

THE PENNSYLVANIA STATE UNIVERSITY
SCHREYER HONORS COLLEGE

DEPARTMENT OF HUMAN DEVELOPMENT AND FAMILY STUDIES

THE EFFECT OF DEPRESSION ON CANCER PROGRESSION AND MORTALITY
AMONG ADULTS

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SPRING 2015

A thesis
submitted in partial fulfillment
of the requirements
for a baccalaureate degree
in Human Development and Family Studies
with honors in Human Development and Family Studies

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ABSTRACT

Receiving a diagnosis of cancer is a stressful life event that affects every individual differently. Most respond to a cancer diagnosis with feelings of shock, anger, helplessness, and sadness. However, for some these feelings do not go away and result in depressive symptoms or depression. The question of how depressive symptoms and depression affect cancer progression and mortality has been investigated in studies. This literature review reviewed and synthesized longitudinal research that examines the effect of untreated depressive symptoms and depression on cancer progression and mortality. Results showed conflicting findings across studies due to a variation of samples, cancer types, cancer stages, and depression measures. This review displayed the need for additional examination of depressive symptoms and depression and the effect it has on cancer progression and mortality.

TABLE OF CONTENTS

LIST OF FIGURES	iii
LIST OF TABLES	iv
ACKNOWLEDGEMENTS	V
Chapter 1 Introduction	1
Cancer	2
Depression.....	3
Cancer and the Effects of Depression and Depressive Symptoms.....	5
Chapter 2 Methods.....	7
Objective.....	7
Search for Studies	7
Selection of Studies.....	7
Chapter 3 Defining Depression and Depressive Symptoms.....	9
DSM-5 Depression Diagnosis.....	9
Changes in Depressive Diagnostic Criteria from DSM-IV-TR to DSM-5	10
ICD-10 Depression Diagnosis.....	11
Chapter 4 Measurement of Depression and Depression Assessment Scales	13
Chapter 5 Results	17
Study Characteristics.....	17
Chapter 6 Discussion	23
Limitations	25
Future Research.....	27
Conclusion	28
BIBLIOGRAPHY.....	30

LIST OF FIGURES

Figure 2-1: Systematic Review Process for the Selection of Studies8

LIST OF TABLES

Table 4-1: Description of Assessment Methods Utilized in Reviewed Studies.....	15
Table 5-1: Characteristics of Reviewed Studies	18

ACKNOWLEDGEMENTS

To start I would like to thank my thesis advisor, Dr. Lynn Martire, for helping me throughout this entire process. Your patience and guidance played an instrumental role in the completion of my thesis.

I would also like to thank my friends, specifically my roommates, for letting me talk about my thesis constantly and vent when I was stressed. Your support and encouragement contributed significantly to completing my thesis. Mom and Dad, thank you for always being willing to lend a listening ear and supporting me. Your faith in me has never wavered and I would not have had the drive to finish this thesis without you. Thank you!

Chapter 1

Introduction

This paper will review the effects of depression and depressive symptoms on patients diagnosed with cancer. Throughout the decades many have believed that a positive mindset affects the progression and outcome of illness and disabilities. Scientists have looked at the psychological aspects of depression, as well as the physiological pathways and effects of depression on the human body. Research has focused on various physical illnesses, including the effects of depression on cancer progression and mortality among patients diagnosed with cancer. Many studies have examined the effects of depression when comorbid with cancer. It has been argued that a patient's attitude is a key component in cancer outcome. Whether positive or negative aspects of attitudes and beliefs affect cancer progression and mortality is a heavily debated and studied phenomenon. According to Makhoul (2013), doctors and cancer patients believe depression and a negative attitude will have a negative effect on cancer outcomes.

It is important to understand the effects of depressive symptoms on the human body, whether the individual has cancer or not. However, it is especially important to examine how depression affects cancer progression and mortality, in an effort to reduce rates of depression among cancer patients and increase survival. According to Watson, Haviland, Greer, Davidson, and Bliss (1999) women who are diagnosed with early stage breast cancer have an increased risk of mortality if they also experience depression. Additionally if depression remains untreated in individuals with or without cancer it will have a significant effect on their mortality (Massie, 2004). A study conducted by Buccheri (1998) showed a relationship between psychological health and lung cancer outcome. They found the more depressed a cancer patient was the higher

their risk of death, then mentioned the importance of positive mental health on a cancer patient's survival (Buccheri, 1998).

Cancer

People are diagnosed with cancer everyday. It is predicted that by 2042 cancer incidence will rise by more than 150 percent (World Health Organization [WHO], 2015). According to the World Health Organization (2015), cancer is considered to be one of the main causes of morbidity and mortality for humans throughout the world. In recent decades cancer research has increased exponentially. Worldwide scientists are working to find cures for various types of cancers. Medical advancements have increased and many forms of cancer are considered to be more treatable today than forty years ago. According to the National Cancer Institute (2015) the passing of the National Cancer Act in 1971 allowed scientists to learn more about cancer prevention, detection, treatment, and survival.

Cancer refers to a group of diseases that may affect any living organism, in any part of the body (WHO, 2015). The types of cancer associated with the highest mortality rates are lung, liver, stomach, and colorectal. Cancer results when an individual cell in the body does not develop correctly, resulting in an abnormal cell. The cell then divides through the process of mitosis resulting in the production of additional abnormal cells. While normal, healthy cells mature and die, abnormal cells do not; therefore, the amount of abnormal cells may increase exponentially and cause tumors to grow. Abnormal cells produced in one region of the body may invade other parts of the body (American Cancer Society, 2014). Cancer treatments focus on the physiological and biological aspects of cancer. Some common forms of treatment are targeted

therapies that will only attack specific areas and substances in the body, as well as immunotherapies, surgery, chemotherapy, and radiation (American Cancer Society, 2014).

While the biological aspect of cancer is key to finding a cure, there are numerous physiological and psychological factors that interact to affect cancer progression, morbidity, and mortality. Therefore it is important to study various social and psychological variables and their effects on cancer.

Depression

One psychological variable that has been studied and shown to affect cancer progression is depression. Depression alone has a negative impact on an individual's life. It can increase the chance of death, specifically in terms of suicide. In 2012 successful suicides accounted for 1.4% of deaths around the world (WHO, 2015). Depression is a disorder of the brain that affects an individual's mental state. The cause of depression is a complex phenomenon. Many psychologists think depression and depressive symptoms stem from multiple variables such as genetic, environmental, biological, and psychological factors (National Institute of Mental Health [NIMH], 2015).

There are several types of depression. Major Depressive Disorder and Persistent Depressive Disorder are two of the most common types of depression. However, there are some variations of depression that develop depending on circumstance. Some examples of these are psychotic depression, postpartum depression, and seasonal affective disorder (NIMH, 2015). Adjustment disorder is another diagnosis that is related to a depression diagnosis or experiencing depressive symptoms. This disorder may be extremely relevant among cancer patients.

Adjustment disorder can be characterized by an emotional reaction to a stressful incident, such as receiving a cancer diagnosis (Patra & Sarkar, 2013). However it is important to recognize that many people who are suffering from cancer may experience some depressive symptoms.

Suffering from fewer and more mild depressive symptoms may qualify these individuals for a minor depression diagnosis (Andrews, 2010). According to the National Institute of Mental Health (2015) the existence of depression in addition to another diagnosis results in more severe depressive symptoms as well as medical symptoms.

The prevalence of depression is high throughout the world. It is estimated that around 121 million individuals suffer from depression during their lifetime. In the United States it is estimated that one in five people will develop depressive symptoms during their life, and one in ten children will experience depression during adolescence (Massie, 2004). It is important to note that post-pubescent females are more likely to develop depression than males by a two to one (2:1) ratio (Massie, 2004).

Although depression is a mental illness, those suffering from depression tend to experience a wide array of physical consequences. Depression affects an individual's sleep cycle. People who are depressed tend to experience less time in "deep sleep" and more time in REM sleep. This causes their immune system to weaken making them more susceptible to illness and disease (Tyrrell & Elliott, 2013). Serotonin levels play a key role in the development, maintenance, and treatment of depressive symptoms. Selective serotonin reuptake inhibitor medications (SSRIs) used to treat depression affect the amount of serotonin produced in the brain. Serotonin helps block pain receptors in the brain; therefore, the decreased levels of serotonin that characterize some types of depression intensify patient pain (Tyrrell & Elliot, 2013). According to a pioneer study conducted by Derogatis, Morrow, & Fetting (1983) of the

cancer patients who were diagnosed with a psychiatric disability, thirty-nine percent reported substantial pain, while only nineteen percent of patients without a psychiatric disability reported pain. Decreased levels of serotonin in depressed patients may enhance their experience of cancer-related pain.

Cancer and the Effects of Depression and Depressive Symptoms

It can be anticipated that patients suffering from cancer experience varying levels of stress, anxiety, and depression following a cancer diagnosis. When an individual experiences increased levels of stress for a long period of time, as many cancer patients do, it can cause several physical problems (American Cancer Society, 2014). Moreno-Smith, Lutgendorf, and Sood (2010) found tumor growth and progression may be caused by chronic stress which “activates specific signaling pathways in cancer cells and the tumor microenvironment” (p13). Another study found that patients who better manage their stress levels and negative mood have less cancer metastasis and tumor growth (Antoni, et al., 2006). Stress influences various hormones that contribute to cancer growth. For example, prolactin, a hormone that increases the physiological response to stress, causes cancerous cell growth and cancerous cell survival (McDonald, et al., 2005). Additionally chronic stress suppresses various functions of the immune system such as humoral and cell-mediated immunity, T-cell proliferation, and antigen presentation (McDonald, et al., 2005). According to a study by van Pragg (2004), depression tends to result from life stressors or stressful events that occur in an individual’s life. Stress has been linked to the development of depressive features, specifically anxiety and aggressive symptoms (van Pragg, 2004).

The prevalence of patients suffering from both depression and cancer may be underestimated. One study found a 42% prevalence of depression among 62 cancer patients who were hospitalized (Bukberg, Penman, & Holland, 1984). Another study found 33% of eighty patients in the hospital being treated for cancer had a depression diagnosis (Plumb & Holland, 1977).

Researchers have investigated whether some types of cancer cause and exacerbate depression in patients more than other types of cancer. Individuals with pharyngeal cancer have a 22%-57% risk of depression (Davis, Davis, & Deplo, 1986; Cavusoglu, 2001), pancreatic cancer patients have a 33%-50% risk (Fras, Litin, & Pearson, 1967; Joffe, Rubinow, Denicoff, Maher, & Sindelar, 1986), and breast cancer patients have a risk of 1.5%-46% (Sneeuw et al., 1993; Sachs et al., 1995). In addition, Ciaramella and Poli (2001) found that cancer patients who experienced depression or depressive symptoms were more likely to have cancer that metastasized or was in an advanced stage.

The purpose of this review is to review and synthesize longitudinal research that examines the effect of untreated depression and depressive symptoms on cancer progression and mortality. It is important for scientists, doctors, psychologists, and other health professionals to understand the effect of depression on cancer outcomes in order to better diagnosis and treat depression among cancer patients. An improved understanding of depression's effect on cancer, may lead to increased screening and better treatment of depression, and thus improve survival rates. Therefore it is important to investigate whether having depression or experiencing depressive symptoms increases the risk of cancer progression and mortality.

Chapter 2

Methods

Objective

The objective of this paper is to review evidence for the effects of untreated depression and depressive symptoms on cancer progression and mortality in adults.

Search for Studies

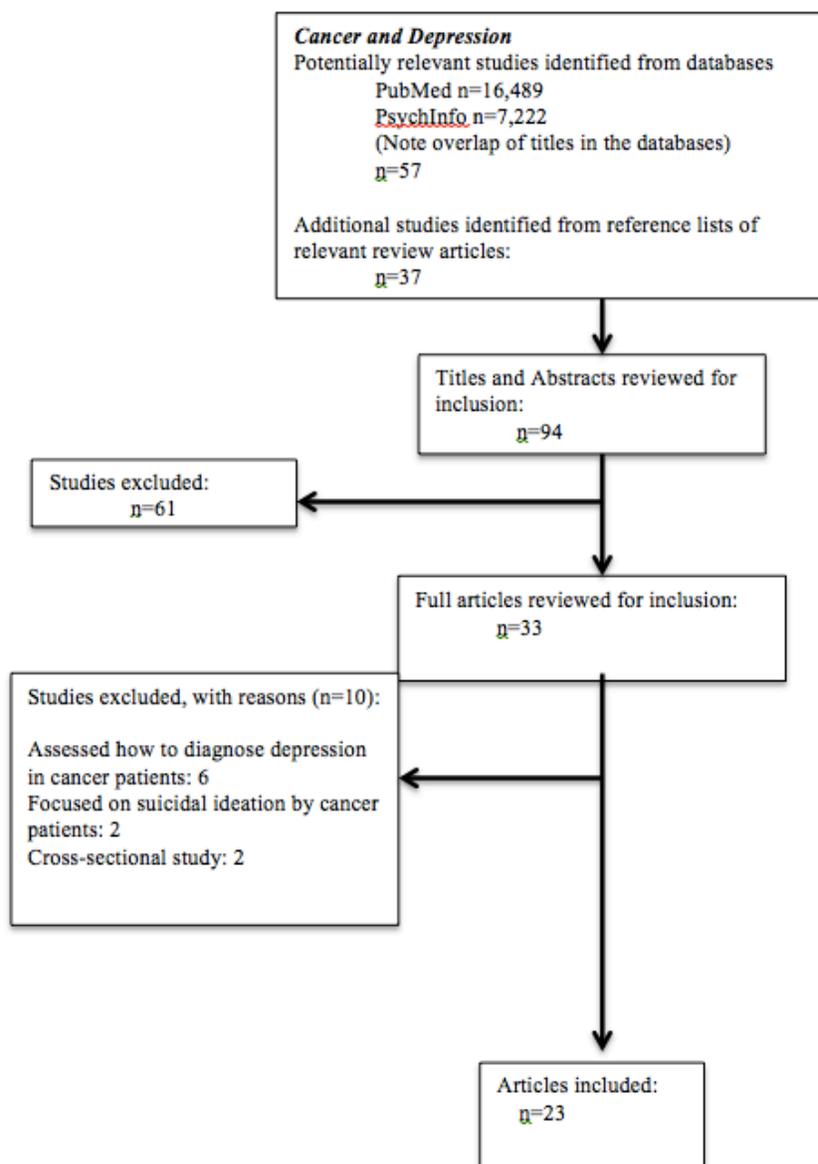
A search was conducted using the electronic databases PubMed and PsychInfo. The search terms entered were used as keywords: cancer and depression and [mortality or hazards or survival]. Ninety-four abstracts were reviewed as a preliminary step in examining relevance of articles. In addition reference lists of several review articles were examined in order to identify additional studies not retrieved in the search.

Selection of Studies

All studies followed a cohort of individuals suffering from cancer. Included articles had to meet the following criteria: 1) longitudinal design with measurement of depression or depressive symptoms using survey(s) or interview questions; 2) examined the potential effects of depression, depressive episodes, or depressive symptoms on cancer progression and mortality; 3) published in the English language; 4) enrolled participants over the age of eighteen. Articles were excluded if the study: 1) focused on how to diagnosis and treat depression in cancer

patients; 2) focused on the effects of treating depression in cancer patients 3) examined whether patients suffering from depression were more likely to develop cancer as a result of their depression; 4) focused on suicidal behaviors. Please see Figure 2-1.

Figure 2-1: Systematic Review Process for the Selection of Studies



Chapter 3

Defining Depression and Depressive Symptoms

Depression is defined according to the definition set forth by The Diagnostic and Statistical Manual of Mental Disorders (DSM) and the International Classification of Diseases (ICD). The DSM is compiled by the American Psychiatric Association and sets the diagnostic criteria for the classification of mental disorders in the United States (American Psychiatric Association, 2014). The ICD, developed by the World Health Association, also gives diagnostic criteria for depression and other mental health disorders (WHO, 2015). As depression is a diagnosed mental disorder, individuals who receive a diagnosis of depression must meet the diagnostic criteria set forth by either the DSM-5 or the ICD-10. Since their formal inception the DSM and ICD have been updated and revised. This has led to changes such as changing criteria for depression diagnoses. The current manuals used to diagnosis depression are the DSM-5 in 2013 and the ICD-10 in 1992 (American Psychiatric Association, 2014). However due to the publication dates of several articles examined in this analysis some studies used the DSM-IV or the DSM-IV-TR to diagnose depression.

DSM-5 Depression Diagnosis

According to the DSM-5 (2013) depression is divided into four main disorders: Major Depressive Disorder (MDD), Persistent Depressive Disorder (PDD), Disruptive Mood Dysregulation, and Premenstrual Dysphoric Disorder. The articles examined in this literature

review focus on a depressive diagnosis of either MDD, PDD, or exhibiting depressive symptoms outlined in the DSM-5.

Major Depressive Disorder (MDD) is diagnosed when five or more symptoms are present for a week or more, cause significant distress or impairments in an individual's functioning, and are not due to another condition or substance. These symptoms include: depressed mood, decreased interest or pleasure in activities that used to be enjoyable, weight loss, decrease or increase in appetite, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or excessive guilt, decreased concentration, and/or recurrent thoughts of death and suicide (DSM-5, 2013).

Persistent Depressive Disorder (PDD), formerly known as Dysthymia, is when depressive symptoms occur on most days for at least two years or more. Symptoms, must cause significant distress or impairment in an individual's functioning and not be due to another condition or substance. An individual must exhibit two or more the following symptoms: change in appetite, change in sleep patterns, low energy, decreased concentration, decreased self-esteem, and feelings of hopelessness (Long, 2015).

Changes in Depressive Diagnostic Criteria from DSM-IV-TR to DSM-5

Several articles examined in this review were published before the publication of the DSM-5. The Diagnostic Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR), published in 2000, and the Diagnostic Statistical Manual of Mental Disorders, 4th Edition (DSM-IV), published in 1994, were used to identify depressive disorders and symptoms in cancer patients.

The diagnostic criteria for depressive disorders is the same as the criteria stated in the DSM-5. However, there are a few significant changes that should be noted. The DSM-5 added new disorders under the Depressive Disorders category, such as disruptive mood dysregulation disorder and premenstrual dysphoric disorder. Another change is that psychologists recognize depression due to the death of a loved one may last longer than the specified two months in DSM-IV. Therefore depression from bereavement now falls under a symptom of Major Depressive Disorder. A final change is the emphasis that is now placed on anxiety and the effect of anxiety on depression, depressive symptoms, and suicidal behaviors. Although these changes are minimal it is important to note how current diagnostic methods may differ from those used in past research.

ICD-10 Depression Diagnosis

According to the ICD-10 (1992) depression is categorized by episode. There are varying levels of depressive episodes: mild, moderate, severe without psychotic symptoms, severe with psychotic symptoms, other, and unspecified. The level of the depressive episode is determined by the amount of symptoms exhibited and the severity of symptoms. Depressive episodes occur when an individual experiences: decreased mood, decreased self-esteem, a decrease in the enjoyment of activities, lowered concentration, changes in sleep pattern, change in appetite, feelings of worthlessness, and psychomotor retardation. Additionally the ICD-10 (1992) identifies specified criteria for a depressive disorder diagnosis. Depressive disorder occurs when an individual experiences repeated depressive episodes and symptoms associated with mild,

moderate, severe without psychotic symptoms, severe with psychotic symptoms, other, and unspecified depressive episodes.

A mild depressive episode requires at least two depressive symptoms whereas a moderate depressive episode requires four or more depressive. A severe depressive episode without psychotic symptoms requires several symptoms and a severe depressive episode with psychotic symptoms requires several symptoms of depression in addition to hallucinations, delusions, or stupor that drastically reduce the ability to participate in everyday functioning. Other depressive episodes may be a single depressive episode, or “masked” depression.

Chapter 4

Measurement of Depression and Depression Assessment Scales

Throughout the world scientists use various techniques and methods to assess adults for depression. Among the studies included in this review, several methods were used to evaluate cancer patients for depression and depressive symptoms. Each method assesses depressive symptoms differently. Self-report questionnaires, surveys, and scales are commonly used to assess depression. Structured interviews and admittance to psychiatric treatments were also used for diagnoses. Some instruments focus only on depressive symptoms outlined by the DSM-IV, DSM-V, or ICD-10, while others assess anxiety, patient reactions to a physiological diagnosis, feelings of helplessness, optimism, and energy levels [Table 4.1].

The most common methods of assessment for depression among cancer patients was the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Smith, 1983), the Center for Epidemiologic Studies Depression Scale (CES-D) (Radloff, 1977), and the Mental Adjustment to Cancer Scale (MAC) (Watson et al., 1988). Researchers employed several other self-reported questionnaires as well. Scientists utilized these scales to diagnosis depression among cancer patients by administering the scales to patients who had recently received a diagnosis of cancer. The score depicts whether an individual experiences depressive symptoms and the severity of their symptoms.

Interviews were the other method of assessment used to identify patients diagnosed with cancer who were experiencing depression or depressive symptoms. The interviews used were the Structured Clinical Interview from the Diagnostic and Statistical

Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR) (Othmer & Othmer, 2002), the International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998) and the Structured Interview Guide for the Hamilton Anxiety/Depression Scales (Bech, 2009).

Table 4-1: Description of Assessment Methods Utilized in Reviewed Studies

Measures Used to Assess Depression/ Depressive Symptoms	Number of Studies That Used Measure	Type of Assessment	Description of Measure
HADS	7	Self-report questionnaire	Measures anxiety and depression
CES-D	6	Self-report questionnaire	Assesses depressive symptoms
MAC	4	Self-report questionnaire	Assess patients' reactions to having cancer in five dimensions: fighting spirit, helplessness or hopelessness, anxious preoccupation, fatalism, and avoidance
HADS-D	1	Self-report questionnaire	Subset; measures anxiety and depression
GHQ-12	1	Self-report questionnaire	Inquires about levels of happiness, experience of depressive symptoms and anxiety symptoms, and changes in sleep over the previous four weeks
Affect Balance Scale	1	Self-report questionnaire	Measures mood
EDS	1	Self-report questionnaire	Assesses depression in women in the postnatal period; excludes somatic symptoms of depression
BDI	1	Self-report questionnaire	Assesses depressive symptoms according to criteria in the DSM-IV
LOT	1	Self-report questionnaire	Assesses levels of optimism and pessimism
PSSCAN	1	Self-report questionnaire	Assess anxiety and depressive symptoms based on criteria from DSM-IV-TR, perceived social support, desire social support, and quality of life; specifically used with cancer patients
GWB-D	1	Self-report questionnaire	Assess overall subjective well-being; six subscales assess: freedom from health worry, energy level, satisfying and interesting life, cheerful vs. depressed mood, relaxed vs. anxious, and emotional behavior control
SCID	3	Interview	Interviews focus on mood, anxiety and adjustment disorders
MINI	1	Interview	Depression diagnosis based on DSM-IV criteria
SIGH-AD	1	Interview	Assess symptoms of depression and anxiety over the past week
DSMI-IV-TR	1	Diagnostic Criteria	Diagnostic and Statistical Manual Fourth Edition Revised
Admission to a psychiatric department	1	-----	Admission into a psychiatric department due to a patient experiencing depressive symptoms

Notes. HADS=Hospital Anxiety and Depression Scale, MINI=International Neuropsychiatric Interview, CES-D= Center for Epidemiologic Studies Depression Scale, SCID=Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, 4th Ed. Text Revision, GHQ-12=General Health Questionnaire, EDS=Edinburgh Depression Scale, LOT= Life Orientation Test, SIGH-AD =Structured Interview Guide for the Hamilton Anxiety/Depression Scales, PSSCAN=Psychosocial Screen for Cancer, GWB-D=General Well-being Schedule, MAC=Mental Adjustment to Cancer Scale

Chapter 5

Results

Study Characteristics

The studies included in this review evaluated predictors of survival for patients suffering from cancer, and potential hazards associated with depression and depressive symptoms that led to patient mortality, or death. The articles reviewed were published in different countries, had varying sample sizes, examined diverse types of cancer, and included samples of males, females, or both. Studies used data from baseline survey(s) and interview question(s), and from follow-up data collected at varying points following baseline, depending on the study. These studies also varied in terms of the types of measures they used to assess depression [Table 5.1].

Table 5-1: Characteristics of Reviewed Studies

First Author, Year, Country	No. of Participants, Cancer Type, Sex	Outcome, Length of Follow-Up	Measure of Depression & Depressive Symptoms
Arrieta 2013, Mexico	n=82, lung cancer, both	Mortality and Health-related quality of life, 6 months	HADS, MINI
Bergenmar 2004, Sweden	n=436, melanoma, both	Mortality, 1-17 months	HADS
Brown 2003, United States	n=205, mixed, both	Mortality, 15 months	CES-D
Chan 2014, Malaya	n=467, mixed, both	Mortality 24 months	HADS, SCID DSM-IV-TR
Chen 2010, Taiwan	n=90, advanced lung cancer, both	Mortality, 10-20 months	HADS-D
Faller 2004, Germany	n=59, lung cancer, male	Mortality, 4-6 years	Sub-Scale of HADS
Graham 2002, United Kingdom	n=202, breast cancer, female	Recurrence of disease, 5 years	Structured Clinical Interview
Hamer 2009, United Kingdom	n=15,453, mixed, both	Mortality, 3-11 years	GHQ-12
Hjerl 2003, Denmark	n=20,593, breast cancer, women	Mortality, death	Admission to any psychiatric department or hospital in Denmark
Levy 1988, United States	n=36, breast cancer, women	Mortality, death/end of study	Structured Interview; Affect Balance Scale
Lloyd-Williams 2009, United Kingdom	n=90, mixed, both	Mortality, 12 months	EDS
Maino 2006, Finland	n=101, brain tumors, both	Mortality, 12-13 years	BDI
Nakaya 2008, Japan	n=1178, lung cancer, both	Mortality, 6 months–5 years	Japanese versions of HADS, MAC,
Onitilo 2006, United States	n=10,523, none/mixed, both	Mortality, ~8 years	CES-D
Schulz 1996, United States	n=238, mixed, both	Mortality, 8 months	LOT, CES-D
Steel 2007, United States	n=103, hematologic, both	Mortality, death	CES-D
Stommel 2002, United States	n=871, breast/colon/lung/prostate, both	Mortality, 19 months or death/end of study	CES-D, questioned if they were diagnosed for emotional, nervous, or psychiatric problems
Sullivan , 2014, United States	n=3,869, lung cancer, both	Mortality, 24 months	Depression-related hospitalizations and mental health care visits
Telepak 2014, United States	n=87, endometrial cancer, women	Mortality, 60 months	SIGH-AD
Vodermaier 2014, Canada	n=1,646, breast cancer, women	Mortality, median 76 months	PSSCAN
Watson 1999, United Kingdom	n=578, breast cancer, women	Mortality, 5 years	MAC, HADS
Watson 2005, United Kingdom	n=578, breast cancer, women	Mortality/progression, 10 years	MAC, HADS
Zonderman 1989, United States	n=2814, mixed, both	Mortality, 15 years	CES-D, GWB-D

Notes. HADS=Hospital Anxiety and Depression Scale, MINI=International Neuropsychiatric Interview, CES-D= Center for Epidemiologic Studies Depression Scale, SCID=Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, 4th Ed. Text Revision, GHQ-12=General Health Questionnaire, EDS=Edinburgh Depression Scale, LOT= Life Orientation Test, SIGH-AD =Structured Interview Guide for the Hamilton Anxiety/Depression Scales, PSSCAN=Psychosocial Screen for Cancer, GWB-D=General Well-being Schedule, MAC=Mental Adjustment to Cancer Scale

There were mixed findings across studies. Fifteen of the studies (65%) described a significant association between depression and shorter survival time among cancer patients, while four of the studies found no significant association between depression and mortality. Four additional studies found it was not depression that was associated with decreased survival time but other psychological factors (i.e., hopelessness and helplessness). However, some studies found an association between depression and mortality for certain subgroups, such as age groups or men/women.

Studies that found a positive association between depression and cancer progression and mortality used various measures of depression and depressive symptoms. These include the HADS, MINI, CES-D, SCID, GHQ-12, Affect Balance Scale, EDS, admission to any psychiatric department or hospital, BDI, MAC, and PSSCAN (Arrieta et al., 2013; Brown et al., 2003; Chan et al., 2014; Chen et al., 2010; Hamer et al., 2009; Hjerl et al., 2003; Levy et al., 1988; Lloyd-Williams et al., 2009; Maino et al., 2006; Nakaya et al., 2008; Onitilo et al., 2006; Stommel et al., 2002; Sullivan et al., 2014; Vodermaier et al., 2014; Watson et al., 1999). Studies that did not find a significant association between depression and mortality also used various measures to diagnosis depression and depressive symptoms among cancer patients, including the HADS, Sub-scale of HADS, SCID, LOT, CES-D, SIGH-AD, MAC, and GWB-D (Bergenmar et al.,

2004; Faller et al., 2004; Graham et al., 2002; Schulz et al., 1996; Steel et al., 2007, Watson et al., 2005; Zonderman et al., 1989).

While the same measures were used to assess depression and depressive symptoms in studies that produced conflicting results it is important to identify the different types of cancer that were evaluated across the studies. Five studies (Arrieta et al, 2013; Chen et al., 2010; Faller et al., 2004; Nakaya et al., 2008; Sullivan et al., 2014) examined the relationship between depression and depressive symptoms among lung cancer patients. All except for one (Faller et al., 2004) found a significant positive association between depression and decreased survival time. Arrieta et al., (2013), Chen et al., (2010), Nakaya et al., (2008), and Sullivan et al., (2014), used samples consisting of males and females diagnosed with lung cancer, however Faller et al., (2004) used a sample solely made up of males.

Among the seven studies examining the role of depression and depressive symptoms on female patients diagnosed with breast cancer, there were mixed results (Brown et al., 2003; Graham et al., 2002; Hjerl et al., 2003; Levy et al., 1988; Vodermaier et al., 2014; Watson et al., 1999; Watson et al., 2005). All found a significant association between depression and depressive symptoms and increased mortality risk among breast cancer patients except Watson et al. (1999) and Graham et al. (2002). However it is important to consider what Graham et al. (2002) and Watson et al. (1999) were measuring. Graham et al. (2002) examined the relationship between a depressive episode after a severely stressful life experience, and whether breast cancer reoccurred in the participant. Using the SCID to assess depression and depressive symptoms this study found that experiencing stressful life events did not have a significant association on cancer recurrence. Watson et al. (1999) used MAC to assess depression, and found a non-significant association between depression and decreased survival outcomes for breast cancer

patients. However, they did conclude there is a significant relationship between feelings of helplessness or hopelessness and decreased survival.

Other types of cancer were assessed in the studies included in this review. Researchers examined the effects of depression and depressive symptoms on melanoma (Bergenmar et al., 2004), brain tumors (Maino et al., 2006), carcinoma (Steel et al., 2007), and endometrial cancer (Telepak et al., 2014). Maino et al., (2006) examined the relationship between depression and decreased quality of life among patients suffering from low-grade glioma, a form of cancer in the brain. Depression resulted in a decreased quality of life. These two factors were found to have a significant association with shorter survival times among both male and female patients. The other three studies found non-significant associations between depression and decreased survival outcomes among patients diagnosed with melanoma, carcinoma, and endometrial cancer.

The remaining studies focused on samples of patients suffering from various types of cancer. These are described as “mixed” samples, and consist of both male and female patients. Five of the seven studies reviewed found a significant association of depression or depressive symptoms with higher chances of mortality and lower survival rates (Chan et al., 2014; Hamer et al., 2009; Lloyd-Williams et al., 2009; Onitilo et al., 2006; Stommel et al., 2002). However, two studies that examined mixed samples of male and female patients did not find a significant association between depression or depressive symptoms and risk of mortality (Schulz et al., 1996; Zonderman et al., 1989).

Among the studies reviewed there was variation of cancer stage. Of the fifteen studies that found an association between depression and cancer progression only three (20%) used a sample of only cancer patients diagnosed with an advanced stage of cancer (Arrieta et al., 2013; Chen et al., 2010; Lloyd-William et al., 2009); ten (66%) used a sample of cancer patients

diagnosed with varying stages of cancer (Brown et al., 2003; Chan et al., 2014; Hamer et al., 2009; Hjerl et al., 2003; Levy et al., 1988; Nakaya et al., 2008; Onitilo et al., et al 2006; Steel et al., 2007; Stommel et al., 2002; Sullivan et al., 2014, Vodermaier et al., 2014); and two used a sample of cancer patients diagnosed in the early stages of cancer (Maino et al., 2006; Watson et al., 1999).

The differing methods of each study may explain why conflicting results were produced. Various measurement tools were used to assess and diagnosis depression and depressive symptoms. Additionally several different types of cancer, various cancer stages, and diverse predicted outcomes were examined to see how depression and depressive symptoms affects cancer progression and patient mortality. Finally participant samples included either only males, only females, or both, as well as participants of various ages.

Chapter 6

Discussion

Experiencing depressive symptoms is a common experience, affecting people throughout the world. The estimated lifetime incidence for adults in the United States is twenty percent (Massie, 2004). Depression has a significant impact on an individual's mental state, physical functioning, and quality of life. It is important to understand the side effects associated with depression, particularly how it affects the physiological processes of the human body. Cancer prevalence is high as well. According to Kamanger, Dores, and Anderson (2006) over 25 million people throughout the world are affected by cancer.

It is important to understand the role depression plays in cancer progression and mortality among adults suffering from different types of cancer. Assessing and diagnosing depression in cancer patients remains a challenge for clinicians. It is difficult for psychologists and treating physicians to recognize and effectively treat depressive symptoms found among cancer patients. There are many aspects of cancer and cancer treatments that affect the psychological functioning of patients. Cancer patients may experience depressive symptoms and depression as side effects of treatments (e.g., chemotherapy, radiation, surgery, and various types of medications) (Newport & Nemeroff, 1998). It is believed there are psychological factors that may predispose some patients to become depressed after receiving a cancer diagnosis. These factors include poor coping skills, social isolation, family history of cancer and depression, previously suffering from depression, history of alcoholism or substance abuse, external locus of control, and tendency for conforming personality style (Newport & Nemeroff, 1998).

The biological processes of the human body and the medical treatments used to treat cancer are the most important aspects of successfully reducing cancer progression and mortality. However, the psychological well-being of cancer patients also plays a significant role in overcoming cancer. Cancer patients suffering from depression display several similar characteristics that affect cancer progression and overall survival time following a cancer diagnosis. In several studies researchers have found an association between suffering from depression and increased levels of pain, as well as displaying decreased treatment adherence (Ciaramell & Poli, 2001).

From the studies evaluated in this review there were conflicting findings regarding whether depression has an effect on cancer progression, cancer recurrence, and mortality. Several of the studies found depression and depressive symptoms are associated with cancer progression and greater mortality rates. The findings differed and were affected by type of cancer, stage of cancer, depressive assessment method and depression scales, age of patient, and gender. It is important to note that no two studies in this review examined the same type of cancer, gender, and depression assessment tool.

The majority of studies in this review (65%) found that depression did reduce patient survival time and increases the risk of cancer progression and recurrence. Studies that examined samples of either women or both women and men were more likely to find an association between depression and cancer progression. This may be because women tend to be more susceptible to depression and depressive symptoms than men (Massie, 2004). Therefore it is important for clinicians to properly assess, diagnosis, and treat depression among the cancer population. If depression is appropriately diagnosed and treated, these patients may experience decreased levels of pain, increased treatment adherence, decreased risk of cancer progression,

and better survival outcomes. For doctors and psychologists who are treating patients suffering from depression in addition to cancer, it is important for them to be aware of the adverse consequences associated with suffering from these two diseases. By accurately recognizing, assessing, diagnosing, and treating depression doctors will be able to improve the outcomes of cancer patients, potentially increasing their life span and improving patients' quality of life.

It also is important for patients diagnosed with cancer to understand the effects of the depression on their diagnosis. If patients are aware of the adverse outcomes that may result from experiencing depression and depressive symptoms they may be more aware of their moods and mental state. If cancer patients are more aware of their psychological health they may be more inclined to seek professional help and receive treatment for depression and depressive symptoms. This will decrease their risk of engaging in behaviors that may have a negative effect on their physical health and cancer. For example, depressed patients tend to exhibit higher rates of non-adherence to their treatment (DiMatteo, Lepper, and Croghan, 2000).

Limitations

There are several limitations to the studies examined in this review. One limitation is the variability in depression measures used in the studies. Across the 23 studies there were sixteen different assessment measures used to diagnosis depression among cancer patients. The differing symptomology required for a depression diagnosis may have resulted in the conflicting findings.

A second limitation was the type of depression assessment used. Some used self-report questionnaires, other used interviews, the diagnostic criteria set forth by the DSM-IV-TR, or admission to a psychiatric facility. This is important because the differing diagnostic methods

may have had a significant impact on what symptoms were required to be diagnosed with depression. This would have impacted the amount of participants in each study who received a diagnosis of depression.

Each type of depression assessment tool displays limitations that may have affected how many of the studies' participants received a depression diagnosis. For example, self-report questionnaires may be affected by respondent bias. Participants may not answer the questionnaires honestly or accurately due to fear of being diagnosed with a second disease, fear of being labeled with a mental illness, or for various other reasons. The clinical interview is considered to be the "gold standard" in accurately assessing and diagnosing depression (Onitilo, et al., 2006). However interviews were only utilized in five of the studies examined in this review. Admission to a psychiatric setting also provides a problem for correctly identifying cancer patients suffering from depression. These individuals may have been admitted to a psychiatric setting for other psychological issues instead of or in addition to depression and depressive symptoms.

Another limitation was the various types of cancer examined in these studies. Some examined the effects of depression on mixed cancer samples while others looked at a specific type of cancer. Several studies noted depression may have differing effects on patients depending on the type of cancer and where the cancer is located in the body. For example one study found that patients suffering from lung cancer displayed elevated risk of depression compared to other cancer patients (Zabora, Brintzenhofeszoc, Curbow, Hooker, & Piantadosi, 2001). This study also found patients suffering from brain or pancreatic cancer are at a higher risk for experiencing depression. It is important to consider why some types of cancer have a higher risk of experiencing depression or depressive symptoms. Lung cancer is associated with a poor

prognosis and tends to result from the individual's behaviors, such as smoking. The feeling of being responsible for their condition may play a role in patients' increased risk of depression. In addition, the treatments for brain and pancreatic cancer are not as effective as the treatments for other types of cancer; therefore, patients may experience stronger symptoms of depression (Zabora et al., 2001). The link between depression and certain types of cancer is important in order to understand why depression may affect some patients more than others.

An additional limitation is the differing lengths of follow-ups between cancer diagnosis, depression diagnosis, and observing the survival times of cancer patients over time. Conflicting findings may have been a result of how much time elapsed between diagnosis and follow-up, the amount of follow-up researchers performed to assess cancer progression and survival, and the procedure of the follow-up(s). A final limitation among these studies is the varying sample sizes identified in each study. Some researchers used large sample sizes while others used smaller, more limited sample sizes. The sample size may have played a role in whether the findings found a significant association between depression and cancer progression and mortality.

Future Research

There are many areas researchers should pay attention to in future research. First researchers should use the clinical interview to diagnosis depression, especially among cancer patients. The clinical interview is the most effective way to accurately diagnosis depression. Another improvement would be to conduct follow-ups over longer time periods. Some of the studies only followed cancer patients for a short period of time following diagnosis. The shortest length of time between diagnosis and follow-up was six months, while the longest was fifteen

years. Future research should also use large sample sizes in order to gain the most accurate results. The larger the sample size the more reliable the results would be. Another idea for future research would be to narrow the ages of participants as some researchers looked at specific age groups while others included any participants over the age of eighteen. The age of cancer patients may be a confounding factor in the association between depression and cancer progression and mortality. Therefore future research should attempt to minimize the confounding effects of age on this relationship. A final suggestion for future research would be for researchers to identify and study the effects of depression on specific types of cancer and the stage of the cancer. Past research has noted conflicting findings among various types of cancer and specific cancer at varying stages.

Conclusion

The relationship between depression and cancer progression or mortality is important for doctors, psychologist, cancer patients, and their families to understand. As we expand our knowledge of the physiological effects of depression, we can increase our understanding of the importance of treating depression among all individuals, in particular people suffering from physical diseases such as cancer. Cancer patients face many challenges in regards to their illness. Treatment is physically exhausting and the adverse side effects of medications, chemotherapy, and radiation have a negative effect on an individual's physical and psychological functioning. The quality of life of cancer patients tends to decrease for a period of time increasing their risk of developing depression and depressive symptoms. By accurately assessing, diagnosing, and treating depression doctors and psychologists can improve their quality of life and increase

survival outcomes of cancer patients. Cancer is an illness with physical, psychological, and economic consequences. The more effectively we can reduce depression among cancer patients, the more likely we are to reduce rates of cancer progression and cancer recurrence. Therefore, we must work to improve treatment of depression in order to improve cancer survival outcomes and the lives of individuals suffering from cancer.

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