristics of the sample. The theoretical model for the research relied upon the Interpersonal-Psychological Theory of Suicide which identifies three components leading to suicide. Those components are a sense of thwarted belongingness, a sense of burdensomeness, and the capacity for the act (Joiner, 2005; Joiner et al., 2009).

Suicide is a complex, multifaceted phenomenon. There are many factors that can lead an individual to consider suicide as an option, and then to decide that course of action. The three components of suicide identified by Joiner (2005) (see Figure 1) take into account a multitude of specific variables. This research focused on the capacity to engage in suicidal activity.

The theory hypothesizes that an alteration in one of the three components necessary for suicidal activity to occur, will prevent the suicidal individual from engaging in the act. Thus, this research aimed at identifying if cholesterol levels were a valid and

reliable predictor of who is at risk for suicidality. If a cholesterol level is a reliable and valid predictor, it may help clinicians look for modifiable variables in those individuals.

This research hypothesized the following:

1. Lower cholesterol is expected to increase risk for either suicide ideation, or a suicide attempt.
2. There is a correlation between cholesterol level and the lethality method of the suicide attempt.
3. Suicidality is significantly related to cholesterol medication, which chemically lowers cholesterol.
4. There will be a significant decrease (15% expected) in total cholesterol from T1 (a non-suicidal cholesterol level) and T2 (a suicidal cholesterol level).
5. The characteristics of individuals with suicide ideation or attempting suicide will form individual classes representing various total cholesterol values.

The sample was drawn from the Coatesville VAMC. The suicide prevention coordinators maintain a database containing all suicide ideations, suicide attempts, and completed suicides beginning in 2009 that resulted in an admission to Coatesville VAMC. These veterans, once identified by the coordinators, and included in their database, were provided for the research study. Those cases were then reviewed in the VA's electronic patient care system, CPRS. Unfortunately, there was no data available on completed suicides, thus eliminating the variable from the study. Ultimately, the sample did consist of a wide range of veterans ($n = 188$), mostly white (75%), male (90.4%), single (82.4%) with a high school education (81.9%). The ages ranged from 22 to 79 years of age.

Data were analyzed using SPSS, Mplus, and SAS as necessary for each statistical method. The level of significance for hypothesis testing was calculated at the .05 level.

Hypothesis 1 was supported with through the research findings. The findings suggest that there was a distinct difference between a veteran reporting neither a suicide ideation or a suicide attempt and a veteran reporting either suicide ideation or a suicide attempt. Although previous research identified a total cholesterol of 160 mg/dL as the level of concern for an increased risk for suicidality, this research identified 168 mg/dL as the level of concern.

Hypothesis 2 was not supported through this research. However, the results could possibly have been confounded by being tested on a small sample and on a suicide attempt sample. The results may prove different in a larger sample and in a sample of completed suicides.

Hypothesis 3 was not supported through this research. The results were possibly confounded by the use of alcohol in the sample. As stated earlier, alcohol use in excess is contraindicated by cholesterol lowering medications (Food and Drug Administration). Of the total sample, 64 (34.0%) were diagnosed with alcohol dependence, 73 (38.8%) reported using alcohol, and 21 (11.2%) reported alcohol has become a problem for them. The analysis may produce different results if the hypothesis is tested in another sample without alcohol as a confounder.

Hypothesis 4 was supported through the research findings. The results of the analysis indicated that there was an increased risk for suicidal behavior in an individual with as little as a 20% decrease in cholesterol. This finding suggests clinicians may serve their patients well by looking a little closer on a patient who had a 20% decrease in

cholesterol, and is now at risk for either suicide ideation or a suicide attempt. A veteran who is suffering with a depression, for example, may be served well by not lowering their cholesterol level over 15% while still remaining in the recommended parameters established by the AHA.

Hypothesis 5 was supported with through the research findings. The findings of the analysis of data for this hypothesis identified that there were two distinct classes presented. Latent class one were more likely to be employed, white, have post high school education, from the Army military branch, have a diagnoses documentation for PTSD, sleep difficulty, and war nightmares. Class one was also more likely to have a current suicide attempt than latent class two. The second class on average was 14 years older, heavier, was diagnosed with hyperlipidemia, and hypertension, as well as reporting a lack of a social support system. Class two also had a higher probability of a previous suicide attempt and a higher probability of previous suicidal ideation. The combination of characteristics in class one, PTSD, sleep difficulty, and a current suicide attempt indicates this class may be at higher risk than class two. This suggests that a veteran being treated by a clinician with these characteristics should be evaluated more closely. These results will help guide future research by identifying risk factors for suicide ideation or a suicide attempt in veterans, and also help guide or inform future prevention efforts.

In summary, theoretical positions were tested to determine if cholesterol level had a relationship with a variety of suicidal factors. Those factors included suicide ideation, suicide attempt, lethality method, chemically versus naturally low cholesterol, the individual change, and the characteristics of the suicidality sample.

Implications for Nursing

Findings from this study suggest a link between suicidality and total cholesterol level. Nursing at its heart and core is concerned for the whole person and maintains a holistic approach to the individual's wellbeing. As the military and veteran suicide rates continue to rise, nurses spend a great deal of time with patients and those who need nursing, medical, and psychological care. Nurses are trusted and valued by the populations they serve, and can help identify variables or factors that increase the likelihood of suicide, and guide practice to change those variables in the populations they serve. Clinically, nurses can take the holistic approach, and facilitate a link between the nursing, medical, and psychological care with diet and exercise that will translate into a well-balanced individual.

In the early planning stages of this research project, various departments within the DoD and VA were contacted to find the most optimal source of data. As discussed earlier, cholesterol screening is relatively low cost and simple to perform. Additionally, it is standard on the yearly physicals performed in the military components. However, many departments outside of the those performing yearly screenings do not collect or share this data.

In reference to the two classes that emerged from the LCA model. The models appear to make sense and follow the trajectory of the modern conflicts such as OIF and OEF. Although the initial intent of this research was to isolate a younger sample, more representative of the current active fighting force that has been involved in OIF and OEF, a more diverse sample emerged. As a result, the LCA seems to have dichotomized the sample between the veterans who were engaged in OEF and OIF and the previous

conflicts such as Korea, Vietnam, or Gulf War. For example, the prevalence of PTSD in veterans serving in OIF and OEF may be as high as 55% (Smolenski et al., 2013). Whereas 30% of Vietnam veterans report PTSD symptoms, and 10% of Gulf War veterans report PTSD symptoms (Smith, 2008). Whether this is due to an actual increase of PTSD itself, better diagnosing of PTSD, the symptoms of PTSD from previous conflicts being diminished or treated by other means is not clear. However, PTSD did not first appear in the DSM until the DSM-III in 1980 and revised in 1987 with the DSM-II-R, 1994 with the DSM-IV, and again in 2000 with the DSM-IV-TR (Friedman, 2016). This may indicate that the diagnosing criteria is improving, possibly indicating that if the current criteria existed with the previous conflicts, the rates may be similar. Conversely, the modern conflicts (OIF and OEF) have additional difficulties for service members previous conflicts have not. The two most recent conflicts are the longest period of continuous fighting in our history, and the rate of redeployments have never been as high as these two conflicts. Additionally, class one, the younger class of veterans, have the current suicide ideation or a suicide attempt whereas the older class has previous suicide ideation or a suicide attempt. Research suggests that BMI gradually increases with age (Villareal, 2005). Consistent with the literature, class two also contained the veterans with a higher BMI. Likewise, both hypertension and hyperlipidemia is more prevalent in older adults (Buys, 2014; Navar-Boggan, 2015), and were grouped into class two in the analysis.

Interestingly, the way the veterans were dichotomized into the two classes by LCA may have the variables published in various articles encompassing varying topics. However, a search of the literature did not produce any findings that grouped the

variables such as this or relating to veteran suicides. These findings may help guide future research and clinical practice when working with this demographic. For example, based on the findings, the class of younger veterans are more likely to have a current suicide ideation or a suicide attempt. This is a significant factor to help guide both researchers and clinicians working with this demographic, and perhaps indicate veterans in class one may need clinical priority as they have a more recent suicide attempt which may indicate greater risk. The published VA suicide data indicates the largest group of veterans attempting suicide is under 30 years old and the rate decreases with age (Kemp & Bossarte, 2014). However, the same report indicates that the rate of successful suicides increases with age to age 49, and then decreases. Conversely, the DoDSER (2014) reports the highest rate of suicides are between the ages of 20 and 24, and then decreases with age. The eldest active service member completing suicide reported in the DoDSER is reportedly 74-year-old. The age range of the sample for the current study ranges from 22 to 79 years old. Since completed suicide data was not available for this study, it is an area worthy of future research, not only to possibly identify the variables leading to the opposite results, but to potentially save lives. The results of such data may prove invaluable to clinicians, and may not only help identify those veterans at immediate risk, but those veterans most likely to result in a successful suicide attempt.

Furthermore, this research indicates that the Interpersonal-Psychological Theory may be applicable to veterans. Nurses may be able to alter one of the three components of the theory that are necessary for a suicide to occur. As the theory states, for a suicide to occur, the three components, thwarted belongingness, perceived burdensomeness, and the capacity to commit the act must occur together. An alteration in one component is

sufficient to prevent an individual from desiring to take the actions necessary to complete a suicide. An alteration in diet, which can increase total cholesterol to a level still within the recommended levels suggested by the AHA, can be guided by a nurse.

Recommendations

Based on the findings of this study, inclusive of its limitation, replication of the study in a larger sample and in varying demographic and geographic locations is sagacious. The use of multiple research sites would be useful to generalizability of the findings. Additionally, research has suggested that total cholesterol levels in psychiatric patients may be influenced by gender (de Leon et al., 2011). The current study sample was mostly male, and further studies may benefit from being able to obtain data on a larger female demographic.

The current research was not able to collect data on completed suicides. Future research would likely benefit from capturing that demographic. This may help in addressing the second hypothesis, specifically whether total cholesterol level significantly correlates to the method of suicide. As firearms are the most lethal method of suicide, and the main method for veterans, exploring total cholesterol as a link would be interesting to explore.

Furthermore, the third hypothesis was confounded by the high rate of alcohol use in the sample, which also may alter a clinician's decision on whether or not to prescribe cholesterol medications. Replication of the study using a sample where alcohol use is not so prevalent, is therefore recommended.

The current study also had a wide age range. A larger sample which would allow for comparison between various age ranges may produce more precise results for the

varying age groups. As with the wide age range, the sample obviously served in the armed forces at various points in America's history, thus serving in various conflicts. Each conflict, brought with it varying difficulties and challenges. The current research was not able to extract which conflicts the veterans served in, whether or not they were deployed to a combat theater, or what function the veteran served in the conflict. Future research with these variables may provide useful and insightful results.

Limitations

The study is not without limitations. Most notably, the study had a small sample size. Furthermore, data are limited to the variables entered into the CPRS system by the medical, nursing and psychiatric staff. This limitation makes generalizability difficult to a wider population. Furthermore, the sample is not representative of the Active, Reserve, or National Guard components, and may not represent other geographical veteran samples. Additionally, factors for suicidality vary with age, this study examined the phenomena and groups as a whole and did not differentiate by age due to the sample size. Furthermore, certain variables such as support system, were not clearly defined, but left up to the interpretation of the interviewee. Support system can have varying meanings to each individual.

The study was limited to veterans who have a relationship with the Coatesville VAMC between 2009 and 2015. This somewhat limits the geographical nature of the sample demographics, but not in totality. In evaluating the preliminary sample data, some veterans were transferred to Coatesville from other VAMC centers because of their specialty or previous relationships with the veteran.

Other limitations include limitations to variables that require the veteran to self-report, such as support system, sleep problems, and impulsiveness. While it can be argued that the meaning of these variables is what they are as determined by the individual, a universally understood definition across the sample may have more meaning. Each of these variables are collected during the nursing admission assessment in the form of a narrative. Thus, there is no differentiation or clarification made as to what exactly a support system is, what sleep problems are, or what impulsiveness is. For example, some veterans reported sleep problems as only being able to sleep one hour a night, others reported sleep problems when they reported sleeping eight hours a night. While logical deduction may result in assuming the veteran is not getting eight hours of quality sleep, or that the sleep is interrupted, there is no clarifying statement in the record, leaving it open to a wide interpretation.

Conclusions

The main findings of this study support a link between total cholesterol level and suicidality. While previous research has suggested a link between suicidality and total cholesterol at the 160 mg/dL level, this research found the level 168 mg/dL to be significant. Furthermore, the results of aim 4 found that there was a significant increase in suicidality with as little as a 20% reduction in total cholesterol level. The original research in a civilian sample found an increase in suicidality with a 15% decrease in cholesterol (Dayton, Pearce, Hashimoto, Dixon, & Tomiyasu, 1969). No research has been found that explored that exact finding since the original research. These two findings together may suggest that there may not necessarily be a definitive line or level where the neurobiological processes described earlier take place, but rather there may be

a gradual declination that leads to suicidality. Alternatively, the level may be slightly different for each person and it is the individual change within that person that is the significant factor. This research looked to identify if there was in fact a link between naturally lowered or chemically lowered cholesterol, but failed to find one. Indicating that whether an individual's cholesterol was naturally low due to diet, or chemically low due to medication, was not significant to suicidality. Additionally, when looking to classify suicidal veterans, two classes of characteristics formed. One class is younger, leaner, have higher education, and report more sleep and anxiety issues than the other. This may indicate that societal changes in the younger generations which have pushed individuals to higher education, work more, sleep less, has also led to a more stressed, anxious, and depressed group that sees suicide as a relief or end to the pain (Wilburn, 2005; American Psychological Association, 2014; McLoughlin, 2015).

Aside from the reports from the DoD and the VA that discuss their entire suicidality population in totality, most research focuses in on a specific set of variables for more precise analysis. This research aimed at extracting data that more closely correlated to the demographics of the current active fighting force, but was unable to obtain data with such specificity. Nevertheless, the analysis and results not only provide a foundation for future research, but also contains information that clinicians and other researchers may be able to utilize to save lives. Future research with a larger sample and a clear delineation in variables such as age, medical co-morbidities, familial variables and deployment data may provide evermore expanding avenues of research.

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Appendix 1

VA / DoD DEPRESSION PRACTICE GUIDELINE PROVIDER CARE CARD

Assessment and Treatment Algorithm

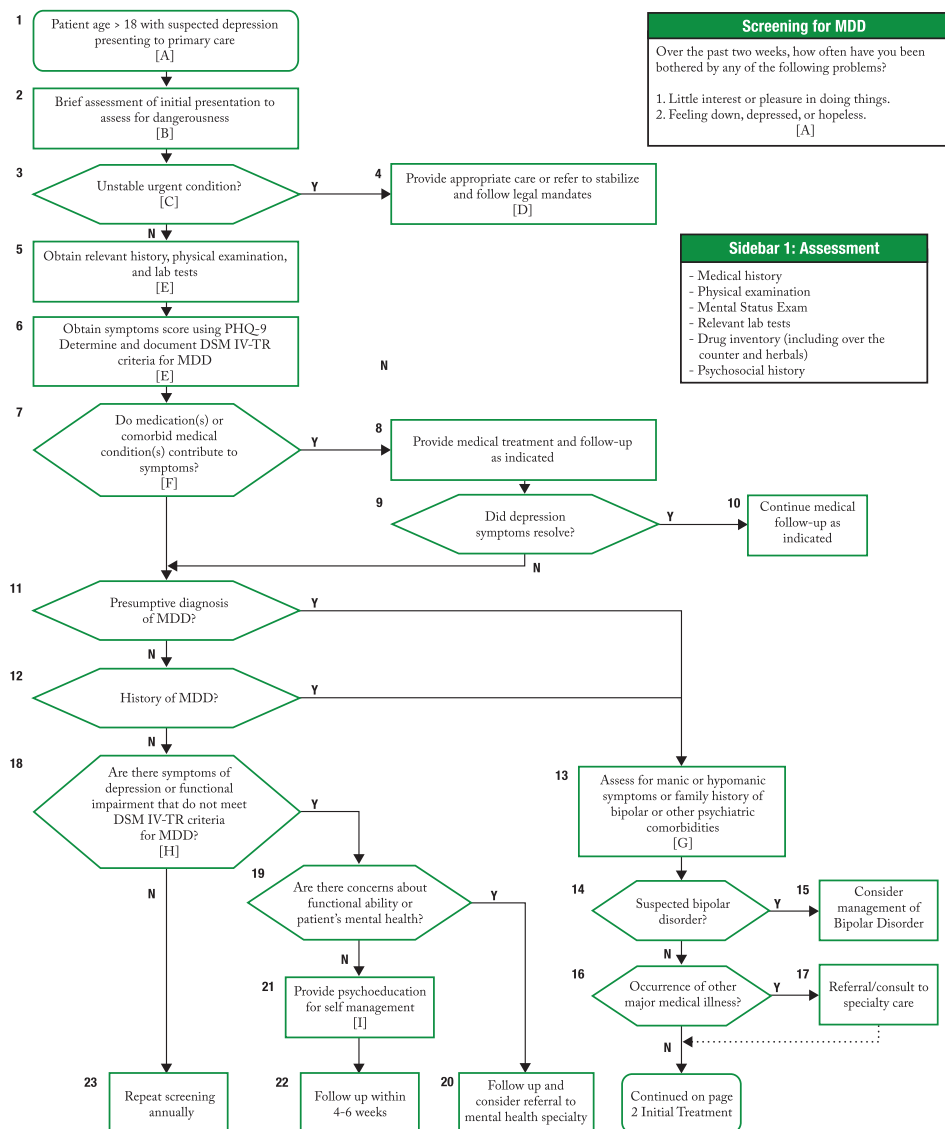


CARD 1

Management of Major Depressive Disorder (MDD) in Adults

Primary Care Initial Assessment and Diagnosis

1



9/08/10

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Assessment and Treatment Algorithm (cont.)



CARD 2



Management of Major Depressive Disorder in Adults

Primary Care Initial Treatment

2

24 Patient with presumptive diagnosis or history of MDD, meets DSM IV-TR diagnostic criteria for MDD

25 Determine level of severity of MDD symptoms and functional impairment [J]

26 Discuss treatment options and patient's preferences
Arrive at shared decision regarding treatment goals and plan [K]

27 Is there indication for referral to mental health specialty? [L]

28 Refer to Mental Health Specialty Care

29 Initiate treatment strategies effective for depression [See Sidebar 4] [M]

30 Address psychosocial needs [N]

31 Schedule follow-up in 4-6 weeks

Continued on page 3

Sidebar 2: DSM-IV-TR Diagnostic Criteria for MDD

MDD diagnosis requires the presence of symptom 1, 2, or both; and at least 5 of 9 symptoms that persist for at least 2 weeks:

1. Depressed mood nearly every day for most of the day, based on self report or observation of others.
2. Marked reduction or loss of interest or pleasure in all, or nearly all, activities for most of the day, nearly every day.
3. Significant non-dieting weight loss or weight gain (>5% change in body weight)
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation (should be observable by others).
6. Fatigue/loss of energy nearly every day.
7. Feelings of worthlessness or excessive/inappropriate guilt nearly every day.
8. Diminished cognitive function (reduced ability to think or concentrate) nearly every day.
9. Recurrent thoughts of death and/or suicide, suicide planning, or a suicide attempt.

Sidebar 3: Indications for Referral to Mental Health

- Unclear diagnosis
- Evidence of psychotic features, past mania, or hypomania
- Signs of comorbid psychiatric conditions
- Unable to treat patient in primary care
- Need for psychosocial interventions
- Patient preference

Sidebar 4: Initial Treatment Strategies for MDD

SEVERITY	PHQ-9 Score	FUNCTIONAL IMPAIRMENT	INITIAL STRATEGY
Mild	10-14	Mild	Monotherapy – antidepressants or psychotherapy – or, possibly combination
Moderate	15-19	Moderate	Antidepressants or psychotherapy, or combination
Severe	≥20	Severe	May start with antidepressants or psychotherapy but should prefer combination or multiple antidepressants

Psychoeducation and self-management should be provided for all severity levels.

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Assessment and Treatment Algorithm (cont.)



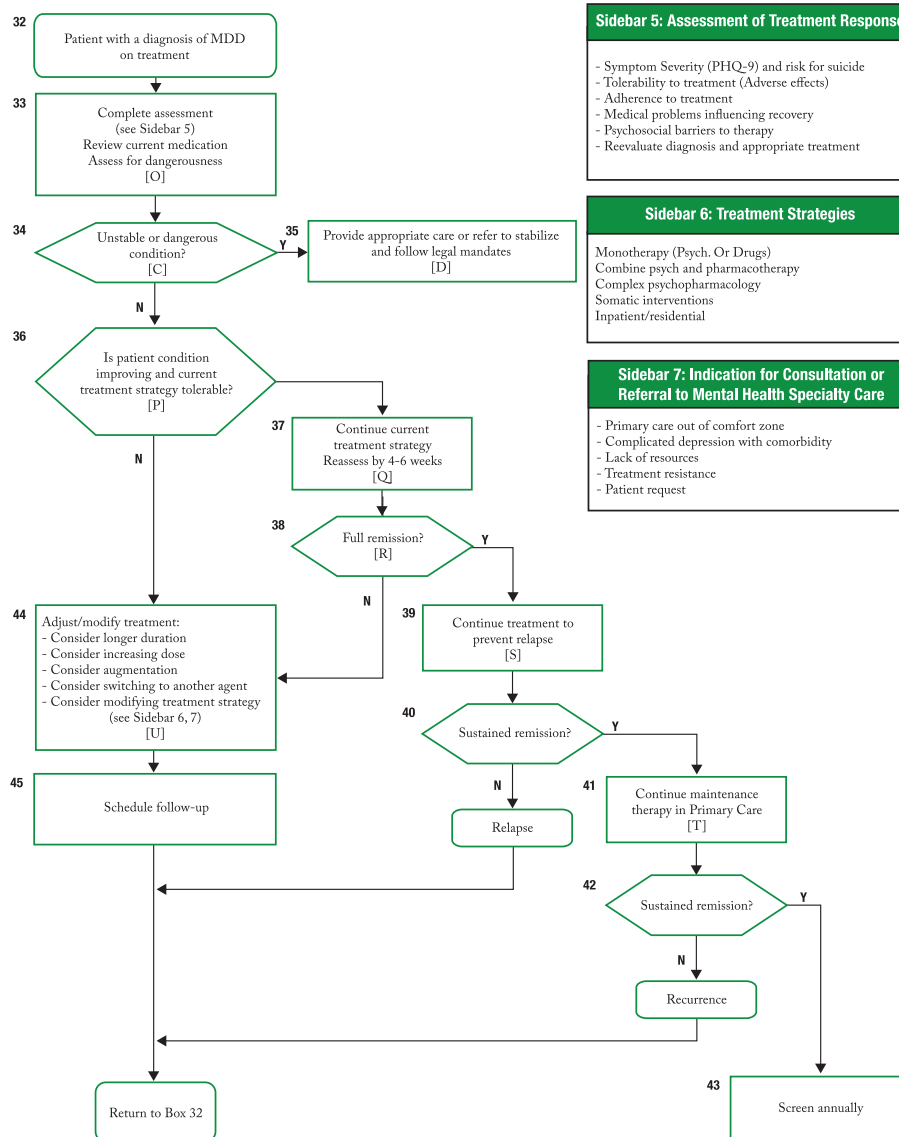
CARD 3



Management of Major Depressive Disorder in Adults

Primary Care Treatment Strategy and Follow-Up

3



6/23/10

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Identification and Assessment



CARD 4

Depression Risk Factors

- Prior Episodes of Depression
- Family History of Depressive D/O
- Prior Suicide Attempt
- Female Gender
- Age of Onset Under 40
- Postpartum Period
- Medical Comorbidity
- Lack of Social Support
- Stressful Life Events
- Current Substance Abuse

Screening Using the Patient Health Questionnaire 2 (PHQ-2)

(see 2009 MDD CPG pp. 17-21)

Screening with PHQ-2 should be completed annually by all patients seen in primary care settings.

Over the past two weeks, how often have you been bothered by either of the following problems?

A) Little interest or pleasure in doing things. (0-3)

B) Feeling down, depressed, or hopeless. (0-3)

Not at all Several days More than half the days Nearly every day
0 1 2 3

Patients with a score of 3 or more should be followed up with the PHQ-9.

Score	% Prob. of MDD	% Prob. of Any Depressive Disorder
1	15.4%	36.9%
2	21.1%	48.3%
3	38.4%	75.0%
4	45.5%	81.2%
5	56.4%	84.6%
6	78.6%	92.9%

Assessment Using the Patient Health Questionnaire 9 (PHQ-9)

(see 2009 MDD CPG Appendix B pp. 149-153)

Purpose: The Patient Health Questionnaire (PHQ) is designed to facilitate the recognition and diagnosis of depressive disorders in primary care patients. For patients with a depressive disorder, a PHQ Depression Severity Index score can be calculated and repeated over time to monitor change.

Making a Diagnosis: Since the questionnaire relies on patient self-report, definitive diagnoses must be followed up on and verified by the clinician, taking into account any presenting functional impairments and/or the patient's understanding of the questions. The clinician should also consider relevant information obtained from the patient, their family, and other sources.

Over the last two weeks, how often have you been bothered by any of the following problems?

	Not at All	Several Days	More Than Half the Days	Nearly Every Day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself in some way	0	1	2	3

Add Columns: + +
Total:

10. If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

☐ Not Difficult at All ☐ Somewhat Difficult ☐ Very Difficult ☐ Extremely Difficult

VA / DoD DEPRESSION PRACTICE GUIDELINE PROVIDER CARE CARD

Identification and Assessment (cont.)



CARD 5

Assessment Using the Patient Health Questionnaire 9 (PHQ-9) (cont.)

Interpreting the PHQ to Make a Provisional Diagnosis: To facilitate interpretation of patient responses, all clinically significant responses are found in the columns farthest to the right. Any symptom endorsed as being present at least “more than half the days” counts toward a DSM-IV-TR diagnosis. (The only exception is for suicidal ideation which counts toward a DSM-IV-TR diagnosis if endorsed as being present “several days” or more.)

Major Depressive Disorder is suggested if Q#1 or 2 and five or more of Q#1-9 are at least “more than half the days” (count Q#9 if present at all).

Other Depressive Disorder is suggested if: Q#1 or 2 and two, three, or four of Q#1-9 are at least “more than half the days” (count Q#9 if present at all). To score the instrument, tally each response by the number value under the answer headings. Add the numbers together to total the score on the bottom of the questionnaire. Interpret the score by using the following guide:

PHQ-9 Score	DSM-IV-TR Criterion Symptoms	Depression Severity	Proposed Treatment Action
1–4	Few	None	None
5–9	< 5	Mild Depressive Symptoms	Watchful waiting; repeat PHQ-9 at follow-up
10–14	5–6	Mild Major Depression	Treatment plan; Consider counseling, follow-up, and/or pharmacotherapy
15–19	6–7	Moderate Major Depression	Immediate initiation of pharmacotherapy and/or psychotherapy
20–27	> 7	Severe Major Depression	Immediate initiation of pharmacotherapy and, if severe impairment or poor response to therapy, expedited referral to a mental health specialist for psychotherapy and/or collaborative management

Note: The diagnoses of Major Depressive Disorder and Other Depressive Disorder require ruling out normal bereavement (mild symptoms, duration less than two months), a history of a manic episode (Bipolar Disorder) and a physical disorder, medication, or other drug as the biological cause of the depressive symptoms.

Additional Clinical Considerations

(see 2009 MDD CPG Appendix B pp. 149-153)

After making a provisional diagnosis with the PHQ, there are additional clinical considerations that may affect decisions about management and treatment:

- Have current symptoms been triggered by psychosocial stressor(s)?
- What is the duration of the current disturbance and has the patient received any treatment for it?
- To what extent are the patient's symptoms impairing his or her usual work and activities?
- Is there a history of similar episodes, and were they treated?
- Is there a family history of similar conditions?

Table 11 – Table of Evidence

Citation	Sample Size and Setting	Design	Major Variables Examined	Results
Al-Delamy, W. K., Jansen, E. H. J. M., Peeters, P. H. M., van der Laan, J. D., van Noord, P. A. H., Boshuizen, H. C., . . . Bueno-de-Mesquita, H. B. (2006). Reliability of biomarkers of iron status, blood lipids, oxidative stress, vitamin D, C-reactive protein and fructosamine in two Dutch cohorts.	30 men from Bithoven 35 women from Utrecht	Cross-Sectional	Daily alcohol consumption, daily energy intake, age, weight, cholesterol, triglycerides, apo lipoprotein-A, apo lipoprotein-B, high-density lipoproteins, low-density lipoproteins	For all biomarkers, except C-reactive protein, there were no substantial changes in the mean levels over time. Uric acid, ferritin, creatinine, HDL, and apo lipoprotein-B levels consistently showed the highest reliability for men and women (intra-class correlation 0.69 and 0.86). With the exception of a few gender-specific differences, most of the 20 biomarkers performed well and can be considered to have sufficient reliability to be used in future cohort studies. Most biomarkers did not change significantly between the two time points and changes in mean values were around 10% or less No substantial change of the selected biomarkers over time for the populations. There was a statistically significant difference ($p < 0.0001$) in the mean duration between the two points of time for women compared with men. Age was not statistically different ($p < 0.18$) between the two populations (55 years for women versus 53 years for men).
Almeida-Montes, L. G., Valles-Sanchez, V., Moreno-Aguliar, J., Chavez-Balderas, R. A., Garcia-Marin, J. A., Cortés Sotres, J. F., & Hheinze-Martin, G. (2000). Relation of serum cholesterol, lipid, serotonin and tryptophan levels to severity of depression and to suicide attempts. <i>Journal of Psychiatry and Neuroscience</i> , 25(4), 371-377. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1407732/	274 subjects with personality disorders	Cross-Sectional	Age Sociopathy Psychopathy Sex Cholesterol Antisocial Personality	The group of subjects with antisocial personality had a clearly lower mean level of serum cholesterol than the group with other personality disorders which was used as a control group. The use of a mean male population with standardized ages as a control group further emphasized the low values of the serum cholesterol of the antisocial personality group.
Asellus, P., Nordstrom, P., & Jokinen, J. (2010). Cholesterol and CSF 5-HIAA in attempted suicide. <i>Journal of Affective Disorders</i> , 125(1-3), 388-392. doi:10.1016/j.jad.2010.02.111	42 medication free suicide attempters during their follow-up after a suicide attempt at Karolinska University Hospital, Sweden	Cross-Sectional	Cholesterol CSF 5-HIAA Serotonin Suicide attempt Depression	Serum total cholesterol and CSF 5-HIAA showed a significant positive correlation adjusted for age, body mass index and substance abuse diagnosis. Cholesterol and CSF 5-HIAA levels did not differ between violent and non-violent suicide attempters or between suicide completers and survivors. Conclusions: These findings indicate that the serotonergic system may be connected to serum cholesterol in patients with a recent suicide attempt.

Citation	Sample Size and Setting	Design	Major Variables Examined	Results
Atmaca, M. (2004). Serum Cholesterol and Leptin: Their Roles in Suicide and Impulsive-Aggressive Behaviors. <i>Psychiatric Times</i> , 21(1), 24-25.	24 suicide attempters	Review Article	BMI Leptin levels Violence level Cholesterol level Suicidal behavior	The mean cholesterol levels in suicidal patients and controls were 152.26 mg/dL \pm 14.39 mg/dL and 186.44 mg/dL \pm 32.56 mg/dL, respectively. Mean cholesterol levels for violent and nonviolent suicide attempters and controls were 140.2 mg/dL \pm 24.1 mg/dL, 164.5 mg/dL \pm 28.4 mg/dL and 193.7 mg/dL \pm 27.9 mg/dL, respectively
Bachynski, K. E., Canham-Chervak, M., Black, S. A., Dada, E. O., Millikan, A. M., & Jones, B. H. (2012). Mental health risk factors for suicides in the US Army, 2007-8. <i>Injury Prevention</i> , 18(6), 405-412. doi:10.1136/injuryprev-2011-040112	255 active duty suicides between 2007 and 2008	Secondary data analysis	Mood disorder Anxiety disorder Adjustment disorder PTSD Substance abuse Rank	Factors associated with higher suicide risk included male gender, lower enlisted rank and mental health disorders treated on an outpatient basis (RR 3.9), as well as a number of mental health disorders (mood disorders, anxiety disorders, PTSD, personality/psychotic disorders, substance-related disorders and adjustment disorder; RR range 4.7-24.5). Analysis of historical trends suggested that 25-50% of the suicides that occurred in 2008 might have been related to the major commitment of troops to combat beginning in 2003.
Beck, A. T. (2008). The evolution of the cognitive model of depression and its neurobiological correlates. <i>American Journal of Psychiatry</i> , 165(8), 969-977. doi:10.1176/appi.ajp.2008.08050721		Review article	Cross-Sectional Model of Depression, Developmental Model of Depression, Biological Correlates of the Cognitive Model, Genetic Vulnerability, Genetic Diathesis and Cognitive Bias, Neuropsychological and Cognitive Factors/Bias	Discussion of neurobiological basis of depression. "A hypersensitive amygdala is associated with both a genetic polymorphism and a pattern of negative cognitive biases and dysfunctional beliefs, all of which constitute risk factors for depression. Further, the combination of a hyper-active amygdala and hypoactive prefrontal regions is associated with diminished cognitive appraisal and the occurrence of depression."
Black, S. A., Gallaway, M. S., Bell, M. R., & Ritchie, E. C. (2011). Prevalence and Risk Factors Associated With Suicides of Army Soldiers 2001-2009. <i>Military Psychology</i> (Taylor & Francis Ltd), 23(4), 433-451. doi:10.1080/08995605.2011.590409	874 Army suicides from Army Behavioral Health Integrated Data Environment (ABHIDE)	Cross-Sectional	Demographics and military risk factors	The demographics of soldiers committing suicide mirror the overall demographics of the Army. The most common method of suicide involved gunshot wounds (66%) and hanging or asphyxiation (20%). Men were somewhat more likely to die by gunshot wounds, whereas women were somewhat more likely to die from drug overdoses.

Citation	Sample Size and Setting	Design	Major Variables Examined	Results
Brenner, L. A., Ignacio, R. V., & Blow, F. C. (2011). Suicide and traumatic brain injury among individuals seeking Veterans Health Administration services. <i>Journal of Head Trauma Rehabilitation</i> , 26(4), 257-264. doi:10.1097/HTR.0b013e31821fdb6e	Soldiers receiving care at the VA between 2001 and 2006. Analyses included patients with a history of TBI (n = 49,626) plus a 5% random sample of patients without TBI (n = 389,053). Of those with a history of TBI, 105 died by suicide.	Cross-Sectional	Any traumatic brain injury (concussion/fracture cerebral contusion/traumatic intracranial hemorrhage) Various other mental health diagnoses such as depression and substance abuse.	Veterans with a history of TBI were 1.55 (95% confidence interval [CI], 1.24–1.92) times more likely to die by suicide than those without a history of TBI.
Briere, J., & Runtz, M. (1986). Suicidal thoughts and behaviours in former sexual abuse victims. <i>Canadian Journal of Behavioural Science/Revue canadienne des sciences du comportement</i> , 18(4), 413.	95 women presenting at the Crisis Intervention program of a community health center	Cross-Sectional	Childhood sexual abuse and suicidality	Previous suicide attempts were more common among former sexual abuse victims (54.9%) than among non-abused patients (22.6%), $X^2(1) = 17.86$, $p < .0001$. Patients who reported themselves to be suicidal at the time of their intakes were also more likely to have a history of 2 sexual abuse (35.6%) than were non-suicidal intakes (22.6%), $X^2(1) = 4.23$, $p < .040$.
Bryan, C. J., Morrow, C. E., Anestis, M. D., & Joiner, T. E. (2010). A preliminary test of the interpersonal-psychological theory of suicidal behavior in a military sample. <i>Personality and Individual Differences</i> , 48(3), 347-350. doi:http://dx.doi.org/10.1016/j.paid.2009.10.023	Three Samples: Active Duty US Air Force personnel (n=88) Non-military undergrad sample (n=309) Non-military clinical sample (n=228)	Cross-Sectional	Age, Sex, Military Status, Race Scale Results, Positive Affect, Negative Affect, Gender, Belongingness, Burdensomeness, Age, Suicidal Behaviors, Belongingness, Burdensomeness, Fearlessness of Self Injury, Positive and Negative Emotional States,	The military sample (M = 1.16, SD = .58) reported significantly lower levels of burdensomeness as compared to the under-graduate sample (M = 1.70, SD = .94; $t(395) = 5.116$, $p < .001$, $d = .69$), but no differences were observed between the military sample (M = 2.28, SD = 1.21) and the undergraduate sample (M = 2.18, SD = 1.15) in belongingness. The military sample's acquired capability (M = 4.38, SD = 1.35) was found to be significantly higher than the acquired capability of the non-military outpatient clinical sample (M = 2.60, SD = .84; $t(314) = 14.078$, $p < .001$, $d = 1.58$). Further analysis revealed that the military sample had a significantly higher acquired capability than the non-military subgroup of multiple suicide attempts (M = 3.13, SD = .87; $t(101) = 3.458$, $p < .001$, $d = 1.10$).
Carr, R. B. (2011). When a Soldier Commits Suicide in Iraq: Impact on Unit and Caregivers. <i>Psychiatry: Interpersonal & Biological Processes</i> , 74(2), 95-106. doi:10.1521/psyc.2011.74.2.95	One soldier's suicide in Iraq	Qualitative	Case study of the affects of a suicide during a deployment	The soldier's suicide closely affected the lives of 13 soldiers on the base where the event took place.

Citation	Sample Size and Setting	Design	Major Variables Examined	Results
Carter, C. S., Braver, T. S., Barch, D. M., Botvinick, M. M., Noll, D., & Cohen, J. D. (1998). Anterior cingulate cortex, error detection, and the online monitoring of performance. <i>Science</i> , 280(5364), 747-749.	13 subjects underwent fMRI scans	Cross-sectional	Anterior Cingulate Cortex, behavior regulation,	The ACC detects conditions that errors are likely to occur rather than the errors themselves.
Cersovsky, S. B. (2011). Fighting the War Within: Suicide as an Individual and Public Health Challenge in the U.S. Army. <i>Psychiatry: Interpersonal & Biological Processes</i> , 74(2), 110-114. doi:10.1521/psyc.2011.74.2.110	Review / Informational Article			Several of the soldiers most affected by the event, including those requiring evacuation from theater, were operating in a combat environment with significant psychological problems diagnosed prior to the deployment. This illustrates the predicament of a military that has been engaged in sustained conflict over many years: how do military leaders balance the ongoing requirements to successfully execute missions with the cumulative stress this places on the force?
Chapman, A. L., & Dixon-Gordon, K. L. (2007). Emotional antecedents and consequences of deliberate self-harm and suicide attempts. <i>Suicide and Life-Threatening Behavior</i> , 37(5), 543-552. doi:10.1521/suli.2007.37.5.543	n=63 Female inmates who attempted suicide	Cross-Sectional	Self-harm, suicide attempt, mental health diagnoses, emotional state	Anger was the antecedent emotion reported by the largest proportion of individuals who had engaged in deliberate self-harm (45.16%), suicide attempts (40.9%), and ambivalent suicide attempts (30%). Relief and other positive emotional shifts were more common in deliberate self-harm (41.94%) than in suicide attempts or ambivalent suicide attempts, particularly for persons with borderline personality disorder.
Craig, S. R., Amin, R. V., Russell, D. W., & Paradise, N. F. (2000). Blood cholesterol screening influence of fasting state on cholesterol results and management decisions. <i>Journal of General Internal Medicine</i> , 15(6), 395-399.	n=181 patients at least 20 years of age receiving medical care at a community hospital general internal medicine clinic.	Cross-Sectional	Age Gender Tobacco use Alcohol use Medication use Comorbid conditions Fasting Total Cholesterol HDL LDL	Several of the soldiers most affected by the event, including those requiring evacuation from theater, were operating in a combat environment with significant psychological problems diagnosed prior to the deployment. This illustrates the predicament of a military that has been engaged in sustained conflict over many years.
Cuijpers, P., de Beurs, D. P., van Spijker, B. A. J., Berking, M., Andersson, G., & Kerkhof, A. J. F. M. (2013). The effects of psychotherapy for adult depression on suicidality and hopelessness: A systematic review and meta-analysis. <i>Journal of Affective Disorders</i> , 144(3), 183-190. doi:10.1016/j.jad.2012.06.025	Review of 13 studies	Meta-Analysis	Hopelessness Depression Suicidality	Thirteen studies (with 616 patients) were included, three of which examined the effects of psychotherapy for depression on suicidal ideation and suicide risk, and eleven on hopelessness. No studies were found with suicide attempts or completed suicides as the outcome variables. The effects on suicidal ideation and suicide risk were small and not statistically significant. A power analysis showed that these studies only had sufficient power to find an effect size. The effects on hopelessness were large and significant, although heterogeneity was very high. Furthermore, significant publication bias was found.

Citation	Sample Size and Setting	Design	Major Variables Examined	Results
D'Ambrosio, V., Salvi, V., Bogetto, F., & Maina, G. (2012). Serum lipids, metabolic syndrome and lifetime suicide attempts in patients with bipolar disorder. <i>Progress in Neuro-Psychopharmacology and Biological Psychiatry</i> , 37(1), 136-140.	220 patients with bipolar disorder	Cross-Sectional	History of lifetime suicide attempts Blood exams testing total cholesterol, triglycerides, and HDL-c levels, metabolic syndrome	Lifetime suicide attempts rate was 32.3%. There were no statistically significant differences between patients with and without lifetime suicide attempts in cholesterol, triglycerides, HDL-c levels, and the prevalence of metabolic syndrome. No differences in the same variables were found in violent suicide attempters compared with nonviolent ones. Clinical characteristics such as gender, low education, higher number of manic and depressive episodes, and taking more medications for bipolar disorder were associated with life-time suicide attempts.
de Leon, J., Mallory, P., Maw, L., Susce, M., Perez-Rodriguez, M., & Baca-Garcia, E. (2011). Lack of replication of the association of low serum cholesterol and attempted suicide in another country raises more questions. <i>Annals of Clinical Psychiatry</i> , 23(3), 163-170.	n = 1284	Cross-Sectional	Psychiatric patients with a previous suicide attempt, psychiatric patients who had not currently attempted suicide served as controls, fasting serum total cholesterol	There were 193 current suicide attempters (cases) and 1091 non-current suicide attempters (controls). In the total sample logistic regression model, low cholesterol levels were significantly associated with lower risk of current suicide attempt (OR, 0.60; confidence interval (CI), 0.39 to 0.92) after adjusting for confounding variables. After sex stratification, low cholesterol levels were significant only among men (OR, 0.47; CI, 0.26 to 0.86).
Engelberg, H. (1992). Low serum cholesterol and suicide. <i>Lancet</i> , 339(8795), 727. Retrieved from https://login.proxy.libraries.rutgers.edu/login?url=http://search.ebscohost.com/login.aspx?direct=true&db=nyh&AN=9204062720&site=ehost-live	Literature review			Primary prevention trials which have shown that the lowering of serum cholesterol concentrations in middle-aged subjects by diet, drugs, or both leads to a decrease in coronary heart disease have also reported an increase in deaths due to suicide or violence. There has been no adequate explanation for this association. I have reviewed the relevant published work and describe a physiological mechanism that might account for this curious finding. One of the functions of serotonin in the central nervous system is the suppression of harmful behavioral impulses. When mouse brain synaptosomal membrane cholesterol is increased there is a pronounced increase in the number of serotonin receptors. Low membrane cholesterol decreases the number of serotonin receptors. Since membrane cholesterol exchanges freely with cholesterol in the surrounding medium, a lowered serum cholesterol concentration may contribute to a decrease in brain serotonin, with poorer suppression of aggressive behavior.
Golier, J. A., Marzuk, P. M., Leon, A. C., Weiner, C., & Tardiff, K. (1995). Low serum cholesterol level and attempted suicide. <i>The American Journal of Psychiatry</i> , 152(3), 419-423.	650 patients, aged 18-59 admitted to a psychiatric hospital	Cross-Sectional	Age, weight, race, socioeconomic status, alcohol use, and depression, cholesterol, suicide attempt	Male psychiatric patients with low cholesterol levels were twice as likely to have ever made a medically serious suicide attempt than men with cholesterol levels above the 25th percentile.

Citation	Sample Size and Setting	Design	Major Variables Examined	Results
Griffith, J. (2012a). Army Suicides: "Knowns" and an Interpretative Framework for Future Directions. <i>Military Psychology</i> (Taylor & Francis Ltd), 24(5), 488-512. doi:10.1080/08995605.2012.716269	Literature review		age, gender, race, type of high school attainment, mental category or MCAT (based on the Armed Services Vocational Aptitude Battery or ASVAB), marital status, rank, prior service, years of service, military status (M-day or part-time versus full-time military service), military occupational specialty (MOS) (coded into combat arms versus others), in training, and ever deployed.	Many of the suicide cases in Army analyses have behavioral and mental health conditions, which—on the face of it—are very different than those having problems in daily living. Additionally, many suicides were associated with earlier, childhood abuses). Very recent research has shown childhood and early adolescent trauma, which here it was argued exacerbates age-specific developmental tasks, predicted later young adulthood suicide behaviors—both as a main effect and interaction effect between these earlier experiences and current stressors
Griffith, J. (2012b). Correlates of Suicide Among Army National Guard Soldiers. <i>Military Psychology</i> (Taylor & Francis Ltd), 24(6), 568-591. doi:10.1080/08995605.2012.736324	Army National Guard (ARNG) (N = 5,390); post-deployed ARNG soldiers (N = 4,567); and home-stationed ARNG soldiers (N = 15,597).	Secondary Analysis	PTSD symptoms (e.g., upsetting memories, difficulties falling asleep) and negative mood (e.g., anger, frustration, and loneliness). PTSD symptoms mediated the relationship between combat experiences and post-deployment negative mood and changed suicidal behavior. Gender Age Race Military experience Suicidal behavior	Combat exposure showed little relationship to changes in suicidal behavior (from deployment to post-deployment). Rather, suicidal behavior was associated more with current and post-deployment stressful events.
Heron, D. S., Shinitzky, M., Hershkowitz, M., & Samuel, D. (1980). Lipid fluidity markedly modulates the binding of serotonin to mouse brain membranes. <i>Proceedings of the National Academy of Sciences of the United States of America</i> , 77(12), 7463-7467.	Mice specimens in a lab setting	Experimental	Membrane fluidity Cholesteryl hemisuccinate Stearic Acid Lipids Serotonin binding	As the membrane lipids become more viscous, the specific binding of serotonin increases steadily.

Citation	Sample Size and Setting	Design	Major Variables Examined	Results
Joiner, T. E., Van Orden, K. A., Witte, T. K., Selby, E. A., Ribeiro, J. D., Lewis, R., & Rudd, M. D. (2009). Main predictions of the interpersonal-psychological theory of suicidal behavior: empirical tests in two samples of young adults. <i>Journal of Abnormal Psychology</i> , 118(3), 634-646. doi:10.1037/a0016500	Two Samples: Test One: n=815 - Miami-Dade County Middle and High Schools Test Two: n=313 from two US Army Medical Centers	Cross-Sectional	Sample One: Age, Sex, School, Ethnicity, Psychiatric Diagnoses, Sample Two: Age, Sex, Marital Status, Diagnoses, Family Hx of Depression, Bipolar DO, and Suicide, Test Scale Results. Lifetime depression, Major depression last six months, Low family social support, Low mattering, Low family social support X Low mattering, Previous suicide attempt, current suicide attempt, Test Scale Results Suicide Ideation, Suicide Intent	6-month and lifetime depression rates significantly predicted suicidal ideation Mattering and family social support significantly predicted current suicidal ideation beyond the covariates Mattering marginally predicted suicidal ideation The interaction of mattering and family social support predicted suicidal ideation The interpersonal-psychological theory does not predict that the two-way interaction will predict suicide attempt (the focus of this study) but rather suicidal ideation The three-way interaction among SPS perceived burdensomeness, SPS low belonging, and lifetime number of suicide attempts predicted current suicide attempt status SPS burdensomeness was a stronger predictor of attempt status in multiple attempters who reported high belongingness than in multiple attempters who reported low belongingness
Jokinen, J., Nordstrom, A. L., & Nordstrom, P. (2010). Cholesterol, CSF 5-HIAA, violence and intent in suicidal men. <i>Psychiatry Research</i> , 178(1), 217-219. doi:10.1016/j.psychres.2008.07.020	13 medication-free male suicide attempters and eight healthy volunteers	Experimental	Age BMI HDL LDL Sex Hypcholesterolaemia 5-hydroxyindolacetic acid (5-HIAA) Suicide intent Suicide attempt	Cholesterol levels did not differ between violent and non-violent suicide attempters or between suicide completers and survivors. In non-violent suicide attempters, HDL-C showed a significant positive correlation with the planning subscale of suicide intent ($r=0.91$, $p<0.05$) and serum cholesterol a trend ($r = 0.83$, $p<0.08$). In violent suicide attempters, the serum cholesterol levels did not correlate with the planning subscale of suicide intent. Serum total cholesterol showed a negative correlation with MADRS scale in suicide attempters ($r=-0.66$, $P<0.05$).
Kaplan, J. R., Shively, C. A., Fontenot, M. B., Morgan, T. M., Howell, S. M., Manuck, S. B., . . . Mann, J. J. (1994). Demonstration of an association among dietary cholesterol, central serotonergic activity, and social behavior in monkeys. <i>Psychosomatic Medicine</i> , 56(6), 479-484.	Juvenile cynomolgus monkeys (eight female and nine male)	Experimental	Diet Norepinephrine Dopamine Serotonin Cholesterol Social behavior Violent behavior	Animals that consumed a low-cholesterol diet were more aggressive, less affiliative, and had lower cerebrospinal fluid concentrations of 5-hydroxyindoleacetic acid than did their high-cholesterol counterparts ($p < .05$ for each). The association among dietary cholesterol, serotonergic activity, and social behavior was consistent with data from other species and experiments and suggested that dietary lipids can influence brain neurochemistry and behavior.

Citation	Sample Size and Setting	Design	Major Variables Examined	Results
Maguen, S., Madden, E., Cohen, B. E., Bertenthal, D., Neylan, T. C., & Seal, K. H. (2015). Suicide risk in Iraq and Afghanistan veterans with mental health problems in VA care. <i>Journal of Psychiatric Research</i> , 68, 120-124. doi:10.1016/j.jpsychires.2015.06.013	All Iraq and Afghanistan war veterans who screened positive for PTSD and/or depression, between January 1, 2010 and June 29, 2014 (n=45,741)	Cross-Sectional	Iraq and Afghanistan war veterans, PTSD depression suicidal thoughts, deployment, alcohol use disorder,	In high-risk veterans, some of the strongest associations with suicidality were with modifiable risk factors, including time to VA care and alcohol use disorder diagnoses.
Mann, J. J., & Malone, K. M. (1997). Cerebrospinal fluid amines and higher-lethality suicide attempts in depressed inpatients. <i>Biological Psychiatry</i> , 41(2), 162-171.	22 drug free inpatients with major depression	Experimental	Suicide attempt, major depression, serotonin,	CSF 5-HIAA levels were lower in depressed patients with a history of a high-lethality or well-planned suicide attempt compared to depressed patients with a history of only low-lethality suicide attempt(s). Other CSF monoamine metabolites did not correlate with suicidal behavior. Low serotonergic activity may correlate with a predisposition to more lethal suicide attempts in major depression.
Neaton, J. D., Blackburn, H., Jacobs, D., Kuller, L., Lee, D. J., Sherwin, R., . . . Wentworth, D. (1992). Serum cholesterol level and mortality findings for men screened in the Multiple Risk Factor Intervention Trial. <i>Multiple Risk Factor Intervention Trial Research Group. Archives of Internal Medicine</i> , 152(7), 1490-1500.	350,977 men aged 35 to 57 years who had been screened for the Multiple Risk Factor Intervention Trial over a 12 year period	Secondary analysis	Cholesterol, health risk factors	A serum cholesterol level less than 4.14 mmol/L (<160 mg/dL) was also associated with a significantly increased risk of death from various factors including suicide.
Persons, J. E., Coryell, W. H., & Fiedorowicz, J. G. (2012). Cholesterol fractions, symptom burden, and suicide attempts in mood disorders. <i>Psychiatry Research</i> , 200.	35 Caucasian adults with major depression or bipolar disorder	Cross-Sectional	Depression, suicide attempt,	Researchers found no significant difference ($p=0.24$) in mean LDL-c levels between individuals with a history of suicide attempts (129.8 (27.7) mg/dL) and individuals with no documented history of suicide attempt (117.9 (25.5) mg/dL), nor did we detect a significant difference ($p=0.52$) in mean (S.D.) HDL-c levels between attempters (53.1 (15.0) mg/dL) and non-attempters (56.0 (11.4) mg/dL). Depressive symptom burden was correlated with neither HDL-c ($r=0.10$, $p=0.56$) nor LDL-c ($r=0.09$, $p=0.62$) levels.
Poorolajal, J., Haghtalab, T., Farhadi, M., & Darvishi, N. (2015). Substance use disorder and risk of suicidal ideation, suicide attempt and suicide death: a meta-analysis. <i>J Public Health (Oxf)</i> . doi:10.1093/pubmed/fdv148	12,413 references, included 43 studies with 870,967 participants	Meta-analysis	SUD, suicidal ideation	There was a significant association between SUD and suicidal ideation: OR 2.04 (95% CI: 1.59, 2.50; $I^2 = 88.8\%$, 16 studies); suicide attempt OR 2.49 (95% CI: 2.00, 2.98; $I^2 = 94.3\%$, 24 studies) and suicide death OR 1.49 (95% CI: 0.97, 2.00; $I^2 = 82.7\%$, 7 studies).

Citation	Sample Size and Setting	Design	Major Variables Examined	Results
Seo, D., Patrick, C. J., & Kennealy, P. J. (2008). Role of Serotonin and Dopamine System Interactions in the Neurobiology of Impulsive Aggression and its Comorbidity with other Clinical Disorders. <i>Aggress Violent Behav</i> , 13(5), 383-395. doi:10.1016/j.avb.2008.06.003		Literature Review		Impulsive aggression is characterized by an inability to regulate affect as well as aggressive impulses, and is highly comorbid with other mental disorders including depression, suicidal behavior, and substance abuse. In an effort to elucidate the neurobiological underpinnings of impulsive aggression and to help account for its connections with these other disorders, this paper reviews relevant biochemical, brain imaging, and genetic studies. The review suggests that dysfunctional interactions between serotonin and dopamine systems in the prefrontal cortex may be an important mechanism underlying the link between impulsive aggression and its comorbid disorders. Specifically, serotonin hypofunction may represent a biochemical trait that predisposes individuals to impulsive aggression, with dopamine hyperfunction contributing in an additive fashion to the serotonergic deficit. The current paper proposes a modified diathesis-stress model of impulsive aggression in which the underlying biological diathesis may be deficient serotonergic function in the ventral prefrontal cortex. This underlying disposition can be manifested behaviorally as impulsive aggression towards oneself and others, and as depression under precipitating life stressors.
Virkkunen, M. (1979). Serum cholesterol in antisocial personality. <i>Neuropsychobiology</i> , 5(1), 27-30.	274 subjects with personality disorders	Cross-Sectional	Age Sociopathy Psychopathy Sex Cholesterol Antisocial Personality	The group of subjects with antisocial personality had a clearly lower mean level of serum cholesterol than the group with other personality disorders which was used as a control group. The use of a mean male population with standardized ages as a control group further emphasized the low values of the serum cholesterol of the antisocial personality group.

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