Major Depressive Disorder: Overview, Treatment and Recurrence Prevention

A Research Paper

Presented to

The Faculty of the Adler Graduate School

In the Partial Fulfillment of the Requirements for

The Degree of Master of Arts in

Adlerian Counseling and Psychotherapy

By:

Stacie L. Nelson

August 2012
Abstract

This literature review presents an overview of Major Depressive Disorder (MDD) followed by summaries of up-to-date research on the pathophysiology and treatment of depression. The incidence of MDD continues to increase despite modern day advances in research and treatment. Those employed in the psychological field, as well as primary care practitioners, will undoubtedly treat those affected by MDD. Treatment preference is often influenced by the mental health professionals’ training and education. In order to give individuals the best care possible, it is imperative that professionals have a thorough and up-to-date understanding of the disorder including the presentation of the illness, pathophysiology, and current treatment recommendations. Treatment choice should be made on an individual basis regardless of the educational background of the provider. A number of psychotherapeutic approaches as well as an array of antidepressant medications are used to treat individuals with MDD. It can be confusing to know which treatment is most effective and appropriate. This review will examine five recent clinical trials and meta-analyses of the treatment options including psychotherapy, pharmacological treatment, and a combination approach. A discussion will then follow addressing which treatment option is most effective.
Table of Contents

Figures

4

Abstract 2

Introduction 5

Background of Major Depressive Disorder 7

Statement of the Problem 8

Major Depressive Disorder 10

   Symptoms 10

   Chronicity 12

   Suicide 14

   Overview of Brain and Neurotransmitters 16

   Etiology of MDD 19

   Summary 23

Treatment 24

   Antidepressant Medication 24

   Psychotherapy 29

   Summary 32

Studies 35

Individual Psychology and Depression 43

   Life Tasks 45

   Summary 48

Conclusion 50
MAJOR DEPRESSIVE DISORDER

List of Figures

Figure 1: Antidepressant Medication, Dosages, and Side-Effects  28
Figure 2: Interpersonal Triad  31
Major Depressive Disorder: Overview, Treatment, and Preventing Recurrences

“Happiness is when what you think, what you say, and what you do are in harmony.”

-Mahatma Gandhi (1869-1948), Indian political and spiritual leader

Evidence of Major Depressive Disorder has been around for thousands of years. In the fourth century BC, Hippocrates referred to a group of symptoms including loss of appetite, insomnia, flat affect, and irritability as melancholia (Jackson, 1978). In the Christian Bible, King David penned psalm after psalm filled with sadness and despair. Psalm 6: 3: reads, “My soul is in deep anguish”, and Psalm 6:6-7: “All night long I flood my bed with weeping and drench my couch with tears. My eyes grow weak with sorrow”.

Melancholy was evident in several of Shakespeare’s characters, Hamlet in particular (Facelmann, 2003). Famed artist, Vincent Van Gogh, hung himself in 1890 after struggling with a lifetime of mental health issues. He was only 37-years-old (Blumer, 2002). Abraham Lincoln suffered his first breakdown, now believed to have been a Major Depressive Episode, at the age of 26. He endured several recurrences and was reported to be suicidal during these times (Shenk, 2005).

One would think that in our medically advanced society we would be able to drastically reduce the occurrence, and recurrence, of Major Depressive Disorder (MDD). Statistics are alarming. They reveal that in 1994, the lifetime prevalence of depression was estimated at 15% for males and 24% for females (Kessler, 2002). More recently, survey data from the National Comorbidity Survey Replication, which gathered data from 2001 to 2003, reported the lifetime prevalence of depression to be 44% (Kessler, Berglund, Demier, Jin, & Walters, 2005). According to another source, it is estimated that 32 to 35 million United States residents will develop MDD at some point in their life (DeRubeis, Siegle & Hollon, 2008).
Even more discouraging is the recurrence rate of MDD. The STAR*D Project (Sequenced Treatment Alternatives to Relieve Depression) studied 1500 individuals with MDD and found that 74% had experienced more than one episode (Hollon, Shelton, Wisniewski, Warden, Biggs, Friedman, Husain, Kupfer, Nierenberg, Petersen, Shores-Wilson, & Rush, 2006). It is imperative that those in the psychological field be educated on treatment and recurrence prevention of MDD.

Seligman (2002) makes a compelling point by stating, “While every objective indicator of well-being in the United States has been increasing, every indicator of subjective well-being is decreasing” (p. 116). Why the spike in the prevalence of MDD in spite of modern luxuries? Perhaps it is due to the growing acceptance of depression, which has led to more accurate reporting. As recent as 30 years ago, the word “depression” was spoken in hushed tones. There was a stigma attached to the disorder. In today’s society television commercials, funded from pharmaceutical companies, are regularly played and promote the newest antidepressant. The increase in prevalence may also be due to more reliable and universal diagnostic criteria. Prior to the publication of the Diagnostic and Statistical Manual, there was no clear distinction between different mental disorders, and no criteria for diagnosing that could be used across the profession. Perhaps the increase is simply due to the daily stresses faced as the complexity of our world increases. Whatever the cause, it is clear that depression is pervasive in our culture. It attacks regardless of gender, race, socioeconomic class, occupation, or age.

Those working with clients in the mental health field will inevitably see people affected by depression. It is the therapists’ responsibility to provide the highest level of care. In order to do so, therapists should have a thorough understanding of the pathophysiology of depression. It is imperative that they are up-to-date on current research and trends in diagnosis and treatment.
This includes relapse and recurrence prevention. They must also be willing to explore different treatment approaches and work alongside other professionals, such as psychiatrists and family physicians.

**Major Depressive Disorder Background**

Major Depressive Disorder (MDD) is a global issue. According to the World Health Organization (2004), unipolar depression is currently in third place worldwide on the burden of disease list. It ranks eighth among low-income countries and first in medium and high-income countries. Depression ranks higher than ischemic heart disease, violence, strokes, and traffic accidents.

While the prevalence of depression is undisputed among mental health practitioners and those in the medical field, the preferred treatment modality varies. Although MDD is often recurrent and chronic, individuals may only seek assistance while in the midst of a depressive episode. Upon returning to a functional level, they may drop off the radar and discontinue treatment until the cycle begins again.

There remains an ongoing debate about the most effective treatment for MDD and prevention of future recurrence. Those that treat mental health issues may include counselors, therapists, psychologists, social workers, psychiatrists, general practitioners, and other physicians. Different fields have different schools of thought on treating MDD. Some are more adamant about sticking to their preferred method than are others. Within each profession, there also is disagreement on the most effective treatment approach. Among non-prescribing professionals, medication may be mentioned in passing or only as a last resort in managing severe depression. Psychiatrists and other medical practitioners, trained extensively in the medical model of mental illness, often prefer to manage depression with medication.
Professionals must be willing to put aside biases when working with clients, and recommend treatment based on current research.

**Statement of the Problem**

Treatment preferences vary among mental health practitioners. Therapists often have biases either for or against medications. There seems to be a divide between the proponents of psychotherapy and those of pharmacological treatment. It is important to provide the highest level of care to clients regardless of the personal preference of the therapist. Mental health practitioners should base treatment on the current research, the individual client’s situation and history, and the client’s preference. This literature review examines the effectiveness of different psychotherapeutic approaches and antidepressant medication in treating and preventing recurrences in adults diagnosed with MDD. The following treatment options are examined: antidepressant medication; psychotherapy without medication; and psychotherapy with medication.

**Purpose of the Review**

The purpose of this review is to research the effectiveness of several treatment modalities in an effort to identify the best approach to treat MDD and avoid recurrences so individuals with MDD are able to receive the best care possible. Modalities researched include antidepressant medication, psychotherapy without medication, and psychotherapy with medication.

**Rationale**

Depression is widespread and commonplace as evidenced by the estimate that 32 to 35 million US residents will develop MDD in their lifetime (DeRubeis et al., 2008). Some professionals have grown complacent and treat every depressed client in the same manner. They utilize their preferred course of treatment, and only in atypical situations do they stray from the
course. Furthermore, there are also practitioners who are not knowledgeable about MDD and the various treatment options.

Without proper training and education, one cannot effectively, and ethically, diagnose and treat a client with MDD. Principle 3.1 in the Code of Ethics (2012) of the American Association of Marriage and Family Therapists (AAMFT) addresses maintenance of competency by stating, “Marriage and family therapists pursue knowledge of new developments and maintain their competence in marriage and family therapy through education, training, or supervised experience”. MDD is a serious mental illness that not only causes the afflicted enormous emotional pain, but also ultimately can lead to death by suicide. It is imperative that highly competent practitioners give clients unbiased care.

**Major Depressive Disorder**

“If there be a hell upon earth it is to be found in a melancholy man's heart.”

-Robert Burton (1577-1640), writer and clergyman

To effectively treat Major Depressive Disorder (MDD), one must have a thorough understanding of what it is, how it manifests, and the potential etiology of the disorder. The DSM-IV TR (American Psychological Association, 2000) identifies and discusses the diagnostic criteria. To meet the criteria for MDD, at least five of the symptoms listed below must be present during the same 2-week period, and must represent a change for the individual. The symptoms must also cause significant distress or impairment in social, work, or other areas. The symptoms must not be due to substance use, a medical condition, another mental disorder, or bereavement. In addition, the individual cannot have a history of a manic, hypomanic, or mixed episode. It is also important to note that those with MDD are at an increased risk for developing co-morbid mental illness such as anxiety, phobias, impulse control, or substance abuse.
Symptoms

Onset of a Major Depressive Episode can be anywhere from days to a few weeks (APA, 2000). Symptoms must be present for most of the day, nearly every day, for at least 2-weeks and include:

- Depressed Mood
- Diminished interest/pleasure
- Significant weight loss or gain
- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Fatigue
- Feelings of worthlessness or guilt
- Difficulty concentrating
- Recurrent thoughts of death/suicidal ideation

**Depressed mood.** One of the hallmark symptoms of MDD is a depressed mood. This can be described as feeling sad, down, or hopeless. Some individuals may not be able to describe the feeling, and some may even deny feeling depressed. Some may complain of irritability in addition to, or in place of, depressed mood. It is important to observe the affect of the individual, paying close attention to facial expressions, posture, and tone of voice. This is especially important if the person is in denial about his or her feelings.

**Loss of interest in activities.** Depressed individuals will often notice they are no longer interested in things previously enjoyed. Some describe it as not looking forward to anything, or being unable to experience joy. Others may notice the affected person withdrawing from his or
her family and friends resulting in increased isolation. A loss of sexual desire may also be noticed.

**Weight changes.** Appetite changes resulting in significant, unintentional weight change are often seen in MDD. This most often manifests as a loss of appetite although some individuals may crave fat and carbohydrate-laden foods.

**Sleep changes.** Insomnia is commonly seen in MDD. Individuals may find they wake-up in the middle of the night and are unable to fall back asleep. Others may lie awake, unable to initiate sleep. In some instances, hypersomnia occurs.

**Psychomotor changes.** Psychomotor changes must be observable by others and include agitation resulting in pacing, leg bouncing, or fidgeting. Conversely, retardation may manifest as slowed speech, movement, or delay in responding to questions.

**Fatigue.** Excessive fatigue is often a symptom that greatly impacts the sufferer. He or she may lack the energy to perform the daily tasks of living. Tiredness, even following a full night’s sleep, is common.

**Feelings of worthlessness or excessive or inappropriate guilt.** Those experiencing a major depressive episode often harbor intense feelings of worthlessness and guilt. He or she may feel undeserving of the things in their life. They may obsess and experience intense guilt over past or present events. They also may negatively misinterpret things said or done by others. This perpetuates the guilt and feelings of unworthiness.

**Indecisiveness and concentration problems.** Those with MDD often experience difficulty concentrating on tasks. This must be a change from normal functioning. Focusing issues also arise, and can result in occupational, educational, and relationship problems. Making decisions can suddenly seem monumental to a depressed person.
**Recurrent thoughts of death and/or suicide.** The biggest concern with Major Depressive Disorder is that of suicide. Thoughts of death are a common occurrence in the afflicted. These thoughts may vary depending on the severity of the depression. It is more concerning if the individual has made a plan of how they would commit suicide. Unfortunately, some follow-through on the plan and take their own lives.

**Chronicity**

Before delving into this section it is important to define a few relevant terms. The goal in treating MDD is remission of the illness. Remission is a complete reversal of the symptoms with a return to pre-illness status. Essentially, the individual is completely better with little to no residual symptoms.

The term response refers to a 50% improvement in depressive symptoms. While response is progress, the best scenario is complete remission. It is considered a relapse if the individual has a return of symptoms within 6 months of remission or response. Lastly, a recurrence refers to a separate major depressive episode that occurs after 6 months have elapsed (Nierenberg, Petersen & Alpert, 2003).

A major challenge in treating MDD is its chronicity. In those who have experienced an initial Major Depressive Episode, the rate of a second MDD episode is approximately 60%. The risk continues to rise with each successive recurrence. By the time an individual has had a third episode, his or her chance of having a fourth is 90% (Solomon, Keller, Leon, Mueller, Lavori, Shea, Coryell, Warshaw, Turvey, Maser & Endicott, 2000).

The previously mentioned STAR*D Project found that those with chronic MDD typically experienced onset of the illness at an earlier age, meaning any time before adulthood. In addition, many also had a family history of MDD (Hollon et al., 2006). According to Nierenberg et al.
(2003), the greatest risk factor for a recurrence or relapse is residual symptoms. These symptoms may not seem serious at first but they often continue to grow in severity. At the same time, other symptoms may return or develop for the first time.

Several approaches to preventing relapses are commonly used by physicians and other practitioners. Most include pharmacological treatment (Nierenberg et al., 2003). Fava, Ruini and Sonino (2003) discuss three different approaches, utilizing antidepressants, in the prevention of MDD. The first approach involves using maintenance medication. Typically prescribers will recommend continuing the antidepressant for an additional 12 to 17 months, after resolution of symptoms, at which time they recommend discontinuing the drug. After reviewing several studies, Fava et al. arrived at the conclusion that discontinuation of the medication returns the individual to pre-treatment risk of a recurrence of MDD. This researcher believes that this is true of those with biological underpinnings rather than situational depression.

Armed with that knowledge, it is logical to look at lifelong antidepressant therapy. Fava et al. (2003) point out an interesting fact: Some physicians withhold the possibility of lifelong antidepressant medication from their patients. This may be because some individuals are hesitant to begin an antidepressant out of fear of side effects, dependence, or cost. Imagine a physician telling an already hesitant patient that they will be on an antidepressant for the remainder of his or her life. That being said, ethically, physicians should exercise great caution when deciding to withhold the knowledge of this possibility. An issue with lifetime antidepressant therapy that was discussed by Fava et al. is that of tolerance. Individuals often find that after years of doing well on a specific antidepressant, they may begin to relapse. At this point it is recommended that the individual switch to another antidepressant.
The third pharmacological option discussed by Fava et al. (2003) is intermittent treatment. With this approach, the individual discontinues medication after achieving remission, but restarts the same, or similar, drug as needed. In most instances the individual will experience a week or so of warning symptoms indicating that a recurrence is imminent. If medication is reinitiated as soon as possible, the severity of the depressive episode can be minimized.

**Suicide**

One cannot look at the topic of MDD without addressing suicide. Suicide is the worse possible outcome of MDD, but it is a reality that must be considered; 0.045% of the general population commits suicide each year (Rihmer, Z., Gonda, Rihmer, A. & Fountoulakis, 2010). Estimates are that 15% of individuals with MDD have attempted suicide. The completion rate is between 2% and 12% (Oquendo, Currier & Mann, 2006). More than 90% of individuals who either attempt or complete suicide have at least one current Axis I disorder. MDD is found in 56-87% of these individuals (Rihmer et al., 2010).

Individuals planning suicide often display certain behaviors. In many instances, he or she will talk with someone else about wanting to die in the weeks leading up to the attempt. They may also begin giving away prized possessions for no apparent reason. Their mood may actually seem to improve shortly before attempting suicide. This may seem peculiar until one realizes that the suicidal person often feels a sense of relief having made the decision to die. He or she believes that the emotional pain and turmoil will soon be gone.

There are factors that put people at high risk of taking their own lives. It is crucial that those working with the depressed population know these. The authors Oquendo et al (2006); Rihmer (2010); and Zalsman (2006), list and discuss the following risk factors:

- Past suicidal attempts
• Recurrent suicidal ideation that has been displayed throughout repeated depressive episodes
• Alcohol or other substance abuse
• Recurrence of MDD or failure to achieve remission
• Comorbid mental disorders, particularly personality disorders
• Family history of suicide and/or MDD

In comparison, the same authors have identified positive predictors that may act as protection against suicide. These include good social support; strong family support; comforting religious beliefs; adequate medical care; post-partum period and a larger number of children. It is helpful to assess these predictors as well as risk factors. Once identified, the professional can place emphasis on, and encourage utilization of, these positive factors.

Overview of the Brain and Neurotransmitters

To better understand MDD and other psychological concepts, it is useful to have information about the basic anatomy and physiology of the brain and neurotransmitters. Those working in the psychological field can benefit from knowing the basics before they begin treating those with mental disorders. Furthermore, this knowledge proves helpful when learning about possible causes of this illness.

The human brain is comprised of three main components (Annenberg Foundation, 2012):

Central core. The central core regulates basic life processes and includes five structures.
• Thalamus: The thalamus is located deep in the center of the brain. It is responsible for beginning the sensory interpreting process. Using this sensory information, it determines whether something is good or bad. It then forwards this information to the cerebral cortex. For example, if you touch a hot pan, the thalamus would be the first
to receive this signal. It would quickly determine it is bad and would relay this to the cerebral cortex.

- **Pons**: The pons is located below the thalamus. Its job is to trigger dreams and wake the body from sleep.

- **Cerebellum**: The cerebellum is located at the posterior base of the brain, and it is the coordinator of the body. It coordinates body movement, maintains equilibrium, and controls posture. Problems in this area of the brain would result in uncoordinated movement, extreme dizziness, and problems standing or sitting up.

- **Reticular Formation**: This is located near the base of the brain, just below the pons. The job of the reticular formation is to signal the cerebral cortex to pay attention to new stimulation and to remain alert.

- **Medulla**: The medulla is located below the reticular formation. It has the life-sustaining job of controlling breathing, beating of the heart, sleeping, and waking. If something were to go wrong in the medulla, the heart and breathing could stop.

**Limbic system**: The limbic system consists of three small sections and has many responsibilities. It mediates memory, emotions, and motivated behaviors as well as regulating body temperature, blood pressure, and blood sugar level.

- **Hippocampus**: The hippocampus is located in the lower, center portion of the brain. It assists with emotions, learning, and memory. An injury to the hippocampus could cause unregulated emotional outbursts, learning difficulties, and dementia-like symptoms.
- Amygdala: The amygdala is a very small area of the brain located next to the hippocampus. It helps regulate aggression and plays a role in sexual behaviors, eating, and drinking.

- Hypothalamus: As the name indicates, the hypothalamus is located to the side of the thalamus. Through its connection to the central and autonomic nervous systems, and endocrine system, it helps to regulate processes throughout the body. It monitors blood glucose, blood pressure, hormone levels, and salt.

**Cerebral cortex.** The cerebral cortex includes the majority of the brain’s mass. It is divided into two hemispheres, each containing four lobes. The cerebral cortex is responsible for the brain’s higher cognitive and emotional functions.

- Frontal Lobe: As the name implies, the frontal lobe is located near the front of the head, and includes the forehead region. It helps relate the present to the future through purposeful behavior. It helps with decision-making, planning, and goal setting. Problems in this part of the brain would manifest as difficulty with cognitions, decision-making, and conceptualizing future implications of actions.

- Temporal Lobe: The temporal lobe is located on either side of brain in the region above the ears. It assists in language comprehension, auditory perception, and visual recognition. Problems in this area would affect hearing and vision, and cause problems with comprehension when spoken to.

- Parietal Lobe: This lobe also assists with language comprehension in addition to spatial interpretation and attention. Short attention span could result if damaged.
• Occipital Lobe: This lobe is located at the back of the brain. It processes visual information and passes it on to the temporal and parietal lobes. Damage to the occipital lobe would affect vision.

The human body contains between 10 and 100 billion specialized nerve cells called neurons. Each neuron consists of an axon, a cell body, dendrites, and terminal buttons. Neurons are connected to one another through a small space called a synapse. Neurons send and receive information at these synapses throughout the body using substances called neurotransmitters.

The process of sending and receiving information occurs through receptors on the synapses. Different types of receptors have their own unique shapes, which match the shape of certain neurotransmitter molecules. When the appropriately shaped neurotransmitter comes into contact with its matching receptor, it activates the receptor. The receptors need time to reset between activations in order to function properly. When resetting, the receptor releases the neurotransmitter back into the synapse where the sender takes it up again (reuptake). The process will repeat once information is ready to be relayed again. (Nemade, Staats Reiss & Dombeck, n.d.)

Three of the main neurotransmitters that have been linked to depression are serotonin, dopamine, and norepinephrine. Serotonin is responsible for regulating many of the body’s functions such as mood, appetite, sleep, aggression, and sexual behavior. Norepinephrine is believed to aid in recognizing and responding to stressful situations. Dopamine regulates the drive to seek out rewards and pleasure. (Nemade et al., n.d.)

**Etiology of Depression**

Despite decades of research, no definitive cause of MDD has been identified. There are multiple theories that have been proposed and studied, resulting in conflicting results. The
possibility that MDD involves several interconnected systems is becoming more likely (aan het Rot, Mathew & Charney, 2009; Kornhuber, Reichel, Tripal, Groemer, Henkel, Muhle & Gulbins, 2009). Furthermore, the vast majority of studies done on MDD have been done on people who were currently depressed (aan het Rot et al., 2009). A few of the most commonly accepted theories follow:

**Neurotransmitters.** Perhaps the most universally accepted explanation of MDD involves neurotransmitters. Any problem that disrupts the chain of neurotransmitter action can lead to imbalances. The main neurotransmitters believed to be responsible are serotonin, norepinephrine, and dopamine. Considering the previous section describing how neurotransmitters communicate through synaptic receptors, one hypothesis explaining MDD is that the receptors are flooded with neurotransmitters. This saturation of neurotransmitters results in little to no refractory period, which leads to inefficiency of the process (Nemade et al., n.d.). Conversely, another hypothesis proposes that the neurotransmitter levels present at receptor sites are low in those suffering from MDD.

Leventhal & Antonuccio (2009) state, “After 40 years of research, in contradiction to prevailing beliefs, neurotransmitter theories have failed to achieve empirical support” (p. 200). The authors go on to point out the inconsistencies in neurotransmitter levels by claiming that most depressed individuals do not have low levels of serotonin or norepinephrine. In fact, some have high levels. Furthermore, there have been low levels found in individuals with no depression. The bottom line is that there is vast inconsistency in neurotransmitter levels in depressed and non-depressed individuals.

To shed some light on this topic, aan het Rot et al. (2009) describe how most of the studies on the neurotransmitter hypothesis were conducted. Participants were given a tryptophan-
deficient amino acid mixture to ingest. This mixture temporarily decreases serotonin levels in the brain. Scientists found that those who were currently taking antidepressants at the time of the study experience a brief relapse of MDD symptoms. Participants who were in remission after a major depressive episode (within the past few months) but not on antidepressants were also likely to experience a relapse.

Very few of the participants with no personal or family history of MDD experienced depressive symptoms. This outcome suggests that lowering serotonin levels does not produce depressive symptoms in all individuals. In fact, it may be the depressive episode itself causing the alterations in the serotonin level (aan het Rot et al., 2009; Leventhal & Antonuccio, 2009; Grisel, Rasmussen & Sperry, 2006). The most recent hypotheses on the neurotransmitter theory propose that depression is a result of faulty signal transduction between neurotransmitters and neurons (Tamatam, Khanum, Bawa, 2012).

**Structural changes.** A second area being researched involves structural changes. Scientists have been able to closely examine the anatomy and vascularity of the human brain using current imaging methods including MRI, CT scans, and PET scans. They have found several changes in the brain of individuals with MDD. These include changes in the prefrontal cortex, anterior cingulated cortex, ventral striatum, amygdala, and the hippocampus (Maletic, Robinson, Oakes, Iyengar, Ball & Russell, 2007). Changes found when compared with healthy brain imaging include changes in size and blood flow. The hippocampus, in particular, has been found to have a volume loss in individuals with MDD (aan het Rot et al., 2009; Meisenzahl et al., 2009). It is unknown if this finding contributes to the etiology of MDD or if it is a result of the illness.
Inflammation. It is commonly accepted knowledge among researchers in the field of depression that those who have been diagnosed with MDD also have an increased incidence of other illnesses including cardiovascular disease, stroke, cancer, diabetes, and asthma (Manji, Drevets & Charney, 2001; aan het Rot et al., 2009; Tamatam, 2012). Medically ill and medically healthy individuals with MDD have been found to have all the markers of inflammation: An increase in inflammatory cytokines and their receptors in blood and cerebrospinal fluid samples, and an elevation in blood values of acute phase proteins, chemokines, adhesion molecules, and prostaglandins (Tamatam, 2012).

Maletic et al. (2007) describe the process of inflammation as follows: elevated levels of glucocorticoids are released which sets off a series of reactions within the body that eventually promote the release of cytokines. This sets off a cycle of inflammation, which affects the brain and other organs. Elevated cytokines may be experienced as fatigue, sensitivity to pain, anorexia, and decreased libido.

Although the presence of inflammation in MDD and comorbid medical conditions are universally accepted, the underlying connection is not known. Perhaps the inflammation causes the depression. Conversely, depression may set-off the inflammatory response which then wreaks havoc on the entire body.

Genetics. MDD is known to have a moderately strong genetic component. Early onset and multiple recurrences correlate with an increased likelihood of this (Tamatam, 2012). Sullivan, Neale & Kendler (2000) estimate the heritability of MDD to be as high as 40%. An earlier family study (Girshon, Hamovit, Guroff, Dibble, Leckman & Sceery, 1982) estimated the risk to be 74% if both parents have MDD and 27% if one parent has MDD. The chance is 7% in an individual when neither parent has had MDD.
Expanding on the meta-analysis completed by Sullivan et al. (2000), findings strongly suggest major depression is a familial disorder resulting mostly from genetic influences. The meta-analysis reviewed five previously published twin studies. Three adoption studies were also reviewed but did not meet inclusion criteria. All eight of these studies supported the assumption that genetic influences are the most important contributor to familial aggregation. Yet, they propose that MDD is due to a combination of genetic and environmental influences.

Scientists have identified a variation in genes, called polymorphisms, that has been linked to an increased risk for MDD. This is significant because genes are involved with neurotransmitters: their metabolism, transduction of signals, and the speed with which they can change in response to stressors. The gene most studied is the serotonin transporter gene. The serotonin transporter gene contains a polymorphism that slows down the synthesis of this gene. The result is serotonin neurons that are slower in adapting to changes. Simply stated, this polymorphism may make an individual more sensitive to stress. Stress exposure does not always precipitate depression but the risk is increased in those with a certain genetic makeup such as the serotonin transporter polymorphism (aan het Rot et al., 2009).

Summary

The desired treatment outcome for an individual with MDD is complete remission. Unfortunately, MDD tends to be a chronic illness with recurrences occurring anywhere from 60% to 90% of the time (Solomon et al., 2000). The risk increases with each depressive episode experienced. Risk factors that increase the risk of a recurrence include onset of MDD at an earlier age and a family history of MDD. There are a few proactive approaches commonly used to prevent recurrences. These include continuing medication for an additional 12 to 17 months
following remission; lifelong antidepressant treatment; and initiation of medication at the earliest onset of symptoms (Fava et al., 2003).

The greatest concern involving individuals with MDD is suicide. Statistics show that as many as 15% of those with MDD have attempted suicide with the completion rate varying between 2% and 12% (Oquendo et al., 2006). Rhimer et al. (2010) have found that MDD is present in 56% to 87% of individuals who have either attempted, or committed, suicide. There are warning signs present in many who are contemplating suicide. It is imperative that one remains alert to these signs as part of the continual assessment of suicide risk.

The exact cause of depression is unknown. One of the most commonly accepted theories involves neurotransmitter imbalances. Recent research has cast doubt on these theories showing inconsistencies in the serotonin levels of depressed and non-depressed individuals (Leventhal & Antonuccio, 2009; aan het Rot et al., 2009). Other theories discussed include structural, inflammatory, and genetic. There appears to be a strong genetic component involved in MDD. Some studies estimate the risk of hereditability at 74% if both biological parents have been affected by MDD (Girshon et al., 1982). As research has advanced, it appears the pathophysiology of MDD most likely involves a combination of factors.

Treatment

“Happiness is not the absence of problems but the ability to deal with them.”

-Author Unknown

Many have heard stories about ancestors self-medicating their sadness with alcohol. Even today one need not look far to find hurting and depressed people using drugs, alcohol, and sex as a band aid. These approaches might numb the anguish for a short while, but once the drug or alcohol wears off, the sufferer is back to square one. In this section, this researcher will focus on
two commonly chosen treatment modalities for MDD: Antidepressant medication and psychotherapy.

**Antidepressants**

Pharmacological interventions, in the form of antidepressant medications, are a common treatment for MDD. In 2006, 5 of the 35 most prescribed drugs were antidepressants. Annual sales are estimated to be between 1 and 2.23 billion dollars (Ioannidid, 2008). Approximately 11 million prescriptions for SSRIs, and other newer antidepressants, were written in 2002 (Grisel et al., 2006). Drug manufacturing companies do a remarkable job of advertising their antidepressants. One need only watch television for an hour to see one or more commercials singing the praises of the newest medication that will purportedly improve the lives of millions (Bostwick, 2010). Drug companies court physicians through free meals, samples, trips, or financial reimbursement. This often results in physicians writing an increased number of prescriptions for the marketed drug.

In reviewing research on antidepressants, it is clear that there are two competing schools of thought regarding medication. There are those who support and prefer to treat MDD with medication alone or in combination with psychotherapy. Conversely, there are others who prefer to avoid pharmacological treatment and prefer to recommend psychotherapy alone.

Antidepressants are not curative but, rather, provide symptom relief. Despite scientific investigation, there has been no evidence found that these medications help to prevent future depressive episodes once discontinued (Leventhal & Antonuccio, 2009; Paradise & Kirby, 2005). Discontinuation of the medication places the client at three to five times the risk of a recurrence than those in the general population (DeRubeis et al., 2008). Therefore, physicians
often instruct clients to remain on the antidepressant for a minimum of six months, but many find they must take it indefinitely.

One area of contention is the effectiveness of antidepressants. Up to 40% of clients fail to improve when using first-line antidepressants (Arroll, Macgillivray, Ogston, Reid, Sullivan, Williams & Crombie, 2005). There exists a gap between the efficacy of antidepressants as reported in clinical trials and the results displayed in the general population. This may be due to inadequate physician guidelines in prescribing as well as the lack of time they are able to devote to clients (Wade, 2006). Considering that family physicians write more than 75% of the prescriptions for these medications, it is imperative that they fully understand MDD and the treatment options (Bostwick, 2010).

Opponents of pharmacological treatment are quick to point out that the neurobiological hypotheses of depression are not backed up by science. Furthermore, they question if pharmaceutical companies are withholding information from the general public. According to Leventhal & Antonuccio (2009), when reviewing 74 trials of 12 antidepressants approved by the FDA, biases were found. Of the 74 trials, 51% (38) had positive outcomes. Of the 38 trials all but one were published. On the other hand, there were 36 studies with negative outcomes. “Of these, 3 were published with negative results (8%), 22 were not published, and 11 (33%) were published as if the results had been positive-directly conflicting with the FDA’s conclusions concerning outcome” (p. 203).

As is true with the majority of medications, antidepressants have side effects. A study examining 401 patients on antidepressant medication found that 86% reported at least one side effect by the 3.5-month mark. 55% experienced an adverse effect that led them to consider discontinuing the medication (Hu, Bull & Hunkeler, 2004). It has been estimated that as many as
70% of primary care clients discontinue medication treatment, largely due to unwanted effects (Nurnberg, Hensley, Gelenberg, Fava, Lauriello & Paine, 2003). The majority of antidepressants have similar efficacy so it is the side effect profiles that are used to tailor treatment. Bostwick (2010) puts it succinctly when stating, “The patient and physician can ‘pick their poison’” (p. 541). Some common side effects include nausea, headache, jitteriness, appetite and weight changes, sexual dysfunction, sedation, and insomnia (Bostwick, 2010; Warren, 2011). Side effects can also be utilized in a positive way. For example, bupropion can increase the energy level in someone who is lethargic and fatigued (Bostwick, 2010).

On the other end of the spectrum are those that prefer antidepressant treatment. They argue that approximately 50% of those with MDD will respond to any prescribed antidepressant. The majority of the remaining 50% will respond to a second or combination of medications (DeRubeis, 2008). Proponents argue that the newest class of antidepressants, selective serotonin reuptake inhibitors, are effective in approximately two-thirds of clients, and have fewer side effects than older antidepressant categories (Serretti & Artoli, 2004).

A meta-analysis completed by Arroll et al. (2005) analyzed 15 studies comparing tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), or both to a placebo. All reviewed studies took place in a primary care setting. They found that both TCAs and SSRIs are significantly more effective than placebos in treating MDD and heterogeneous depression. This clearly shows that there are benefits to antidepressant therapy.

Antidepressant categories. The various categories of antidepressants work in slightly different ways but all improve monoaminergic (neurotransmitter) transmission (Serretti & Artioli, 2004). The three monoaminergic systems include 5-HT, noradrenaline (NA), and dopamine (DA).
The categories of antidepressant medication are discussed briefly below followed by figure 1, which lists common medications, dosage, and side effects.

a) **Tricyclic antidepressants (TCAs)** are also referred to as nonselective reuptake inhibitors. They work by blocking the reuptake of norepinephrine and serotonin. TCAs cause more side effects than SSRIs and typically are not used unless clients fail to respond to SSRIs or medication in the other category. Side effects include dry mouth, drowsiness and blurred vision.

Examples include amitriptyline, clomipramine, doxepin, and nortripyline.

b) **Selective serotonin reuptake inhibitors (SSRIs)** block the reuptake of serotonin. SSRIs are well tolerated and commonly used because of minimal side effects. Common side effects include nausea, nervousness, sweating, and headache.

Examples include sertraline, fluoxetine, citalopram, and paroxetine.

c) **Monoamine oxidase inhibitors** block the breakdown of monoamines (serotonin, dopamine, and norepinephrine) by attaching to monoamine oxidase. MAO inhibitors are used as a last resort due to the danger of high blood pressure when foods containing tyramine are eaten. Caffeine and alcohol can also increase blood pressure. This category of medication cannot be taken with other antidepressants.

Examples include isocarboxazid, phenelzine, and selegiline.

d) Other antidepressants that do not fall into the previous categories include bupropion, which works by inhibiting the reuptake of dopamine. Bupropion is often combined with an SSRI to combat sexual dysfunction caused by other antidepressants. Venlafaxine blocks the reuptake of serotonin, norepinephrine, and dopamine. Mirtazapine blocks the presynaptic auto-receptors, which results in an increase in norepinephrine and serotonin.
Side effects vary but include nervousness, insomnia, headache, and nausea. (Keltner & Kelley, 2003; Warren, 2011).

<table>
<thead>
<tr>
<th>Class and drug</th>
<th>Standard adult dosage (mg per day)</th>
<th>Common side effects and risks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antidepressants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSRIb</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>20–60</td>
<td>Nausea, drowsiness, dry mouth, sexual dysfunction</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>100–250</td>
<td>Nausea, drowsiness, insomnia, sexual dysfunction</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>20–80</td>
<td>Nausea, insomnia, tremor, sexual dysfunction</td>
</tr>
<tr>
<td>Paroxetinec</td>
<td>20–60</td>
<td>Nausea, drowsiness, insomnia, sexual dysfunction</td>
</tr>
<tr>
<td>Sertralinec</td>
<td>50–200</td>
<td>Nausea, insomnia, loose stools, sexual dysfunction</td>
</tr>
<tr>
<td><strong>Tricyclic antidepressants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anapiriniline</td>
<td>50–300</td>
<td>Dry mouth, drowsiness, weakness; risk of cardiac conduction</td>
</tr>
<tr>
<td>Imipramine</td>
<td>50–300</td>
<td>Dry mouth, drowsiness, weakness; risk of cardiac conduction</td>
</tr>
<tr>
<td><strong>MAOIsd</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenelzine</td>
<td>15–90</td>
<td>Restlessness, insomnia, postural hypotension; risk of hypertensive</td>
</tr>
<tr>
<td><strong>Novel antidepressants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupropion</td>
<td>200–450</td>
<td>Agitation, tremor, dizziness, insomnia, excessive sweating;</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>15–45</td>
<td>Somnolence, increased appetite, weight gain, dry mouth; risk of</td>
</tr>
<tr>
<td>Nefazodone</td>
<td>200–600</td>
<td>Nausea, drowsiness, dizziness, weakness, dry mouth; risk of hepatic</td>
</tr>
<tr>
<td>Trazodone</td>
<td>50–400</td>
<td>Drowsiness, fatigue, nausea, postural hypotension; risk of priapism</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>75–225</td>
<td>Nervousness, insomnia, somnolence, dizziness, nausea, anorexia,</td>
</tr>
</tbody>
</table>

Figure 1. Medication table. http://ps.psychiatryonline.org/data/Journals/PSS/3614/in09t1

**Psychotherapy**

Unlike antidepressant medications, the efficacy of psychotherapy is more difficult to objectively measure. Studies on pharmacological approaches have the advantage of comparing specific antidepressants to a placebo pill. It becomes complicated when trying to define and compare different therapy approaches. That being said, researchers have undertaken this task.

In 2008, Cuijpers, Van Straten, Andersson and Van Oppen published a meta-analysis. The authors compared outcomes of the seven most commonly studied psychotherapeutic approaches including cognitive behavioral therapy; nondirective supportive therapy; behavioral activation therapy; psychodynamic therapy; problem-solving therapy; interpersonal
psychotherapy; and social skills training. In total, 2,757 depressed patients participated in the 53 studies included in the meta-analysis.

There were 124 psychological treatments within these 53 studies. The result of this research was surprising. Cuijers et al., “Found very few indications that the efficacy of several important types of psychological treatment for depression differ significantly from each other”. They did find a slight advantage in efficacy of interpersonal psychotherapy and a small disadvantage in nondirective supportive therapy. However, these differences were small and of unknown significance.

Several different psychotherapeutic approaches have been researched in multiple clinical trials. This researcher will briefly describe three types of therapy that are commonly found in the literature.

Cognitive Behavioral Therapy or Cognitive Therapy. Modern day Cognitive Behavioral Therapy (CBT) is not a specific technique but rather a classification of similar approaches. CBT was influenced by several therapists beginning with Albert Ellis in the mid-1950s in response to his opposition to Freud's psychoanalytic approach. Originally Ellis referred to his approach as Rational Emotive Therapy (RET) followed by Rational Emotive Behavior Therapy by the 1990's. In the 1960's Aaron Beck, M.D. began his cognitive approach calling it Cognitive Therapy (National Association of Cognitive-Behavioral Therapists, 2010).

CBT is based on the idea that our thoughts cause our feelings and behaviors, rather than external things like people, situations, and events. Schemata refer to the way information about the world and self are stored in the brain. Dysfunctional schemata can result in illogical thoughts, which lead to unhealthy emotions and behavior. Depressive schemata focus on hopelessness, guilt, and other negative feelings (Driessen et al., 2007).
Cognitive Therapy purposes that individuals can change the way they feel even if the situation does not change. By correcting faulty cognitions, individuals can relieve distress and prevent future problems (DeRubeis et al., 2008). CBT is typically short-term and uses Socratic questioning to help clients examine cognitions. Socratic questioning is a line of questioning used to help clients question the accuracy of their thoughts. Homework is utilized in CBT and aids in the client’s progress. Because of the work required, some people might find CBT to be difficult.

**Interpersonal Psychotherapy (IPT).** IPT was developed in the 1970’s by a group of researchers at Yale University. Originally it was developed for use in a clinical trial evaluating tricyclic antidepressants versus psychotherapy for the treatment of depression. Originally intended for use by social workers, it was designed to be very supportive and involve frequent contact with the clients.

IPT is best explained using the interpersonal triad (see Figure 2). The process begins when a person experiences a stressor or crisis. The person then attempts to manage the crisis. The way they do so is influenced by their biopsychosocial vulnerabilities. Examples of these vulnerabilities include personality, temperament, attachment style, and genetic factors influencing illness. The third side of the triad is social support. Social factors such as current relationships and social life are the setting in which this stress-biopsychosocial vulnerabilities interaction occurs (International Society for Interpersonal Psychotherapy, 2012).

Similar to CBT, IPT is a brief and focused treatment that consists of three phases: beginning, middle, and end. Much of the emphasis of therapy is placed on the relationship between the therapist and client. The therapist’s role is to be an ally and supporter. As the name implies, IPT focuses on interpersonal issues that are causing distress and works toward symptom
resolution, increased functioning, and improved social support (International Society for Interpersonal Psychotherapy).

Figure 2. Interpersonal triad. http://interpersonalpsychotherapy.org/about-ipt/

**Behavioral Activation (BA).** Peter Lewinsohn and colleagues at the University of Oregon developed BA in the 1970s as a treatment for depression. It is similar to Individual Psychology in that it focuses on the function, or purpose, of the client’s behavior. According to Ferster (1973), “The most obvious characteristic of a depressed person is loss of certain kinds of activity coupled with an increase in avoidance and escape activity such as complaints, crying, and irritability” (p. 857). Depression is described as a passive style of responding, which leads to avoidance of difficult life issues (Houghton, Curran & Ekers, 2011). In addition, depressed individuals receive reinforcement from within and from those around them that result in an increase in depressive behaviors.
Treatment using BA attempts to break the cycles of avoidance and withdrawal found in depressed individuals. This is done through increased activation. BA helps identify and encourage engagement with activities and contexts that are reinforcing with the individual’s long-term life goals (Dimidjian et al., 2006). Examples of behaviorally focused activation include: implementing structure into the daily schedule; making a schedule for each day; self-monitoring; assessing the degree of enjoyment received from doing various scheduled activities; and assessment and treatment of behavioral issues.

Summary

At times there appears to be a large divide between those professionals who prefer medication and those who prefer therapy. This most likely is a result of specialized training. Educational approaches between the two groups appear to be polarized. Physicians are trained in the medical, or biological, model of care and therapists are trained in psychotherapy. There are advantages to this educational model such as specialized care and competence, but clients may be better served if professionals were knowledgeable in other approaches.

Primary care practitioners and psychiatrists commonly prescribe antidepressants to treat MDD. 5 of the top 35 prescribed drugs in 2006 were in this category (Ioannidid, 2008). Pharmaceutical companies do a thorough job of advertising their medications through the media and prescribers. Although the exact mechanism by which antidepressants work is unknown, it has been shown to improve the symptoms of depression in a majority of patients (DeRubeis, 2008; Arroll et al., 2005).

Antidepressants do have side effects. The most common include gastrointestinal side effects, headache, weight changes, sedation, and insomnia (Bostwick, 2010; Warren, 2011). It is estimated that as many as 70% of primary care patients discontinue antidepressant therapy due to
the side effects (Nurnberg et al., 2003). The main categories of antidepressants include tricyclic antidepressants (TCAs), Selective Serotonin Reuptake Inhibitors (SSRIs), Monoamine Oxidase Inhibitors (MAO inhibitors), and non-categorized antidepressants.

There are several psychotherapeutic approaches used in treating MDD. While it is difficult to objectively study the effectiveness of these different approaches, studies have been conducted. The outcomes of many of the studies suggest that there is no significant variation in the outcome when comparing approaches (Cuijpers et al., 2008). Rather, effectiveness appears to be a result of the therapeutic relationship formed between the client and therapist.

That being said, three psychotherapeutic approaches repeatedly found to be researched were discussed in this paper. The first is Cognitive Behavioral Therapy (CBT). CBT stresses that one’s thoughts cause feelings and behaviors rather than external factors. This philosophy proposes that one can change his or her feelings even if the situation does not change (Driessen et al, 2007; DeRubeis et al., 2008). CBT is typically short-term and uses homework to facilitate therapy.

The second approach discussed is Interpersonal Psychotherapy (IPT). IPT uses the interpersonal triad to demonstrate the depressive process. The process begins with a stressor, or crisis. The individual then attempts to manage the crisis based on factors such as his or her biopsychosocial vulnerabilities and social support. The therapist’s role in IPT is that of a supporter.

Behavioral Activation (BA) focuses on the purpose of the behavior exhibited in an individual. This approach believes depression results from a pattern of avoidance and withdrawal. Treatment is focused on breaking this cycle through activities such as structuring one’s day, self-monitoring, and self-assessment (Dimidjian et al., 2006).
Studies

Armed with the knowledge of the prevalence of MDD, symptoms, and potential etiology one must ask: What is the most effective treatment? Not only is it necessary to treat an acute case of MDD, but also it is imperative to reduce the likelihood of future recurrences. Several trials have been conducted within the past decade looking at one or both of these goals. This researcher will present an overview of five clinical trials and meta-analyses followed by discussion of the results.

Combined Pharmacotherapy and Psychological Treatment for Depression: A Systematic Review

Pampallona, Bollini, Tibaldi, Kupelnick & Munizza published this review in 2004. The researchers analyzed 16 studies. The diagnosis was MDD in 10 of the studies, dysthymic disorder in 3, unipolar depression in 2, and mixed diagnoses in 1. The breakdown of therapy included CT (7 studies), IPT (2 studies), psychodynamic therapy (2 studies), and 1 study each used marital therapy, social skills training, problem-solving therapy, CBT, and a combination of CT and IPT. The medication used in all studies was the dose equivalent of imipramine.

The results revealed that participants who received a combination of medication and psychotherapy improved significantly when compared to the group receiving medication alone. When analyzing studies lasting more than 12 weeks, the advantage continued. In addition, there was a reduction in the dropout rate in the combined group.
Short Psychodynamic Supportive Psychotherapy, Antidepressants, and Their Combination in the Treatment of Major Depression: A Mega-Analysis Based on Three Randomized Clinical Trials

This mega-analysis of three clinical trials was performed in Amsterdam by Saskia de Maat, Dekkar, Schoevers, van Aalst, Gijsbers-van Wijk, Hendriksen, Kool, Peen, Van, de Jonghe (2008). Short-term Psychoanalytic Supportive Psychotherapy (SPSP) consists of 16 sessions implemented over six-months.

Participants in the trials were between the age of 18 and 65 years and had a diagnosis of MDD. The researchers included only participants with mild-to-moderate major depression with a score of 12 to 18 on the HDRS. Those with severe MDD were excluded because it would be unethical to potentially withhold treatment.

Those in the SPSP treatment arm received psychotherapy as prescribed in this approach, 16 treatments over a 6-month period. Two of the trials used fluoxetine (an SSRI). If fluoxetine was not tolerated or ineffective, they would then switch to nortriptyline (a TCA) and then moclobemide (a RIMA). In the third trial the medication order was venlafaxine XR (an SNRI), then fluoxetine or fluvoxamine (an SSRI), then nortriptyline, and finally lithium (a mood stabilizer) in combination with nortriptyline. The antidepressant groups received 15-minute psychiatry visits every two weeks during the first two months, then once a month until the end of the study. Another arm in these studies included the combined therapy of SPSP and antidepressant medication.

The results of SPSP compared to medication treatment suggest that both are equally effective. There was also no significant difference between the two groups in terms of improvement in quality of life. Results suggest that independent observers, therapists and
participants found the combination of SPSP and antidepressants to be more effective than antidepressants alone. Analysis of data found no actual difference between SPSP and combined therapy contrary to the previous statement.

**Clinical Effectiveness of Usual Care with or Without Antidepressant Medication for Primary Care Patients With Minor or Mild-Major Depression: A Randomized Equivalence Trial**

This study was published in 2007 by Hermens, van Hout, Terluin, Ader, Penninx, van Marwijk, Bosmans, van Dyck, and de Haan. The researchers looked at primary care physicians (PCPs) in the Netherlands. Globally, it is common for primary care physicians to treat a large portion of depressed patients.

This trial included 181 adult participants who were treated by one of 59 recruited PCPs. Participants were randomly assigned to receive usual care in addition to 3 months of antidepressant medication or usual care alone. Usual care consisted of psychoeducational information on dealing with depression. The information recommended focusing on the present, minimizing alcohol use, exercise, setting goals, increasing social contact, and following daily routines.

Participants visited the assigned PCP at 2, 4, 7, and 11 weeks after the initial screening visit. At each visit, part of the group was assigned to receive usual care as previously described. The remaining participants received the usual care plus the SSRI, paroxetine. Sertraline, also a SSRI, was used as an alternative medication in the event that paroxetine was poorly tolerated. Those in the medication group were also given education about the antidepressant.

Diagnosis was obtained using the Composite International Diagnostic Interview (CIDI). At the beginning of the trial and at 6, 13, 26, and 52 weeks, the Montgomery Asberg Depression
Rating Scale (MADRS) was used to monitor the severity of the depression. A self-report assessment used included the Short-Form 36, which measures quality of life. It was sent to the participants' home at 6, 13, and 52 weeks. At 13 and 52 weeks, the participants were also sent the Client Satisfaction Questionnaire, which was used to measure treatment satisfaction.

The trial found that usual care alone and usual care with antidepressants were equivalent in effectiveness over the first six weeks. Beginning at 6 weeks and continuing through 52 weeks, there is a slight advantage to the group who had taken the antidepressant. This difference was too small to make a definitive conclusion, therefore future studies are recommended.

**Randomized Trial of Behavioral Activation, Cognitive Therapy, and Antidepressant Medication in the Acute Treatment of Adults with Major Depression**

This study, conducted by Dimidjian, Dobson, Kohlenberg, Gallop, Markley, Atkins, Hollon, Schmaling, Addis, McGlinchey, Gollan, Dunner & Jacobsen, was published in 2006. There were 241 participants who met the criteria for MDD. They were between the ages of 18 and 60 years old.

Participants were randomly assigned through a computer-generated report to one of four treatment groups: behavioral activation (BA), cognitive therapy (CT), antidepressant medication, or pill placebo. Assessments used to screen and monitor participants included the Beck Depression Inventory (BDI-II) and the 17-item Hamilton Rating Scale for Depression (HRSD). They were re-screened at approximately 8 and 16 weeks and as deemed necessary throughout the trial.

Those undergoing BA and CT participated in a maximum of twenty-four 50-minute sessions over 16 weeks. Participants on either antidepressants or the pill placebo where treated by one of five experienced prescribing therapist. For the first eight weeks the study was triple-
blind but at the eight-week mark, the blind was broken. At this point those on the placebo arm were offered the option of beginning antidepressant medication at the expense of the study. Paroxetine was used as the medication. Paroxetine is a SSRI. The most common side effects reported for the active medication included decreased libido and sexual performance, nausea, insomnia, somnolence, and dry mouth.

The results of this study found that when comparing the antidepressant medication with the placebo, high-severity participants receiving the active medication improved significantly more than the placebo group on a week-to-week basis. This difference was insignificant when analyzing low-severity participants.

Analysis of the three active groups displayed significant overall improvement in the high-severity participants on a week-to-week basis. This indicates the importance of severity level when choosing appropriate treatment. Those in the BA or antidepressant groups improved significantly over the CT group. Interestingly, BA and antidepressant treatment had a similar response. This contradicts previously published studies showing CT to be comparable to antidepressant treatment.

**Rational Emotive Behavior Therapy, Cognitive Therapy, and Medication in the Treatment of Major Depressive Disorder: A Randomized Clinical Trial, Posttreatment Outcomes, and Six-Month Follow-Up**

This randomized clinical trial was conducted in Romania by David, Szentagotai, Lupu and Cosman. 170 participants were included after meeting the criteria for MDD, scoring 20 or higher on the BDI, and at least 14 on the HRDS.

Participants were divided into one of three arms: CT, rational emotive behavior therapy condition (REBT), or antidepressant therapy. Those assigned to CT or REBT underwent 20
sessions with a qualified therapist. Those in the medication arm of the trial were given the SSRI, fluoxetine, in addition to brief weekly session with a psychiatrist. The study lasted for 14-weeks with assessment given along the way. At the end of the 14-weeks, participants were offered up to three follow-up appointments over the following 6 months. They could choose whether to utilize these or not.

The results of this study suggest that REBT, CT, and antidepressant therapy are equally efficient in treating individuals with MDD. When reviewing the results from a 6-month follow-up, REBT was found to be significantly better than medication, and CT was slightly more efficient than medication.

**Discussion**

Finding clinical trials comparing efficacy of psychotherapy and pharmacologic treatment proved to be challenging. This researcher was particularly interested in trials comparing the efficacy among three groups: those on antidepressants, those undergoing psychotherapy, and those utilizing the combination of the two approaches.

That being said, the reviews published by de Maat et al. (2008) and Pampallona et al. (2004) were thorough and informative. Between the two analyses, 19 studies were reviewed. There were key differences between the two. De Maat et al. looked specifically at one type of therapy, SPSP. Pampallona et al. included 16 studies encompassing eight different psychotherapeutic approaches. The antidepressants used in the trials also varied. In the review of SPSP, treatment consisted of 16 sessions and lasted for six months. In contrast, the other review included trials of various time frames. Diagnosis was another major difference. De Maat et al. examined trials in which the participants were diagnosed with mild-to-moderate major
depression. Pampallona et al. included participants with several depression-related diagnoses including MDD, dysthymia, unipolar depression, and mixed diagnoses.

Statistically speaking, the results of the two reviews conflicted. De Maat et al. found that SPSP alone was comparable to SPSP combined with antidepressant medication. Even though the data analysis showed no difference, those involved in the studies felt that the combination treatment was more effective. The review of 16 studies (Pampallona) found significant advantages in both improvement and adherence to treatment among the participants in the combination groups.

The trial performed by Hermens et al. (2007) was unique among the five studies. This trial looked at primary care and the treatment of depression. This study was included because of the high number of depressed individuals being treated by their PCPs. Therefore, it is important that PCPs are adept at diagnosing and treating depression.

This trial was also different than the others discussed in that it did not include a specific psychotherapeutic approach. Instead, the researchers used an educational approach that could be used during brief doctor visits. In reality, many patients fail to seek psychotherapy or drop out prematurely, despite their PCP’s recommendation. The usual care approach can be easily implemented and done at regular medication check-ins.

Hermens et al. found that there was no significant difference between the usual care alone and usual care with antidepressants groups. They did recommend further research, as there was a very slight advantage to the medication group that could be further explored.

The remaining two trials were similarly structured. Both compared efficacy among two different psychotherapeutic approaches and medication alone. All participants in both studies had a diagnosis of MDD. Dimidjian et al. (2006) compared BA, CT, antidepressants, and placebo
pills; lasted 16 weeks; and utilized an SSRI (paroxetine). David et al. (2008) compared REBT, CT, and antidepressants; lasted 14-38 weeks; and utilized an SSRI (fluoxetine).

The trial by Dimidjian et al. differed by including a placebo arm in the study. At 8 weeks this blind was broken and antidepressant medication was offered to those in the placebo arm. David et al. offered three follow-up visits during the six months immediately following the initial 14 weeks. This was done to study post-treatment outcomes.

Results differed between the two studies. Dimidjian et al. found that response to treatment was dependent on the severity of the depressive symptoms. The data showed that there was significant improvement in all three active groups in the high-severity participants. The researchers found BA and antidepressants to be significantly more effective than CT. BA and antidepressant treatment had a similar response.

Interestingly, David et al. concluded that REBT, CT, and antidepressant therapy are equally effective in treating MDD. The results from the 6-month follow-up showed REBT was significantly better than medication, and CT was slightly more efficient than medication. In light of the earlier discussion, it is not surprising that REBT and CT appear to be more effective than antidepressants in the 6-month follow-up. Antidepressants are symptom suppressing and have no effect after discontinuing.

Overall, results are inconclusive and conflicting. It appears that all treatments, excluding placebo pills, have comparable efficacy in most situations. No psychotherapeutic approach proved to be superior over the others. Perhaps it is more about the quality of the relationship between the therapist and client rather than technique.
Individual Psychology and Depression

“The chief danger in life is that one may take too many precautions.”

-Alfred Adler

Alfred Adler was the founder of Individual Psychology and a pioneer in the psychotherapeutic field beginning with his first publication in 1907 (Ansbacher & Ansbacher, 1956). In order to understand his view of depression, it is helpful to understand a few relevant, basic tenets of Individual Psychology.

Adler identified one dynamic force that was responsible for all human behavior: Striving from a felt minus to a felt plus (Ansbacher & Ansbacher, 1956, p. 1). Humans are always striving for superiority and perfection. They attempt to avoid feeling less than others at any cost. This innate desire is present from birth and doesn't need to be taught (p. 104). This drive is what keeps humans moving forward.

Striving toward a felt plus is driven by a person's fictive goal. Mosak & Maniacci (1999) explain that fictive, or fictional, goals are subjective and identify what must be achieved in order to belong in life (p. 16). Belonging and feeling significant are powerful human desires. The final fictive goal directs and guides individuals as to how they should behave in order to accomplish their goal. Humans are largely unaware of their fictive goal but it impacts every aspect of life. When working with clients, Adlerian therapists help them uncover their fictive goal. Once this goal is realized, the client may no longer have use for it and can form a new, more realistic goal.

Humans are social beings. Even the most introverted person needs to feel a sense of belonging within a community. It is necessary to understand a person's private logic and lifestyle as well as how they relate, and live in, the world (Mosak & Maniacci, 1999, p. 97). Adler
believed that social interest is imperative in a person's adjustment (Ansbacher & Ansbacher, 1956, p. 2).

Individuals each have their own unique lifestyle or way of engaging with the world. It is the lens through which one experiences life. Furthermore, every person has his or her own internal private logic that consists of attitudes and beliefs about oneself, others, and the world. Stress results when one's life desires conflict with reality. Stress can then lead to mental disorders, including depression. Humans are not born as blank slates. Biological dispositions and early life experiences contribute to emotional responses. That being said, biology can be altered by experience (Grisel, Rasmussen & Sperry, 2006).

Slavik and Croake (2006) further describe Individual Psychology’s view of depression. They explain that depression may result when two factors collide. The first has to do with the individual’s psychological tolerance, which is defined as the amount of the threat a person will bear before withdrawing from a difficult situation (p. 429). People with low tolerance are hypersensitive and are ready to withdraw and stagnate when faced with adversity. Combine the conviction that “the world is unsafe” and “I am unable to deal with it” with the second factor: a mistaken belief that “I must be perfect” or “I must always be in control”. These two factors result in discouragement. The depressed individual gives up without attempting to resolve the perceived conflict.

Adlerian therapists are also taught to look at the purpose of behavior. Depression serves a purpose for the individual who identifies him or herself as depressed. Depression may be a way of protecting oneself from useless or harmless circumstances. It may be used as a way of avoiding responsibilities and/or life's circumstances.
Life Tasks

Depression can also be a result of difficulty within the life tasks. Failure and struggles within a specific life task often lead to stress. The threat facing the individual then stimulates a stress reaction within the brain releasing hormones and neurotransmitters throughout the body.

The individual suffering from MDD is impacted in many ways. In his writings, Alfred Adler identified three life tasks that individuals are continually challenged to balance. Alfred Adler, as quoted in Ansbacher & Ansbacher (1956), stated:

For a long time now I have been convinced that all the questions of life can be subordinated to the three major problems-the problems of communal life, of work, and of love. These three arise from the inseparable bond that of necessity links men together for association, for the provision of livelihood, and for the care of offspring. (p. 131)

The better a person is functioning in the life tasks, the more psychologically healthy he or she is. Therapists can use the life tasks to assist with identifying the client's problems. In addition to work, social interest, and love, Adler also wrote of two other areas but did not specifically label them as life tasks. Self and spirituality are commonly accepted as the fourth and fifth life task in Individual Psychology (Mosak & Maniaci, 1999, p. 98). As therapy moves forward, progress can be measured by periodically reevaluating the five life tasks.

When questioned, individuals are usually able to evaluate how they are doing in each area. Someone with MDD could be struggling in any, or all, of these areas as described in the following sections.

Work. The area of work includes an individual's occupation as well as homemaking, school, volunteer positions, and other tasks that contribute to basic survival and improvement of
the community. The majority of people find a sense of accomplishment and satisfaction when contributing through work.

Productivity is affected when an individual is experiencing an episode of MDD. MDD is the number one cause of disability worldwide (Murry & Lopez, 1997) resulting in loss of income, increased financial burden on others, and loss of contribution to the community. Even if the client is not technically disabled, their work can suffer. They may have frequent absences and decreased productivity.

Those who are unable or unwilling to work due to MDD are psychologically impacted. They may experience a wide range of emotions. This may include guilt because they are not providing for their family or anger at oneself for not functioning as they previously did.

**Social Interest.** Belonging is a fundamental desire. From the time of birth, humans long to be near others. As children, humans find the most efficient way to belong within their family of origin. They often carry this role, or set of behaviors, into adulthood and use it to fit in (Mosak & Maniacci, 1999, p. 102). Unfortunately, the role they’ve become accustomed to does not work in every situation. This can result in tension and relationship problems.

Those suffering from MDD typically experience social changes. They often withdraw from friends and family and seem to turn inward. They may lack the energy and motivation to interact with others. Conversely, others may actually begin to avoid the depressed individual due to feelings of frustration or helplessness when they are together.

**Love/Sex.** This task may be the most challenging due to the level of intimacy necessary (Mosak & Maniacci, 1999, p. 104). This category includes identifying with one of the genders as well as one’s sexual orientation. Furthermore, it is the task through which humans bond. This is accomplished through intimate relationships including dating, cohabitation, and marriage.
Society would cease to exist without sex. It is within these bonds that children are born and cared for.

Individuals with MDD often experience instability, or dissolution, within a relationship. The partner may not know how to relate to the afflicted and may begin pulling away. The depressed partner may isolate himself or herself, have little to no sex drive, and take their frustration out on their loved one.

**Self.** The self-task was not specifically labeled by Adler as a life task, but has since been incorporated by many practitioners of Individual Psychology. According to Mosak and Maniacci (1999), “People need to come to a conclusion about themselves, and that process, and its outcome can greatly influence functioning in all of the other tasks” (p. 106). This task includes how we view, and feel about, ourselves.

Individuals who have successfully incorporated the self-task have a healthy body image and genuinely like themselves. They also physically and emotionally take care of themselves. Similarly, they refrain from dangerous, and compromising, situations.

An individual with MDD often struggles with the self-task. It is unlikely he or she would be successful in the other life tasks. They most likely would engage in negative inner talk and feel as though they hate, or distrust, themselves. Struggles with body image may be present. Risky behavior, such as drugs, alcohol, or self-harm, are commonly seen.

**Spirituality.** Similarly to the self-task, spirituality is included as a life task by some Adlerian therapists. This task includes answering questions such as: Do I believe in God? If not, what do I believe in? What is my view of humankind? What happens when we die? Is there an afterlife? What is the meaning of life? (Mosak & Maniacci, 1999)
MAJOR DEPRESSIVE DISORDER

MDD may lead one to question their previously held beliefs of God, others, death, and life. It may be a time of soul-searching that results in deeper faith or a change in opinion. One may feel anger toward God, believing He is responsible for the current situation. Conversely, MDD may lead to a deepening of faith. Some find strength and solace in God when going through difficult times.

Summary

Individual Psychology has similarities to the psychotherapeutic approaches discussed earlier in this paper. For example, CBT refers to the way information about the world and self is stored as schemata. This idea is quite similar to the Adlerian concept of lifestyle. IPT incorporates a triad when looking at how an individual deals with life’s stressors. The triad identifies biopsychosocial factors and social support as influencing the response to these stressors. Adler believed that social interest was extremely important. Increasing social interest was believed to help improve depression and other mental disorders. BA focuses on the function of the individual’s behavior. This is similar to Individual Psychology’s view of behavior as purposeful.

The ideas of Alfred Adler, the founder of Individual Psychology, continue to be applicable in the psychological field today. Much of his theory on depression’s etiology and treatment continue to be relevant. That being said, many of Adler’s writings lack reference to potential biological causes and treatment of depression. This makes sense when considering at the time of his death (1937) antidepressant medication had not been invented, and research into depression’s etiology was minimal. Modern-day research tools and methods were not yet available. It is important to keep this in mind when looking at Adler’s teachings.
Individual Psychology’s view of depression has evolved somewhat to include biological considerations. Even so, the main focus continues to be on purposeful behavior, faulty private logic, mistaken beliefs, and problems with the life tasks. It is this researcher’s opinion that they all do contribute to depression, but in cases of major depression there are most likely biological underpinnings.

**Conclusion**

For thousands of years, perhaps since life began on earth, evidence of depression has existed. Treatments have evolved and new antidepressant medications are being introduced on a regular basis. Life in medium and high-income countries has advanced beyond what one could have imagined three thousand years ago. Convenience is an important goal in many of these countries. We want more, and we want it now. We live in comfortable houses and drive reliable automobiles. We can drive through to pick-up dinner and can hire others to clean our homes and mow our grass. We have the ability to connect to anyone, anywhere, in the world with a click of a computer mouse. Yet, the incidence of Major Depressive Disorder continues to increase. Therefore, the assumption can be made that MDD is not solely the result of external circumstances but rather a combination of factors.

Why should mental health professionals be concerned with the rising incidence of MDD? Some who deal with depressed clients on a regular basis may become desensitized, in a sense, to the magnitude of this disorder. The symptoms of MDD impact sufferers in nearly every area of their lives. Due to its chronic nature, some are not able to maintain employment and end up receiving disability benefits. In turn, this impacts society at-large by decreasing productivity and increasing the financial burden of those who are employed. On a personal level, individuals on
disability are not successfully functioning in the work life task. The remaining four life tasks may also be affected. This in turn contributes to MDD, creating a self-defeating cycle.

Suicide is the ultimate concern of everyone involved in the life of a depressed individual. MDD is found in many who attempt, or complete, suicide. It goes without saying that the impact of suicide is profound. It impacts not only family and friends but also all who learn of the tragedy. In addition, future generations of those who attempt or complete suicide are at an increased risk of suicidal behavior. Effective treatment and prevention of MDD is a top priority, more so when considering the potential lethality of the illness.

Current treatment for MDD focuses on two categories: antidepressant medication and psychotherapy. Some professionals also recommend the combination of the two categories. This researcher initially hypothesized that the combination of medication and therapy would be more effective than either approach alone. Under this assumption, it would make sense that practitioners and therapists would recommend both when treating MDD. The combination does occur in some cases, but the biological and the psychosocial groups often continue to be polarized when recommending treatment options.

It proved challenging to find relevant research comparing the effectiveness of medication, psychotherapy, and the combination of the two. As previously discussed, many studies did not include all three approaches. Furthermore, results varied and were inconsistent with other similar studies. Only two studies were found that included the three approaches. The first study, a systematic review, did find significant improvement in those who received a combination of therapy and medication when compared to groups receiving therapy alone. The second study, a mega-analysis, found all three approaches comparable in efficacy based on the data. Clearly these two examples contradict each other.
The remaining three studies discussed in the paper compared various therapeutic approaches with antidepressant medication. Again, some inconsistency was noted in the results. One study found that psychoeducation delivered in the primary care setting was as effective as medication during the first six weeks of treatment. After six weeks, the medication was slightly more effective than the educational approach. Another study compared CT, BA, and medication. Results showed those in the BA or medication group improved significantly more than the CT participants. The last study compared REBT, CT, and medication and found all three approaches to be similar in efficacy. Results from a 6-month follow-up found CT to be slightly better than medication, and REBT was significantly better than medication. Again, there are conflicting results among these studies.

After reviewing the information found, it is this researcher’s opinion that a main factor influencing the efficacy of treatment for MDD is the quality of the relationship between the professional and the client. It is crucial that a sense of trust, caring, and respect are present in the therapeutic relationship. Perhaps just initiating treatment, regardless of approach, helps the individual begin to heal. Furthermore, there cannot be a one-size fit all approach to treating MDD. There are numerous variables to consider when treating clients affected by this disorder. Some possibilities include: family history, patient preference, financial resources, mental ability, social support, severity of depression, and personal beliefs.

Major Depressive Disorder is a serious, and oftentimes, chronic illness. Those in the mental health and medical field have a responsibility to stay up-to-date on the latest research and treatment options. In doing so, clients will receive the highest quality of care. Ultimately it is the client who will decide which treatment approach is most appropriate for him or her. A caring, knowledgeable professional will naturally build a trusting relationship with his or her clients, and
will remain open to various effective treatment approaches. The combination of competence, caring, and communication will greatly benefit clients.

**Future Research Recommendations**

Taking these results into consideration, one can deduce that all treatment approaches discussed are effective to some degree in the treatment of MDD. Based on the reviewed studies, combination therapy using medication and therapy has not been shown to be consistently more effective than other approaches. More research is needed into the combination approach and long-term results.

One of the problems with the existing research is the lack of continuity. Studies vary in what psychotherapeutic approaches and medications are used. They also do not use uniform assessment tools when confirming a diagnosis of MDD. These factors could account for some of the inconsistency in results.

The research cited in this paper included adults, defined as age 18 and older. Further research is recommended specifically looking at children and adolescents with MDD. As previously discussed, early onset of MDD tends to have a biological underpinning. It would be interesting to see how individuals under the age of 18 would respond to medication, therapy, and/or a combination of both. Based on the biological hypothesis, medication may be superior to therapy.

In conclusion, when looking at the effectiveness of various treatment modalities it is difficult to make an adequate comparison among the studies. Future research using the same therapeutic approach, assessment techniques, and medication is recommended. Results should be consistent assuming the same protocols are used in each study. Research into other age groups is also recommended and may lead to further discoveries in the etiology and treatment of MDD.
References


randomized clinical trial, posstreatment outcomes, and six-month follow-up. *Journal of Clinical Psychology, 64*(6), 728-746.


between major depression and schizophrenia: A comparative neuroimaging study.

_European Archives of Psychiatry & Clinical Neuroscience, 260_(2), 127-137.


