EVIDENCE-BASED TREATMENT OF UNIPOLAR DEPRESSION IN ADOLESCENTS

by

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As members of the Scholarly Inquiry Project Committee, we certify that we have read the scholarly inquiry project report prepared by Gladys Loyola entitled "Evidence-Based Treatment of Unipolar Depression in Adolescents" and recommend that it be accepted as fulfilling the scholarly inquiry project requirement for the Degree of Doctor of Nursing Practice.

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ABSTRACT

Untreated depression has a detrimental effect in the lives of the adolescents suffering from this disorder. Depression is a multidimensional phenomenon that has been linked to biological, psychosocial and cognitive risk factors. Adolescents may be at risk for depression because adolescence is a time of physical, hormonal, emotional and intellectual changes. Depression may lead to impaired social and school performances and to poor physical health. In addition to a reduced quality of life, depression has also been linked to suicidal ideation and attempts. Suicide is the third cause of death in adolescents in the United States.

The purpose of this practice inquiry was to conduct a critical review and synthesis of the literature on evidence-based treatment of unipolar depression in adolescents and to make recommendations for health care providers. This topic was chosen because of the high prevalence of depression in adolescents and because of the devastating effects of not treating this disorder.

The methods used to synthesize the literature are described in the *Guide for Literature Reviews* by Cooper (1998). After the problem was identified, a literature search was conducted in PubMed, Cinahl, Psych Info, Complementary and Alternative Medicine and AMED. Next, the literature yielded 93 articles. The evidence from the literature was ranked according to the Oncology Nursing Society (ONS), *Putting Evidence into Practice (PEP), Levels of Evidence* scale. This system is an adaptation of the *Rating the Quality of Evidence for Clinical Practice Guidelines* developed by Hadorn and others (1996). Lastly, the recommendations for practice were made based on the ONS PEP, *Weight of Evidence Classification Schema* by Mitchell & Friese. Based on the evidence found in the literature, a guideline with the recommendations for practice was developed.

The need for the treatment of adolescents with depression was supported in this synthesis of the literature. Future research is needed to explore treatment modalities tailored to the developmental, biological, psychosocial and cultural needs of adolescents and their families.

CHAPTER ONE: INTRODUCTION TO THE PROBLEM

The purpose of this project is to conduct a critical review and synthesis of the literature on evidence –based treatment of unipolar depression in adolescents and to make recommendations for health care providers. This topic was chosen because of the high prevalence of depression in adolescents which, if left untreated, can have detrimental consequences in this population throughout their lifetimes (Birmaher, et al., 2007). Depression is a common disorder in adolescents and it is considered a disabling and, at times, a life-threatening disorder (Loo, McFarquhar, & Walter, 2006). It affects millions of adolescents every year. The prevalence of depression in adolescents is estimated, in adolescents ages 12 to 18, as 6% to 9% of the total adolescent population (Callan & Howland, 2009) with 15% to 20% of adolescents experiencing a depressive episode before they are 18 years old (Meredith et al., 2009).

It is well-documented that depressive symptoms affect all aspects of an adolescent's life in a negative manner (Lewis, 2002; Lynch, 2005; Melvin, 2002). Depression may be responsible for changes in mood, a decrease in social and school performances and poor physical functioning (Lewis, 2002). Symptoms of depression may include constant feelings of sadness, discouragement, low self-esteem, and loss of interest and enjoyment (Substance Abuse and Mental Health Services Administration, 2009). Depression has been linked to hopelessness, helplessness, poor academic performance, lack of energy, increased sleep, changes in appetite, substance abuse, pregnancy, early parenthood, adult depression, suicidal ideation and suicide attempts (Birmaher, 2007, Lynch, 2005; Meredith et al., 2009). Furthermore, suicide is the third leading cause of death in adolescents in the United States (Arias, McDorman, Strobino, & Guyer, 2002; Depression Center, 2006; Gould et al., 2004; Temple, 2004; Thapar, Collishaw, Potter, & Thapar, 2010). The number of completed suicides in adolescents in the United States grew from

5%, in 2001, to 14% in 2006 (Centers for Disease Control, 2008). The consequences of not treating depression are severe, thus, it is important that mental health specialists assist adolescents and their families to obtain effective treatment to prevent further complications. This evidenced-based review and synthesis will add to the literature about different treatment modalities for the treatment of depression in adolescents.

Background

Unipolar depression is a type of major depression without symptoms of mania or hypomania (Rey & Birmaher, 2009). The age of onset of depression usually occurs between ages 14 to 19 in adolescents, and the prevalence of mood disorders by the end of this age period has been estimated as high as 25% (Kessler et al., 2001; Kuyken, Watkins, Holden & Cook, 2006). Also, 1 to 6% of adolescents experience depression annually (Thapar, et al., 2010).

Adolescents may be prone to depression because adolescence is a time of physical, intellectual and of hormonal changes (Weller, Kloos, Kang & Weller, 2006); as well as, of social development (Jacka, Kremer, Leslie, Berk, Patton, Toumbuorou, & Williams, 2010). These changes take place as adolescents face different stressors, such as separation from their parents, the need to make personal, academic and vocational decisions that will impact their future the formation of their own identity, and the emergence of their sexuality (Weller et al., 2006) and sexual identity.

Sexual identity has been linked to the development of depression and suicidal behavior in adolescents (Garofalo, Wolf, Kessel, Palfrey, & Durant, 1998; Rose, Rogers, & Small, 2006). Most adolescents are heterosexual, but about 2.5% report to be homosexual (Garofalo et al., 1998; Rose et al., 2006). It is estimated that 20 to 40% of gay, lesbian and bisexual adolescents

have a history of suicide attempts (Remafedi, Farrow, & Deisher, 1991). They are also at higher risk for increased depression and suicide than heterosexual peers (Rutter & Behrendt, 2004).

Rose et al., (2006) hypothesized those adolescents who are already identified as gay or lesbian experienced more stress than adolescents who were confused about their sexual identity. Contrary to this hypothesis, the results from this study showed that confused students had more suicidal thoughts, especially if they were female and had less protective factors (Rose et al., 2006). Identified protective factors were higher socioeconomic status, good parenting, feeling connected at school, having a supportive adult to talk to and church involvement (Rose et al., 2006). Confused adolescent males had more problems with delinquency and substance abuse (Rose, et al., 2006).

Early adolescence is also the time for the developmental state of operational thoughts according to Piaget (Kuyken et al., 2006). During this stage, adolescents learn how to give meaning to their emotions and how to adapt to different mood changes (Kuyken et al., 2006; Lakdawalla, Hankin & Mermelstein, 2007). Adolescents having difficulty adapting to their emotions have been found to suffer from neuroticism. Neuroticism has been defined as a behavioral response that is characterized by extreme emotional reactions to stimuli and with inability to return to a euthymic mood (Kuyken et al., 2006). However, depression not only involves emotions, but it affects all aspects of the person suffering from this disorder, ranging from mood to attitude and behavior (Rey & Birmaher, 2009). Since depression involves multiple systems, depression usually has two components: Cognitive and biological symptoms which are discussed below.

Cognitive Symptoms

The cognitive symptoms of depression are formed by the way people interpret their life experiences (Greening, Stoppelbein, Dhossche, & Martin, 2007; Lakadawalla et al., 2007). Depressed individuals may have a tendency to interpret life events in a negative way due to the presence of symptoms of guilt, hopelessness, low self-esteem and suicidal ideation (Lewis, 2002). Adolescents with negative thinking or rumination styles fail to respond appropriately to difficult situations and may constantly ask themselves if their actions are responsible for their stressors. Furthermore, there is evidence that females have a higher tendency to ruminate than males, possibly making females more prone to depression (Kuyken et al., 2006).

Biological Symptoms

The biological symptoms of depression include changes in sleep, appetite, libido and physical activity. These tasks are thought to be controlled by the hypothalamus, which is responsible for maintaining homeostasis by regulating the body's metabolism, autonomic activity and circadian rhythms (Roy, Largen, & Claghorn, 1979). Common biological symptoms of depression include dysphoria, anhedonia and low energy (Lewis, 2002). Next, the negative and biological symptoms of depression will be further expanded because mental health specialists must learn about the role of biological, psychosocial and cognitive risk factors in the development of depression.

Risk Factors Involved in the Development of Depression

It is difficult to separate factors such as genetics, brain chemistry, cognition and environment because they are in constant interaction, and they influence each other (Diamond, 2009). Because of the multiple factors involved in the development of depression, this disorder is considered to be a biopsychosocial phenomenon (Gilbert, 2006). Depression is also

multidimensional because it is usually rooted in a variety of risks factors: individual, familial and social risk factors (Rey & Birmaher, 2009).

Individual Risk Factors

Individual risk factors include: a) genetic predisposition, b) gender, c) stressful events and d) cognitive styles (Boyce & Ellis, 2005; Gilbert, 2006). The separation of these risk factors is difficult because they all could be present when a patient needs treatment (Rey & Birmaher, 2009).

Genetic predispositions.

The link between genetic predispositions and the development of depression has been examined (Rey & Birmaher, 2009; Thapar & McGuffin, 1996). Studies have reported that genetic factors influence the development of depression, and it is estimated that genetics is responsible for 40% of risk for depression in adolescents while the environment accounts for 60% (Rey & Birmaher, 2009; Thapar & McGuffin, 1996). Genetic studies have also shown that heredity appears to play a stronger role in women than in men. One longitudinal study in Sweden showed that for women the risk of inheriting depression was 42%, while the risk for men was 29% (Kendler, Gatz, Gardner, & Pedersen, 2006; Rey & Birmaher, 2009).

One of the most studied genes is the serotonin transporter gene (Gillespie, Whitfield, Williams, Heath, & Martin, 2005; Goodyer, Bacon, Ban, Croudace, & Herbert, 2009). Individuals who are heterozygous or homozygous for the short allele of the serotonin transporter gene promoter (5-HTTLPR) have been found to have difficulty modulating serotonin levels because the short allele has less transcription capability. However, studies have failed to replicate a relationship between the development of unipolar depression in the presence of psychosocial stressors (environmental factors) in carriers of the short allele of the 5-HTTLPR (Gillespie et al.,

2005; Goodyer et al., 2009). Researchers attribute these negative results to the role of physiological, cognitive and behavioral phenotypes in the development of depression. To support that physiological factors contribute to the development of depression, the activity of the hypothalamic-pituitary-adrenal-axis (HPA) in people who have the short allele of the 5-HTTLPR has been studied (Goodyer et al., 2009).

The HPA may be measured by cortisol levels, and higher levels of cortisol have been found in children of depressed parents and in adolescents facing psychosocial stressors (Halligan, Herbert, Goodyer, & Murray, 2007; Mannie, Harmer & Cowen, 2007). In a study of 403 of white participants, ages 12 to 17, the authors found a higher incidence of depression in those who had not only the 5-HTTLPR short serotonin allele, but also had higher waking-cortisol levels. This study also found that the possibility of recurrent episodes was the same for males and females when they had high cortisol levels (Goodyer et al., 2009).

Gender.

Depression usually does not present before puberty; but, if present in early childhood, it affects boys and girls equally (Abela, Parkinson, Stolow & Starrs, 2009; Rey & Birmaher, 2009). However, during adolescence, the rate of depression is two to three times higher in girls (Abela et al., 2009; Rey & Birmaher, 2009; Weller et al., 2006). Females are at higher risk of developing depression between 13 and 14 years of age. Early maturity in girls, before age 11, and late maturity in boys, after age 12, has shown trends leading to depression (Canals, Domech-Laberia, Fernandez-Ballart, & Marti-Henneberg, 2002).

The higher incidence of depression in female adolescents has been attributed to hormonal changes and to psychosocial factors; however there is also a possibility that adolescent boys may report and express low mood differently than girls. Gender socialization and social learning

patterns may dictate how the child behaves according to a learned sexual role (Diamond, 2009; Shaw & Dallos, 2005). In addition, environmental factors, such as living conditions and affiliations, may affect female adolescents more than males. African American adolescent females living with an adult who abused substances or those who were exposed to physical violence and had relationships with peers with a history of delinquency were more prone to develop depression symptoms (Tandon & Solomon, 2009).

Stressful life events.

The third component of individual risk factors is stressful life events. Stressful life events may be a risk and vulnerability for the development of depression. For example, children with a history of sexual abuse are at higher risk of suffering from depression, anxiety, eating disorders and self-mutilating behaviors. Also, individuals with a history of physical and sexual abuse may be vulnerable to depression in adulthood (Rey & Birmaher, 2009). Other stressful events, such as the death of a family member and the loss of a friend are also associated with creating a high vulnerability to depression (Danielson, Kilpatrick, Saunders, & Resnick, 2005; Rey & Birmaher, 2009).

Other sources of stress in adolescence are the presence of impaired school relationships, such as when the youth is the victim of bullying. Bullying is a problem that affects children and adolescents in all parts of the world and is characterized by both psychological and physical attacks on a victim. Students who are bullied have higher rates of depression associated with difficultly in adjusting to social situations, poor self esteem, loneliness and anxiety (Fleming & Jacobsen, 2009).

Mental health specialists need to inquire if the adolescent had any recent stressors in their lives and to assess their experiences according to their cognitive style. This is because while

some adolescents are able to handle stressful situations, others handle the same incidents with exaggerated pessimism.

Cognitive styles.

Finally, the way adolescents cognitively process stressful events may predispose them to depression (Lakdawalla et al., 2007). Beck divided negative cognitive styles into three negative schemas, the self, the world and the future (Greening et al., 2007). The self involves seeing one as worthless, inadequate and defective. Negative thinking about the world involves ideas that others are making irrational demands that prevent the person from achieving goals. Regarding the future, people have pessimistic thoughts, and perceive the future as hopeless, and full of hardship, failure and frustration (Greening et al., 2007; Grewal & Porter, 2007). For example, adolescents, who have a negative cognitive style, have low self-esteem, feelings of hopelessness (pessimistic thoughts about the future) and are at a higher risk for depression when facing stressful situations (Rey & Birmaher, 2009; McGrath & Repetti, 2002; Morris, Ciesla & Garber, 2008).

Morris et al. (2008) tested different cognitive styles in the presence of stress. The cognitive diathesis-stress model of depression was examined taking into consideration three different types of cognitions: attributional style, self worth and hopelessness in a sample of 240 students, whose mothers suffered from depression. The subjects were transitioning to junior high, a time of change in academic and social surroundings, also marked by physical development. This study found higher levels of depression and anxiety in subjects with negative cognitive styles. When taking into consideration gender, females had higher negative cognitive styles (Morris et al., 2008). Also, adolescents with negative cognitive styles are critical of their academic and social skills, and underestimate their performance (McGrath & Repetti, 2002).

Familial Risk Factors

Familial risk factors such as parental depression are one of the most common predictors of depression in children and adolescents (Fear et al., 2009). This association has been linked to both genetic and environmental factors. Genetic factors refer to inherited traits (Kuyken et al., 2006). Environmental factors include factors, such as parental depression (Kuyken et al., 2006). It is documented that when a parent is depressed, the risk for marital discord increases affecting the emotional security of the adolescent (Cummings, Schermerhorn, & Davies, 2006). Parental discord not only affects the emotional security of adolescents, but it may also deteriorate the parent-child relationship (Cummings et al., 2006).

Children of depressed parents have not only shown to have greater peer conflicts and increased aggression, but they are three to four more times likely to suffer from depression. Parental depression can also increase the risk for substance abuse and anxiety disorders in children and adolescents (Rey & Birmaher, 2009).

Social Risk Factors

Different social risk factors are involved in the development of depression in adolescents. Two important social risk factors for adolescent depression are the adolescent's social network and the adolescent's support system.

Social network.

Children do not depend entirely on their parents or caregivers to achieve psychological development; they also need support a sense of belonging to different entities, such as families, communities and peer groups (Rutter & Berendt, 2004). Adolescents who feel rejected by peers may develop depression because for adolescents the opinions of their peers are of utmost importance (Gould, 2009; Knowles, 2009). Acceptance by their peers is highly valued by

adolescents and they are prone to imitate the behavior of other adolescents, even when this might include suicide (Gould, 2009; Knowles, 2009). In addition, decisions that adolescents make are also influenced by their social network since adolescents tend to request advice from their peers rather than requesting help from an adult (Gould et al., 2004).

Support system.

Another factor, which may also lead to depression and suicidality in adolescence, is a limited support system. Adolescents with limited support systems present as hostile, with a poor self-concept, and hopeless (a feeling that certain situations will not improve). Hopelessness, in the presence of impulsive behavior, increases the risk for suicidality (Hollander, 2000; Rutter & Berendt, 2004). On the contrary, adolescents with higher support systems suffer from less isolation, have a higher level of coping mechanisms and are more positive about the future (Rutter & Berendt, 2004).

Support also comes from communities. Social capital, the resources offered by their schools, neighborhoods and their recreational activities, also affect a child's vulnerability to depression. A sense of community and neighbors' willingness to help each other has shown to decrease depressive and anxiety symptoms (Rey & Birmaher, 2009).

Mental health specialists should be aware of the incidence of depression in adolescents, and of the risk factors that that may promote the development of depression. Mental health specialists must also learn about the role of risk factors in the development of depression and how these risk factors relate to different theories of depression.

Theories of Depression

These theories explain how the previously discussed risk factors influence the development of depression. Among the theories of depression are the evolutionary,

psychoanalytical, interpersonal and social theories; as well as the theory of learned helplessness and the theory of hopelessness.

Evolutionary Theories

Evolutionary theories explain how genetic predispositions and environmental factors are interrelated since genes can be turned on and off according to life experiences (Boyce & Ellis, 2005; Gilbert, 2006). There are scientists who believe exposure to social environments; such as, empathetic care or neglect and abuse, can play a role in gene expression because the environment can impact brain development and phenotypes can develop to fit life circumstances (Boyce & Ellis, 2005; Gilbert, 2006). Furthermore, genetic and biological research of depression has found that this illness can be inherited. For example, children of depressed parents are at greater risk of suffering from this mental illness (Badger, 2001).

Psychoanalytical Theories

Psychoanalytical theories describe how symptoms, thoughts, feelings and behavior could be based on unconscious psychological processes. In this theory, unconscious factors, such as childhood experiences, could determine the content of psychological symptoms later in life (Sadock & Sadock, 2003). Psychoanalytical theories also explain how environmental factors influence the development of depression (Gilbert, 2006). For example, psychoanalytical theories link the rate of depression in adolescents to the suffering associated with external losses, such as the death of a relative or the loss of a relationship (Rey & Birmaher, 2009). These losses could also be the result of impaired parent-child relationships observed in cases of depressed parents or in the presence of parental conflicts (Cummings et al., 2006). The effect of lost relationships in the development of depression can also be explained by interpersonal theories (Davidson, Rieckmann, & Lesperance, 2004).

Interpersonal Theories

Interpersonal theories take into consideration not only the present relationships, but also the role of the psychosocial environment in mood disorders (Davidson et al., 2004). For example, psychosocial factors may play a role in the development of depression in female adolescents because girls tend to be more social, they have more acquaintances, they may change friends frequently, and they might also end relationships often (Rey & Birmaher, 2000).

It is also important to note that even though certain events can lead to depression, depression can also affect how a person performs social roles, and impaired functioning can lead to poor interpersonal relationships with negative outcomes (Davidson et al., 2004). For example, when a parent is depressed, an adolescent can also develop depression because of the loss of the perfect parent (Rey & Birmaher, 2009).

In addition, interpersonal theory links the adolescent's relationships to the parenting style they are exposed to because parental interaction is the child's primary experience about associations with others (Yiliu & Kuo, 2007). The love, support and warmth that the child receives from his parents influence the child's acceptance and closeness to peers and satisfaction with relationships (Yiliu & Kuo, 2007). On the other hand, parental depression may also trigger the development of depression in adolescents because children of depressed parents could be at risk for poor parenting techniques which may lead to poor attachment (Rey & Birmaher, 2009) and attachment theory is one of the most studied social theories.

Social Theories

The social theories of depression state that lack of a support system or the exposure to traumatic events does not necessarily entail the development of depression (Gilbert, 2006). Two

of the most researched social theories of depression are the theory of attachment and the theory of resilience.

Theory of attachment.

The best known social theory is the theory of attachment (Gilbert, 2006). This theory explains how young children exhibit certain behaviors to obtain reassurance, support, nurturance protection and closeness to a caregiver (American Academy of Child & Adolescent Psychiatry, 2005). The type of response that infants receive will determine if they become emotionally secure or insecure. Secure infants are the ones who can anticipate a positive and consistent response from the caregiver; while insecure children get inconsistent responses and are not soothed by the reaction they receive (Hornor, 2007). In adolescence, children change their thinking from an egocentric manner to a more global style in which they are no longer the center of the universe. Secure adolescents with a good support system can make this transition easier with less risk for the development of depression (Shaw & Dallos, 2005).

Theory of resilience.

Resilience has been linked to environmental, genetic and neural mechanisms, and it explains how stressful life events are not good predictors of depression by themselves. The theory of resilience has studied how children exposed to difficult situations are able to develop normally; factors associated with positive outcomes are a bond with a primary caregiver and positive relationships with peers (Feder, Nestler & Charney, 2009). Also, resilience has been studied in different environmental and developmental stressors, in illnesses and in catastrophic incidents. Hence, resilience explains how adolescents react to the same stressors differently based on their capacity to deal with adverse situations (Tusaie, Puskar & Sereika, 2007). One of the factors that will influence the development of depression is a negative attributional style as

explained by the cognitive theories of learned helplessness and hopelessness (Gibb & Allow, 2006). These two theories explain how adolescents who have a negative attributional style are more susceptible to develop symptoms of depression when faced with stressful live events (Gibb & Alloy, 2006). Negative cognitive styles have also been linked to low self-esteem, hopelessness and helplessness (Rey & Birmaher, 2009; McGrath & Repetti, 2002; Morris et al., 2008).

Theory of Learned Helplessness

Individuals who are exposed repeatedly to negative events over which they have no control may develop learned helplessness. Adolescents with learned helplessness attribute negative incidents to internal (involving the individual), stable (a permanent, not a transient situation) and global (as opposed to a specific reason) factors (McLaughlin, Lefaivre, & Cummings, 2010). For instance, a student, with a negative attributional style, who fails a geography test, may interpret this as being a poor student (internal cause) and will not name external causes, such as the test not being fair. It will also not consider it a transient problem; for example, being ill the day of the exam. The adolescents will also not recognize having a difficulty learning geography (a specific reason) (McLaughlin et al., 2010).

Theory of Hopelessness

Hopelessness has been defined as the presence of "negative cognitions about the future." A hopeless individual will have a pessimistic view of the self in the future. Hopelessness has been identified as a risk for depression and suicide. To measure hopelessness, the Beck Hoplessness Scale (BHS) is used. This scale measures feelings and expectations about the future and motivation (Grewal & Porter, 2007).

In summary, depression is a multidimensional phenomenon and the theories of depression will facilitate the understating of how individual (genetic predisposition, gender,

stressful events and cognitive styles) familial and social risk factors may influence the development of depression in adolescents. Knowledge about the theories of depression will guide mental health professionals when choosing the appropriate treatment modalities for adolescents and their families.

Mental health specialists should also be informed that the consequences of not treating depression are severe, thus, it is important that adolescents and their families understand the significance of this problem. Knowledge about the effects of untreated depression in adolescents may decrease complications and decrease the burden of depression.

Significance of the Problem

The Burden of Depression

The burden of depression has direct, indirect and intangible costs. Untreated depression in adolescents can cause severe impairment in the lives of adolescents (Lynch et al., 2005). However, when depression is not addressed, it affects not only the adolescents and their families, but it has a larger societal impact by increasing health care costs (Kuyken et al., 2006; Lynch et al., 2005).

Direct costs consist of inpatient, outpatient and medication expenditures. It also involves nonmedical costs, such as social services and transportation needs. Indirect costs are the loss of productivity related to work or school absenteeism, and early death by suicide. Lastly, intangible costs are the reduced quality of life of the afflicted adolescents and their families (Luppa, Heinrich, Angermeyer, Konig, & Riedel-Helter, 2007; Rey & Birmaher, 2009).

To reduce the burden of depression, it is crucial that adolescents receive appropriate and timely interventions. Primary care clinicians (PCC's) and mental health specialists must have the

necessary knowledge to screen, assess, diagnose and treat adolescents (Committee of Psychosocial Aspects of Child and Family Health and Task Force on Mental Health, 2009).

Screening of Depression in Adolescents

The United States Preventive Services Task Force (USPSTF) recommends that adolescents, ages 12-18 should be screened for major depressive disorder in primary care clinics when these clinics have a system in place for treatment and for follow-up services (USPSTF, 2009). Primary Care Clinicians (PCC's) are often the providers who may first come in contact with a depressed adolescent during a routine visit. PCC's also provide the majority of care to minority and low-income families (USPSTF, 2009). Because of the regular contact with PCC's, the USPSTF recommends the screening of adolescents for depression by their primary care provider during all routine check-ups, especially when the adolescents are positive for four risk factors: parental depression, comorbid mental health disorders, chronic physical health problems, and a history of having experienced a recent disappointing event (Raphael, 2009; USPSTF, 2009). The USPSTF advises primary care providers to screen adolescents by using either the Patient Health Questionnaire for adolescents or the Beck Depression Inventory-Primary Care version (USPSTF, 2009). Also, some families may opt to have their children treated by a PCC, rather than by a mental health clinician, because they already have an established therapeutic relationship, which may facilitate treatment (USPSTF, 2009). However, PCC's need to know how to distinguish between mild, moderate and severe psychiatric symptoms since some adolescents will not be appropriate to receive treatment at primary care settings (Committee on Psychosocial Aspects of Child and Family Health and Task Force on Mental Health, 2009).

Depending on the acuity of symptoms, some adolescents must be referred to a psychiatric provider or to a community mental health agency (Raphael, 2009; USPFSTF, 2009; Williams,

O'Connor, Eder, & Whitlock, 2009), and it is important for primary care providers to have a collaborative relationship with all types of mental health clinicians, such as psychiatric providers, counselors, and case managers (Committee on Psychosocial Aspects of Child and Family Health and Task Force on Mental Health, 2009).

Assessment of Depression in Adolescents

The PCC or the mental health specialist must gather information from different sources to properly evaluate adolescents, such as the adolescent, their parents and their schools (AACAP Official Action, 2007). The evaluation should not only include the adolescent's symptoms, but also his/her strengths and weaknesses, and personal, family and community resources (Kazak, Hoagwood, Weisz, Hood, Kratochwill, Vargas, & Banez, 2010). Mental health specialists are also advised to take into consideration environmental and cultural factors during the assessment period (Kazak et al., 2010). Information about the adolescent's peer and family relationships and developmental history, which will include the child's physical, cognitive, social, and emotional milestones, will help the mental health specialist have a more thorough clinical picture of the adolescent (AACAP Official Action, 2007) and to make the appropriate diagnosis.

Diagnosis of Depression in Adolescents

Depression is often untreated because of not being properly diagnosed (Temple, 2004). Symptoms of depression are often unrecognized because parents, teachers and medical providers may interpret the changes in mood as a common phase in adolescence (Temple, 2004). Depression may also go undetected when the adolescent presents mostly with behavioral problems, use of illicit substances, educational problems and physical pain of unknown origin, especially musculoskeletal discomfort (Thapar, 2010).

Since the presentation of symptoms of depression vary, adolescents might not recognize they are suffering from depression even when they are experiencing impairment in school and work activities, such as inability to participate in activities they used to enjoy, preferring to isolate from friends and family and lacking motivation to engage in new projects or to finish tasks (Sadock & Sadock, 2003). Irritability, quick to anger or easily aggravated, is also a common symptom of depression in adolescents (Thapar et al., 2010). Because of this, the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) permits the use of "irritable" mood instead of "depressed" mood when assessing for the symptoms of depression in this population (Thapar, et al., 2010). Primary health providers also play an important part in the recognition of depression in adolescents since the identification and treatment of depression in this group is essential to decrease morbidity and mortality (Rey & Birmaher, 2009).

The American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) is used to diagnose depression and other psychiatric disorders (Herman, Ostrander, Walkup, & Silva, 2007). However, when diagnosing depression, the PCC or mental health specialist needs to be aware of the person's developmental stage (Beck & Alford, 2009; Ginicola, 2007; Lewis, 2002). For example, children, ages 6 to 12, have the tendency to express depression with symptoms of aggression, but as children reach developmental milestones, their behavioral presentation changes to a more cognitive clinical picture (Ginicola, 2007). Young children usually express depression through externalizing factors, while adolescents may present with internalizing factors. The externalizing and internalizing factors of depression are explained by action-thought theory. This theory states that behaviors such as aggression and psychomotor retardation or agitation are known as the externalizing factors of depression. Low mood,

hopelessness, irritability, guilt, suicidal ideation and suicide attempts constitute the internalizing aspects (Ginicola, 2007; Philips & Zigler, 1996).

Other indicators of depression, psychotic symptoms and excessive sleep are also more prevalent in adolescents. In the case of anhedonia, inability to experience pleasure, a child may report this symptom as not wanting to play with toys while an adolescent may complain of constant boredom (Beck & Alford, 2009). In addition to these symptoms, adolescents may also present with negative thoughts, such as fear of separation from their parents because they worry their parents may die. These negative thoughts are often followed by refusal to go to school stating they are sick (Institute of Mental Health, 2009).

To facilitate the diagnosis of depression, mental health specialists should have knowledge about developmental stages in the presentation of depression. Another factor that must be considered when diagnosing depression is the adolescent's cultural background, preferences, beliefs and practices. An understanding of culture will aid mental health specialists to detect symptoms of depression because adolescents from different ethnic groups may describe their symptoms differently (Pumariega, Rothe, & Rogers, 2009). Somatization is more common in anxiety and in depressive episodes in minority groups (Beck & Alford, 2009; Pumariega et al., 2009). For example, African American and Hispanic adolescents might not be diagnosed with depression because they express symptoms of depression by reporting somatic and physical complaints (Kennard, Stewart, Hughes, Patel, & Emslie, 2006). Also, in Latin cultures, adolescents may refer to depression as suffering from "nerves" and headaches, while Asian adolescents may complain of problems with feeling weak, tired or "imbalanced" (Beck & Alford, 2009). Depressed adolescents of Asian descent show less externalizing symptoms, and they may appear with an incongruent bright affect (Pumariega et al., 2009) and because of this,

Asian adolescents may not receive appropriate treatment for depression because they try to project an image of success even when they are facing adjustment difficulties (Zhou, Siu & Xin, 2009). Furthermore, the avoidance of eye contact in older Asian, Native American, African Americans and Latino adolescents is a sign of respect, but it could be diagnosed as paranoia or uncooperativeness (Pumariega et al, 2009) unless one understands the culture influences.

Once an adolescent has been diagnosed with depression, mental health specialists and the adolescents and their families can discuss the importance of treating adolescents with depression. Part of this discussion should include the impact of untreated depression in the quality of life of the affected adolescents and their families.

Treatment of Depression in Adolescents

Early detection of symptoms and appropriate treatment may help reduce the high incidence and prevalence of depression in adolescents (Birmaher et al., 2007). For example, it is recommended that depression in adolescents should be treated even when the depressive symptoms do not meet full DSM-IV criteria not only because of the complications associated with untreated depression (Kuyken et al., 2006), but also because there is a 67% possibility that a sub-threshold level of depressive disorder could escalate to a depressive episode that will meet criteria for diagnoses (Klein, Shankman, Lewinsohn, & Seeley, 2009) or to the development of a more serious illness, such as major depressive disorder (MDD). MDD have 5% prevalence in adolescents and it is associated with high morbidity (The TADS team, 2007; Shafer, Gould, & Fisher, 1996; Gould et al., 1998). Morbidity is defined as the number of cases that present in any given year in a particular population per a set population unit (Mosby's Dictionary, 2009); for example, the number of depression cases occurring in 1,000 adolescents in a specific year. MDD has also been linked to suicidal ideation and to the completion of suicide in adolescents (The

TADS team, 2007; Shafer et al., 1996; Gould et al., 1998), and it is the source of severe psychosocial impairment and long term disability in adulthood (Canals, Domenech-Llaberia, Fernandez-Ballart, & Marti-Henneberg, 2002; Lewis, 2002).

To prevent the ramifications of untreated depression, it is important for mental health specialists to realize that the treatment of depression needs to be tailored to the needs of the individual (Birmaher et al., 2007) To facilitate this process, mental health specialists need to be aware of the three phases in the treatment of adolescent depression, which are: acute, continuation and maintenance phases (Hughes et al., 2007).

Acute Phase

During the acute phase, the initial treatment may involve a "watchful period" (Hughes et al., 2007). In cases of mild depression, a period of 6 to 8 weeks should be considered prior to starting treatment (Hughes et al., 2007). During this time, the adolescents are to receive monitoring and supportive weekly or biweekly meetings (Cheung et al., 2007). This "watchful period" is suggested because 1 in 5 subjects showed improvement with an initial brief psychosocial intervention (Goodyer et al., 2007), and also because of the high response to placebo during clinical trials (Hughes et al., 2007). If improvement is not achieved within 6 to 8 weeks, treatment with psychotherapy or antidepressant should be recommended for mild symptoms of depression (Cheung et al., 2007). However, according to symptoms, antidepressant medication and/or psychotherapy could be prescribed during the initial assessment (Hughes et al., 2007). The acute phase is followed by the continuation phase.

Continuation Phase

A depressive episode has a mean duration of 7 to 9 months (Emslie et al., 2004). After the patient experiences a decrease in symptoms, continuation of treatment is recommended for 6

to 12 months to avoid relapse (Hughes et al., 2007). For example, Emslie et al. (2008) recommend continuation treatment for six to nine months. However, when patients are stabilized after suffering their third depressive episode, they are candidates for maintenance treatment (Hughes et al., 2007).

Maintenance Treatment

There is no established duration time for the maintenance phase in adults or in children and adolescents. A period of three years to lifetime treatment is often recommended depending on risk factors; such as family history, severity of symptoms, and suicidal ideation (Hughes et al., 2007).

Since the complications of untreated depression are well documented, understanding the different subtypes of depression will help mental health specialists to diagnose this disorder. It will also be of assistance in determining the type of treatment that will better fit the needs of the adolescent.

Subtypes of Depression

Experts have divided depression in different subtypes: primary or endogenous, secondary or reactive, and psychotic (Rey & Birmaher, 2009). Knowledge of these different subtypes will facilitate the selection of the most appropriate treatment for depression.

Primary Depression

Primary depression is also called *endogenous depression*. It refers to depression caused by biological causes, such as chemical imbalances involving neurotransmitters. This depression does not relate to symptoms caused by life stressors as is the case of secondary depression (Beck & Alford, 2009; Depression Help for You, 2009).

Secondary Depression

This subtype of depression has also been called *reactive depression* because it is usually the result of external stressors, such as emotional trauma and important losses. It may also develop secondary to neurological disorders or to traumatic brain injury, brain surgery, stroke, tumors or epilepsy. In addition, both primary and secondary depressions have been linked to pathophysiology involving decreased levels of serotonin (Robinson, Chemerinski, & Jorge, 2009).

Psychotic Depression

Lastly, psychotic depression refers to patients who, in addition to suffering from severe depression, may also experience hallucinations and/or delusions (Gilbert, 2006). However, the term psychotic depression is no longer used and instead the current diagnosis is *major depressive disorde***r**, severe with psychotic features (Depression Help for You, 2009).

Knowledge about the subtypes of depression will allow the clinicians to access the best-evidence based treatments for adolescents with depression according to their needs (Lewis, 2002). Also, to design a treatment plan, mental health specialists need to be well-informed about other psychiatric and medical disorders that may co-occur with depression and how the treatment of depression may impact other conditions. In the next section, co-occurring problems will be discussed.

Co-Occurring Problems with Depression

Depression may not present in isolation, and it may co-occur with other mental health disorders and with chronic medical conditions (Callan & Holland, 2009). Depression may also co-occur with other mental health disorders, such as post-traumatic stress disorder, obsessive compulsive disorder, panic disorder and generalized anxiety disorder (Birmaher et al., 2007;

Callan & Howland, 2009). Adolescents suffering from depression may also have problems with conduct disorders and alcohol and substance abuse (Birmaher et al., 2007; Callan & Howland, 2009; National Institute of Mental Health, [NIMH], 2009), and with body dissatisfaction (Chaiton et al., 2009).

The NIMH is an organization whose mission is the understanding and treatment of mental disorders by promoting translational research from bench to bedside to practice (NIMH, 2009). According to the NIMH (2009), depression may also co-occur in the presence of chronic medical conditions. It is estimated that 9 - 14% of children suffer from chronic medical conditions (Bennett, 1993), such as heart disease, stroke, cancer, HIV/AIDS, and diabetes (NIMH, 2009). Furthermore, the recognition of depression in adolescents suffering from chronic medical conditions by mental health specialists may lead to a better management of their conditions (NIMH, 2009).

Knowledge about the incidence of depression in other psychiatric and medical conditions will help the mental health specialist understand the best treatment options that will fit the needs of adolescents. However, even when adolescents and their families have agreed to treatment of depression, there are obstacles that may impact their decision.

Barriers for Treatment of Depression in Adolescents

Different barriers to access treatment for adolescents with depression have been identified (Substance Abuse and Mental Health Services Administration, 2009). In addition to lack of access to health care, stigma related to mental illness, time and transportation constraints, the provider's clinical skills and cultural preferences may also interfere in adolescents entering a treatment program.

Access to Health Care

The National Research Council (NCR) and Institute of Medicine (IOM) have highlighted the need for increasing mental health services for adolescents because of the lack of services for this population. In the past year, 8.2%, or 2 million, of adolescent's ages 12 to 17 years, suffered a major depressive episode in the United States, but only 38.9% of these adolescents received treatment. Access to services was determined largely by whether or not the adolescents had health insurance, but the knowledge of parents and educators also played a role on whether or not the adolescents received treatment. Because of this, the NRC and IOM also recommend that caregivers and teachers should be aware of symptoms of depression in adolescents and assist them in obtaining a timely diagnosis and sustaining adequate treatment (Substance Abuse and Mental Health Services Administration, 2009).

Stigma

Meredith et al., (2009) found that the stigma associated with disclosing the adolescent's symptoms of depression by parents and the fear of being perceived as different by peers prevented adolescents from receiving treatment. These researchers also found that the stigma regarding taking medications was higher than attending psychotherapy sessions possibly due to the concerns about side effects, such as weight gain, and also because of children seeing themselves as ill because they needed medicine (Meredith et al., 2009). Stigma is also linked to individual health beliefs. Children and parents consider psychotherapy a safe and effective treatment for adolescent depression while the use of antidepressants is considered useful, but of higher risk (Campo & Bridge, 2010).

Time and Transportation Constraints

The most mentioned barriers by parents and children in a study by Meredith et al., (2009) were time constraints because of scholastic and recreational activities, trouble getting time off to take the child to appointments, the need of baby-sitting services for other children, lack of transportation, distance to the clinic, and difficulty with the hours the treatment was offered (Meredith et al., 2009). In summary, the adolescents who recognized more barriers to treatment were less likely to receive it (Meredith et al., 2009).

Provider's Clinical Skills

Most of the adolescents first come in contact with health care services in during regular check-ups and lack of knowledge and the level of comfort of primary care clinicians (PCC's) treating adolescents with depression will determine whether or not the adolescents will receive treatment (Glied et al., 1999; Kazak et al., 2010). For example, PCC's might feel more prepared to diagnose and treat attention deficit hyperactivity disorder (ADHD) than depression, anxiety and conduct disorder (Kazak, et al., 2010). Also, some PCC's might be reluctant to initiate treatment for adolescents because of concerns about "labeling" them with a mental disorder (Temple, 2004). In addition, PCC's have cited time constraints as a barrier to providing mental health care in primary care clinics (Committee on Psychosocial Aspects of Child and Family Health and Task Force on Mental Health, 2009).

Because of the problems encountered in primary care, the American Academy of Pediatrics has recognized the need for PCC's to become more knowledgeable about addressing mental health problems in children and has issued a policy statement proposing competencies needed by PCC's to identify risk factors for depression, promote healthy lifestyles and to prevent or alleviate mental health disorders in children and their families (Committee on Psychosocial

Aspects of Child and Family Health and Task Force on Mental Health, 2009). Also, a therapeutic relationship with the adolescents and their families will help decrease barriers to treatment. Good communication between the PCC or mental health providers and the adolescents and their parents is recommended to understand the treatment preferences of adolescents and their support system (Birmaher et al., 2007; Meredith et. al., 2009).

Cultural Preferences

Cultural preferences also need to be taken into consideration when discussing options for the management of depression (Birmaher et al., 2007; Pumariega, Rogers, & Rothe, 2005; Pumariega et al., 2009). Treatment of mental illness might be also be influenced by spiritual beliefs and the adolescent and family might prefer to address their symptoms by seeking treatment with a cultural healer (Pumariega et al., 2009).

Since it is documented that treatment of depression will improve the quality of life of adolescents and their families, it is important that health care providers are aware of the barriers that could interfere with the treatment of depression in adolescents.

To decrease the burden of depression, mental health specialists need to be aware of the importance of screening, assessing, diagnosing, and treating adolescents with depression according to their cultural preferences. Mental health providers also need knowledge to address the barriers that might impede the appropriate treatment of adolescents with depression. Next, a review of the definitions of the main terms used in this paper will follow.

Definitions

Adolescent Population

Adolescents are the population between the ages 12 to 17 years old (March, 2004). However, the literature databases used in this project limited adolescence as the ages of 13 to 18 years old.

"Black Box" Warning

The Food and Drug Administration issued a warning about an increase in suicidality in children and adolescents who are prescribed an antidepressant, such as fluoxetine, sertraline, mirtazapine, paroxetine, venlafaxine, citalopram, bupropion, fluvoxamine and nefazadone among others. The American Academy of Child and Adolescent Psychiatry (AACAP) was first concerned this warning was going to interfere with the treatment of depression in this population because parents could be fearful of dispensing these medications to their children. However, the AACAP urged mental health specialists to monitor children and adolescents more carefully, and to establish a benefit vs. risk ratio at the beginning of therapy. AACAP also recognized the need for further research to determine the effectiveness and the accurate incidence of suicidal thoughts and behaviors in adolescents being treated with antidepressants (Regan, DeWire, Whithy, Bess & Wright, 2005). The FDA issued this black box warning on October 15, 2004 (Bridge et al., 2005; Temple, 2004).

Brain Stimulation Techniques

Even though the most used psychiatric treatment approaches are pharmacological or psychotherapeutic treatment, there are also biological, invasive and noninvasive approaches that have been studied. Among these noninvasive treatments are repetitive transcranial magnetic stimulation (rTMS) and electroconvulsive therapy (ECT) (Fitzgerald, 2008).

Electroconvulsive therapy (ECT).

ECT involves the induction of seizure activity while the patient is under general anesthesia. This type of treatment is reserved for extreme symptoms that could put the adolescent in danger (Fitzgerald, 2008).

Repetitive transcranial stimulation (rTMS).

This technique stimulates nerve cells by the use of a magnetic field in a coil that is placed on the scalp. This electrical field causes a magnetic pulse that induces depolarization of nerve cells (Fitzgerald, 2008).

Evidence-Based Practice

Evidence-Based-Practice (EBP) is the use of the best evidence available when trying to make a clinical decision while taking into consideration the preferences of the patient (Dicenso, Guyatt & Ciliska, 2005; Titler & Everett, 2001).

Integrative Review

The purpose of an integrative review (clinical review) and synthesis of the literature is to describe existing research to increase understanding of a topic of interest. Different methods to review the literature have been developed since the 1970's. Integrative reviews have been defined as "research of research," and it is expected that they comply with the same methodological rigor demanded from primary research (Whittemore & Knafl, 2005).

Major Depression

For a diagnosis of major depression, 5 of 9 possible symptoms indicating social or occupational impairment have to be present for a period of two weeks on a daily basis. These symptoms include: 1) depressed/irritable mood, 2) loss of pleasure in activities previously enjoyed, 3) weight gain or weight loss, 4) decreased or increased sleep, 5) psychomotor agitation

or retardation, 6) loss of energy, 7) feelings of worthlessness or excessive guilt, 8) difficulty concentrating and making decisions, and 9) thoughts of death with or without plan or intent (American Psychiatric Association, 2000).

Mental Health Specialist

This is a qualified individual who is involved in improving and treating mental disorders in individuals, couples and families. It includes psychiatrists, clinical psychologists, clinical social workers, advanced psychiatric nurses, mental health counselors, neurologists, pediatricians, substance abuse counselors and other professionals (Committee on Psychosocial Aspects of Child and Family Health, 2009).

Treatment of Depression

In this paper, the treatment of depression will include different approaches, such as the use of psychotherapy, pharmacological management and a combination of psychotherapy and medication management (Asarnow et al., 2009). The use of complementary and alternative medicine; as well as, the use of other interventions will be explored. The use of psychotherapy includes different modalities. This paper will include the following approaches.

Psychotherapeutic Modalities

Three different types of therapy are the most mentioned in this paper: 1) cognitive-behavior therapy (CBT), 2) Interpersonal Therapy (IPT) and 3) Supportive Therapy.

Cognitive-behavioral therapy (CBT).

This model of psychotherapy focuses on how internal cognitive processes and the environment are responsible for individual performance. CBT was developed by Beck in the 1970s. It usually consists of 16 to 20 sessions with the goal of correcting negative cognitive processes (Craighead & Wilcoxon-Craighead, 2001).

Interpersonal psychotherapy (IPT).

IPT studies the connection between onset of depression and current interpersonal problems. It works with the "here and now." For example, if the depression began after the death of a relative, the therapist facilitates the grief and loss process. IPT has been modified to include adolescents and the problem area of single-parent family as a trigger for depression (Weissman & Markowitz, 2009).

Supportive therapy (ST).

Even though support is part of all the psychotherapeutic approaches, in Supportive Therapy (ST), support is a mode of treatment for a particular group of patients. ST is difficult to define, but it is considered to have an informal psychotherapeutic content, "good clinical care." ST has been ranked in the middle between formal psychotherapeutic modalities, such as CBT, and routine clinical care (Holmes, 1995).

Significance to the Doctor of Nursing Practice Mental Health Specialist

Doctor of Nursing Practice graduates are educated to apply research to practice and provide a foundation for clinicians and researchers to join their efforts to facilitate the translation of research into practice (Chism, 2009; Driever, 2002). Clinicians used to determine how patient care was delivered only based on their experience, but there is a growing awareness that care needs to be based on scientific evidence. The aim of using evidence-based practice is to utilize the best available scientific approaches when deciding the care that is required for the patient, while involving the patient in the decision-making process (McPheeters & Lohr, 1999).

Healthcare providers, the public and health care organizations recognize that clinical decisions should be made based on the best available evidence (Sheldon & Haines, 1998). The importance of using evidenced-based interventions in clinical settings is well documented

(Westfall, Mold, & Fagnan, 2007), and the Institute of Medicine (IOM) identified a "chasm" or a lack of fidelity, between evidenced-based interventions and how health care is delivered in clinical settings (Glasgow & Emmons, 2006). To address this problem, the IOM issued a report in 2001 to improve patient care and to reduce errors by educating healthcare providers on a set of competencies. These competencies include knowledge about how to deliver patient-centered care, the ability of clinicians to work in interprofessional teams, the use of evidenced-based practice to guide practice, knowledge about how to incorporate quality improvement methods in clinical settings and familiarity with different information system to facilitate the delivery of care (Chism, 2009; "Crossing the Quality Chasm: A New Health Care System for the 21st Century," 2001).

The implementation of evidenced-based care has also been addressed by The Joint Commission on Accreditation of Health Care Organization. This organization has reported a need for cost containment by using treatments that have shown to be effective (Driever, 2002). As a DNP student working with adolescents, this student has the opportunity to make a difference in the lives of adolescent patients and their families. By assessing, and if needed, treating adolescents with evidence-based treatments of depression, this student will help improve the lives of depressed adolescents and their families while decreasing health care costs.

Doctor of Nursing Practice graduates are aware of the importance of bringing the results of basic research to the public (Woolf, 2008). I work with adolescents diagnosed with depression in community and mental health settings. As a mental health specialist, I recognize the need for recommendations based on evidence-based practice to guide mental health providers in the treatment of adolescents with depression. The need for these recommendations is especially relevant at this time because of the controversial information regarding the use of antidepressant

medications in adolescents. Mental health specialists, like myself, need to be informed of the effectiveness and safety of the different approaches when treating adolescent depression.

In order to develop evidence-base practice recommendations for the treatment of unipolar depression in adolescents, Chapter 2 describes the method used to conduct a critical review and synthesis of the literature, the process to grade the evidence and the technique used for the development of the recommendations for practice.

CHAPTER TWO: METHODS

The methods used to conduct a critical review and synthesis of the literature on evidence-based treatment of unipolar depression in adolescents and to make recommendations for advanced nursing practice are discussed in this chapter. Cooper's *Guide for Literature Reviews* (1998) will be used to structure the review. This method was chosen because it permits the integration of different methodologies used in nursing studies, such as experimental and non-experimental research (Cooper, 1998; Whittemore & Knafl, 2005).

Cooper's *Guide for Literature Reviews* (1998) consists of five steps: 1) problem formulation, 2) data collection or the literature search, 3) data evaluation 4) analysis and interpretation and 5) presentation of results (Cooper, 1998; Whittemore & Knafl, 2005). All steps are discussed, and to accomplish step 4, the pertinent data will be ranked by using the Oncology Nursing Society, *Putting Evidence into Practice,* (ONS/PEP) *Levels of Evidence* scale. This system is an adaptation of the *Rating the Quality of Evidence for Clinical Practice Guidelines* developed by Hadorn and others (Hadorn, Baker, Hodges & Hicks, 1996; ONS/Tables). Lastly, for step 5, after the evidence for each study is ranked, recommendations for practice are presented based on the ONS/PEP, *Weight-of-Evidence Classification Schema,* developed by Mitchell and Friese (Eaton & Tipton, 2009).

Step 1: Problem Formulation

The first step in Cooper's *Guide for Literature Reviews* (1998) is problem formulation. It consists of identifying the problem that will guide the review process. For this paper, the problem is: Evidence-based treatment of unipolar depression in adolescents ages 12-18. Once the problem was formulated, the variables of interest: concepts, target population and the problem being addressed are clearly identified to allow for the extraction of the appropriate data (Cooper,

1998; Whittemore & Knafl, 2005), and to facilitate a literature search. Most of the articles found refer to major depressive disorder or to depressive disorder. Articles on bipolar depression are not included.

Step 2: Data Collection or the Literature Search

A professional librarian was consulted to ensure that the search was properly carried out. Medline (PubMed) was searched first because this database includes articles that have not been necessarily published in journals. Other databases used were: Medline (Ovid), Cinahl, PsycInfo and Complementary and Alternative Medicine sites. The main search terms used in this literature review were depression, adolescents, and treatment. The search was limited to: a) adolescents, ages 13 to 18, b) English Language, and c) the past five years.

An initial search in Medline (PubMed) was conducted by choosing MeSH for the subject heading of depression. The terms gave two results: 1) Depressive disorder and 2) Depression. These two options were exploded to include: Depressive Post Partum, Depressive Disorder Major, Dysthymic Disorder and Seasonal Affective Disorder. The search was limited to the subsets: a) diet therapy, b) drug therapy, c) nursing and d) therapy, full text. The term depressive disorder yielded a total of 36 articles for systematic reviews and meta-analysis and 297 citations for randomized control trials and clinic trials. In the depression term, 36 articles for systematic reviews and meta-analysis and 101 studies for randomized control trials and clinic trials were found.

The Medline (Ovid) database search was limited to English language, humans, full text, and core clinical journals from 2004 to present. The keyword depression was entered and this term yielded 54,337 articles. Once the subheadings for drug therapy, and therapy were chosen from the subheading list, the search was narrowed to 15,199 entries. Next, this search was

combined with the terms (adolesc* or young* or youth or child* or teen*), and 109 entries were obtained.

The term depression in CINAHL **(**Cumulative Index to Nursing and Allied Health Literature) was limited to peer reviewed, clinical queries for therapy and best balance. This search resulted in 37 results. In PsycInfo, the term depression in scholarly (peer reviewed) journals provided 59 articles. A search in the Complementary and Alternative Medicine (CAM) site provided no results, and the Allied and Complementary Medicine (AMED) database was then searched. This database provided 104 articles.

Following the literature search, the articles were evaluated in step 3. The purpose of step 3 was to find the studies involving an intervention related to the treatment of unipolar depression in adolescents ages 13-18. Also, duplicate studies were identified in Step 3.

Step 3: Data Evaluation

Data evaluation is the third step in the Cooper (1998) method. According to Whittemore and Knafl (2005) there is no gold-standard to evaluate and interpret the quality of research reviews. However, it is advised to choose high-quality data that provide strength and credibility to the topic of interest. Data need to be accurate, relevant, and precise. It also needs to be authoritative, the result of methodological research (Machi & McEvoy, 2009). In this step, the articles yielded by the different databases were reviewed, and a total of 93 articles were selected because they involved an intervention in the treatment of adolescents with depression. After these articles were selected, the literature review continued to step 4, analysis and interpretation.

Step 4: Analysis and Interpretation

The goal of the fourth step of Cooper's method (Cooper, 1998) is to present an unbiased synthesis of the evidence related to the problem of interest. Data analysis includes several

phases: a) data reduction, b) data display, c) data comparison, and d) conclusion drawing and verification (Whittemore & Knafl, 2005). In this step, data obtained were ordered, coded, categorized and summarized (Cooper, 1998; Whittemore & Knafl, 2005).

Data Reduction

The purpose of data reduction is to develop techniques for organizing, extracting and coding data. The use of valid coding is recommended to ensure rigor (Whittemore & Knafl, 2005). During this step, the articles chosen on step 3 are assigned a level to yield the recommendations from practice. To accomplish this task, the Oncology Nursing Society, *Putting Evidence into Practice,* (ONS/PEP) *Levels of Evidence* scale is used (ONS/Tables) (Figure 1). This system grades the evidence in levels, from Level I, strongest, to Level III, weakest, and it is an adaptation of the *Rating the Quality of Evidence for Clinical Practice Guidelines* developed by Hadorn and others (Hadorn et al., 1996).

The source of evidence for Levels I and II is based on quantitative research, while Level III consists of qualitative methods and case studies. In addition, each category also offers subcategories within the different levels (Figure 1). These subcategories allow the investigator to distinguish between different ranks of strength among Levels I, II and III (Hadorn et al., 1996; ONS/Tables).

Level I is the strongest evidence and contains subcategories 1 thru 3. Subcategory 1 consists of meta-analysis, systematic reviews and "well" designed randomized, controlled clinical trials. Subcategory 2 consists of "well-controlled," randomized clinical trials with sufficient sample size, and subcategory 3 covers the non-randomized, but "well-designed" trials, such as cohort and time series designs (Hadorn et al., 1996; ONS/Tables).

ONS Levels of Evidence

ONS Level	Level of Evidence Subcategory	Evidence Source	Strength of Evidence
		Research Based Evidence	
I	1	Meta-analysis or systematic reviews of multiple well designed, randomized, controlled clinical trials	Strongest
	2	Well-controlled, randomized clinical trials with adequate sample size	
	3	Well-designed trial without randomization (single group pre/post, cohort, time series studies)	
II	4	Well-conducted, systematic review of nonexperimental design studies	
	5	Well-conducted case-control study	
	6	Poorly controlled (flawed randomized studies) or uncontrolled studies (correlational descriptive studies)	
	7	Conflicting evidence or meta-analysis showing a trend that did not reach significance	
		National Institutes of Health Consensus Report	
		Published practice guidelines, for example by professional organizations, healthcare organizations, or federal agencies	
		Non-research Based Evidence	
III	8	Qualitative designs Case studies, opinions of expert authorities, agencies or committees	Weakest

Note. Reprinted from *Journal of Clinical Epidemiology*, 49, D.C. Hadorn, D. Baker, J.S. Hodges, & N. Hicks, Rating the Quality of Evidence for Clinical Practice Guidelines, 749-753, 1996, with permission from Elsevier.

Oncology Nursing Society (ONS). *Rating the quality of evidence for clinical practice guidelines table*. Retrieved on 09/27/09 from: http://onsopcontent.ons.org/toolkits/evidence/Process/levels.shtml#table

FIGURE 1. *Rating the Quality of Evidence for Clinical Practice Guidelines*.

Level II includes subcategories 4 through 7. Subcategory 4 refers to systematic reviews of non-randomized studies, and subcategory 5 is composed of case studies. Subcategory 6 encompasses the descriptive studies. It also includes inaccurate randomized control trial studies. Subcategory 7 consists of the studies that show conflicting evidence or meta-analysis that did not reach significance (Hadorn et al., 1996; ONS/Tables).

Level III only has one subcategory; number 8.This last level is used for studies with qualitative designs. It also includes case studies and expert opinions (Hadorn et al., 1996; ONS/Tables).

After data were coded, four subgroups were formed: 1) psychotherapy 2) pharmacological management, 3) combined treatment of psychotherapy and pharmacological management and 4) other treatment modalities to make data more manageable. This last category, other treatment modalities, included the use of dance, exercise, repetitive transcranial magnetic stimulation and of electroconvulsive therapy.

Data Display

To help find the patterns and relationships in the data, tables summarizing the information found in the studies are used. These tables displayed the data and facilitated the process of grading the evidence and making the recommendations for practice. Tables addressing the same treatment modality are presented in ten tables. For example, Table 1 displays the trials for Cognitive Behavioral Therapy, Table 2 contains the results for Interpersonal Therapy, and Table 3 shows the studies for Supportive Therapy. Other Psychotherapy Approaches are shown in Table 4. The results for Pharmacological Management can be found in Table 5. The studies for Combination Treatment (Psychotherapy plus Pharmacological Management) are presented in Table 6. The trials for physical activity are in Table 7. Table 8 exhibits the studies on Complementary and Alternative Medicine. The trials on Repetitive Transcranial Magnetic Stimulation can be found in Table 9. Lastly, Table 10 contains the evidence on Electroconvulsive Therapy.

Data Comparison

Once the tables displaying the evidence were created, these tables were used to aid in the process of comparing results from different studies, as well as the identification of patterns, themes and relationships among the different types of treatment of depression (Cooper, 1998). After step 4, was completed, it was determined that out of the 93 articles included, 30 involved the use of psychotherapy, 28 utilized pharmacological management, 27 used the combination of psychotherapy and pharmacological management and 8 were classified under the category of other types of treatment.

Step 5: Presentation of Results

During this step, the recommendations for practice were offered by using the ONS/PEP Weight-*of-Evidence Classification Schema*, also known as the PRISM categorization, developed by Mitchell and Friese (2009). The purpose of the classification schema is to help in the evaluation process and to make recommendations about a topic of interest. The *Weight-of-Evidence Classification Schema* consists of six categories or panels (Eaton & Tipton, 2009) (Figure 2).

The *Weight-of-Evidence Classification Schema* is based on three principles which include: quality of the data, magnitude of the outcome and concurrence. For example the quality of the power refers to randomized trials and meta-analysis with the highest power. The magnitude of the outcome includes the effect size of the studies, and concurrence refers to the clinician's level of confidence when the results found in the evidence yield similar findings (Eaton & Tipton, 2009).

In this paper, the six panels of the *Weight-of-Evidence Classification Schema* are indicated as: 1) recommended for practice, 2) likely to be effective, 3) benefit is balanced with

harms, 4) effectiveness not established, 5) effectiveness unlikely, and 6) not recommended for practice (Eaton & Tipton, 2009) (Figure 2).

CLASSIFICATION	DEFINITION
1. Recommended for practice	Interventions for which effectiveness has been demonstrated by strong evidence from rigorously designed studies, meta-analyses or systematic reviews, and for which expectation of harms is small compared with the benefits.
2. Likely to be effective	Interventions for which the evidence is less well established than for those listed under "recommended for practice"
3. Benefit is balanced with harms	Intervention for which clinicians and patients should weigh the beneficial and harmful effects according to individual circumstances and priorities.
4. Effectiveness not established	Interventions for which data currently are insufficient or of inadequate quality.
5. Effectiveness unlikely	Interventions for which lack of effectiveness is less well established than for those listed under "not recommended for practice."
6. Not recommended for practice	Intervention for which ineffectiveness or harmfulness has been demonstrated by clear evidence, or the cost or burden that is necessary for the intervention exceeds anticipated benefit.

Note. Based on the work of Mitchell & Friese (Eaton & Tipton, 2009).

FIGURE 2. *ONS/Putting Evidence into Practice: Weight-of-Evidence Classification Schema*

Recommended For Practice

This category consists of studies showing strong evidence from trials that have been rigorously designed, to meta-analysis, and to systematic reviews. In this category, the benefits highly outweigh the harm (Eaton & Tipton, 2009).

Likely To Be Effective

Interventions include one single control trial with less than 100 participants. Evidence may also originate from meta- analysis or systematic review with less than 100 patients and it did not include effect size and confidence intervals. Guidelines not founded in the synthesis and rating of evidence, but rather in the information consensus or expert opinion also fall in this category (Eaton & Tipton, 2009).

Benefit Is Balanced With Harms

In these interventions, the evidence for this category may originate from one or more randomized trials, meta-analysis or systematic reviews. However, the clinician and the patient need to weigh the benefits against the side effects taking into consideration specific circumstances. This recommendation is based on evidence showing adverse effects related to the possibility of mortality, morbidity, disability and increase of hospital days (Eaton & Tipton, 2009).

Effectiveness Not Established

In this case, the evidence originates from a well-controlled case study, or from a poorly designed controlled or uncontrolled study. In addition, the evidence may show conflicting data, such as, meta-analyses not reaching statistical significance (Eaton & Tipton, 2009).

Effectiveness Unlikely

The lack of effectiveness is not as well-defined as the evidence under "Not Recommended for Practice." For example, the evidence from a single, well-designed trial with a minimum of 100 subjects, or from a trials including more than one clinical site, which failed to show any benefit. This category also includes evidence from a well-controlled case study, an

uncontrolled study, or randomized trials with multiple biases showing multiple adverse events without benefits (Eaton & Tipton, 2009).

Not Recommended For Practice

The evidence shows that the ineffectiveness or harmful effects of an intervention exceed the benefit. In addition, these interventions may show that the cost or burden do not justify the adverse effects of the intervention (Eaton & Tipton, 2009).

Summary

Chapter 2 described the methods used to synthesize the literature, grade the evidence and present the results. The synthesis of the literature was done following the *Guide for Literature Reviews* (Cooper, 1998) which consists of five steps. The first step, the identified problem that guided the review process was the treatment of depression in adolescents, ages: 13-18. Next, in step two, a literature search was conducted in PubMed, Cinahl, Psych Info, Complementary and Alternative Medicine and AMED. To accomplish step three, the literature was reviewed as this process yielding 93 articles. Step four was accomplished by ranking the evidence with the ONS/PEP, *Levels of Evidence* scale (ONS/Tables) (Figure 1). This system is an adaptation of the *Rating the Quality of Evidence for Clinical Practice Guidelines* developed by Hadorn and others (Hadorn et al., 1996; ONS Tables). Lastly, after the evidence for each study was ranked, recommendations for practice were presented based on the ONS/PEP, *Weight-of-Evidence Classification Schema* developed by Mitchell and Friese, (Eaton & Tipton, 2009). The results of 93 articles will be presented in Chapter 3.

CHAPTER THREE: RESULTS

The results for the studies found in the literature search for the treatment of unipolar depression in adolescents are presented in this chapter. Even though the focus of this practice inquiry is for adolescent depression, most of the studies also included children, ages 6 to 12. The main treatment modalities included in this practice inquiry are the use of psychotherapy, pharmacological management, and combined approaches (psychotherapy plus pharmacological management). Other treatment options, such as physical activity, complementary and alternative medicine, repetitive transcranial magnetic stimulation and electroconvulsive therapy are also presented.

Tables with the data for every treatment modality are numbered. For example, Table 1 displays the trials for Cognitive Behavioral Therapy. Table 2 contains the results for Interpersonal Therapy. Table 3 shows the studies for Supportive Therapy. Other Psychotherapy Approaches are shown in Table 4. The results for Pharmacological Management can be found in Table 5. The studies for Combination Treatment (Psychotherapy plus Pharmacological Management) are presented in Table 6. The trials for physical activity are in Table 7 while Table 8 exhibits the studies on Complementary and Alternative Medicine. The trials on Repetitive Transcranial Magnetic Stimulation can be found in Table 9. Lastly, Table 10 contains the evidence on Electroconvulsive Therapy. The results for psychotherapy will be discussed first.

Psychotherapy

The main types of psychotherapy found in the literature search for the treatment of depression in adolescents were Cognitive Behavioral Therapy (CBT), Interpersonal therapy (IPT) and Supportive therapy (ST). However, some articles studied the effect of psychotherapy by including a combination of multiple psychotherapeutic approaches, as in meta-analysis and

systematic reviews. A total of 30 studies addressing the use of psychotherapy were included in this practice inquiry. From these studies, 18 studies utilized CBT, six IPT, three supportive therapy and three used other psychotherapy approaches.

Cognitive Behavioral Therapy (CBT)

Strong evidence about the effectiveness of CBT in the treatment and prevention of depression in adolescents was found in two meta-analyses and in eight randomized controlled trials (See Table 1). These two meta-analyses reported results by calculating an effect size (ES). An effect size of 0.2 is categorized as small, while 0.50 reports a moderate effect and 0.80 a large effect (Munro, 2005). The first meta-analysis, conducted by Weisz, McCarty, and Valeri (2006) found an ES in favor of psychotherapy of 0.34 in 31 RCTs of adolescents, while a meta-analysis by Klein, Rachel, Jacobs, and Reinecke (2007) reported a mean weighted post -treatment ES of .53 significantly different from zero in favor of CBT ($z = 3.58$; $p < .01$). However, the benefits of CBT are reduced in children whose parents are depressed (Garber et al., 2009). The previous two meta-analyses included trials of individual psychotherapy; however, this treatment modality is also often delivered to families.

Individual and family CBT.

Individual and Family CBT have been compared to each other. It was reported that they were both equally effective (Trowell et al., 2007). In addition to individual and to family CBT, other types of CBT were included. For example, the following study used the primary and secondary control enhancement training (PASCET) method.

The PASCET method.

This method was compared to usual care in a randomized controlled trial. In this study, adolescents, in the treatment and in the control group, were treated to “normal” termination

which was until the therapists detected improvement. Adolescents in the CBT group needed fewer sessions, and also incurred in fewer costs, such as medications, but no statistical difference between groups was detected (Weisz, Southam-Gerow, Gordis, Connor-Smith, & Chu, 2009). In addition to the effectiveness of psychotherapy, the emergence of suicidality during treatment of depression with psychotherapy has also been studied. An individual trial and a meta-analysis addressing suicidality were found.

Suicidality.

Researchers studied the problems of emergent suicidality during psychotherapy with CBT and they recommended assessing for suicidality prior to starting any intervention by using specific and systematic assessment tools, such as the Beck Depressive Inventory, item 9. This recommendation was made because patients could be suicidal before the initiation of therapy (Bridge, Birmaher, Kolko, & Brent, 2005). Also, a meta-analysis found that there was a small reduction of suicidality attributed to psychotherapy, mean ES of 0.18 (Weisz et al., 2006). In addition to the effectiveness and safety of CBT, another important topic in the treatment of adolescent depression is the cost-effectiveness of CBT. This topic is discussed in the next study.

Cost-effectiveness of CBT.

Lynch et al. (2005) found that costs for CBT were not statistically cost-effective following a group intervention, but it was found to be cost-effective one year after the CBT trial was over. CBT has not only been examined in clinical settings. Researchers have also conducted school interventions addressing the prevention and treatment of adolescent depression.

CBT in School Settings

The use of CBT interventions has also been applied to school settings. School interventions to prevent the development of depression in adolescents have been divided into three categories: universal, selective and indicated approaches.

Universal, selective and indicated interventions.

Universal approaches involve whole populations regardless of their risk level in contract to selective interventions directed at adolescents who are at risk of developing depression due to a trigger in the environment, such as family relationship problems, divorce of parents, and death of a parent. Indicated actions are aimed at adolescents who already have mild to moderate symptoms of depression and are deemed to be candidates to suffer a mood disorder in the future (Sheffield et al., 2006).

In this literature search, two individual trials, one meta-analysis and one systematic review involving universal, selective and indicated approaches were found. For example, in two randomized controlled trials, researchers found no differences between groups. One of these studies used universal, indicated and combined behavioral approaches and found no differences across all the prevention treatment modalities (Sheffield et al., 2006). In another study to test the efficacy of a long-term, universal approach, authors reported that there was no difference between the adolescents that received the intervention, but that subjects with the highest degree of depression at baseline had the greater improvement in problem solving scores at the end of an eight-week intervention (Spence, Shetfield, & Donovan, 2005). In addition to these studies, a systematic review by Horowitz & Garber (2006) found a small to moderate effect for selective and indicated therapeutic approaches.

The previous interventions were individual school trials, but this literature search also found a systematic review and a meta-analysis. For example, a systematic review focused on screening and in early psychological interventions for depression in schools included six studies that used CBT and two that utilized relaxation training. The mean effect size was 0.55 (95% CI: 0.35–0.76), "moderate to high" effect in favor of the psychotherapeutic modalities (Cuijpers, Van Straten, Smits, & Smit, 2006). Also, a meta-analysis found a small effect size for the treatment group that received a brief group cognitive intervention (CB), (Stice, Shaw, Bohon, Martin, & Rohde, 2009).

In addition, the prevention of depression in schools has been addressed by utilizing other CBT approaches (See Table 1 in Appendix A). For example, the "Coping with Stress" and the "Penn Prevention Program" models; as well as, the Mood GYM modality have also been employed in school settings.

Coping with stress and the Penn prevention program.

In a systematic review, the "Coping with Stress" approach, a CBT modality, had a "modest" effect. However, two other studies using the "Penn Prevention Program" did not show this intervention to be beneficial (Waddell, Hua, Garland, Peters, & McEwan, 2007).

MoodGYM.

The Internet was used to deliver this CBT modality, MoodGYM. This study did not show immediate significant results for CBT. However, students with the highest baseline depression scores in the CBT group had the most benefit at 20-week follow-up (O'Kearney, Kang, Christensen, & Griffiths 2008).

CBT has also been compared to other psychotherapeutic interventions. In the first study, CBT was compared to supportive-expressive therapy and bibliography. Three other articles, a

systematic review and two randomized controlled trials compared CBT to IPT in the treatment of adolescents with depression.

CBT, supportive-expressive therapy and bibliotherapy.

Brief CBT, CB, was found to be more effective than supportive-expressive therapy and bibliotherapy in adolescents at post-test. At six-month follow up, improvement in social improvement was still higher for the CB group (Stice, Rhode, Seeley, & Gau, 2008).

Comparison of CBT and IPT.

A systematic review found a benefit for both CBT and IPT especially in patients with moderate to severe depression (Watanabe, Hunot, Omori, Churchill, & Furukawa, 2007). This high response to psychotherapy in high risk adolescents was also found in an individual trial. This trial also found a small effect for both CBT and IPT (Horowitz, Garber, Ciesla, Young, & Mufson, 2007). However, in another randomized controlled trial of individual and group CBT and IPT, CBT was the most effective modality. This study also found that the efficacy of individual over group therapy was small and researchers suggested the possibility of using the group format as a cost-effective method to decrease depression symptoms (Rosello, Bernal, & Rivera-Medina, 2008).

Weight-of-Evidence Classification Schema (CBT)

In conclusion, the use of cognitive behavioral therapy (CBT) has been found to be effective when delivered directly and through the Internet. CBT has also demonstrated to be helpful in individual, family and school treatment modalities. Based on this evidence, and according to the ONS/PEP *Weight-of-Evidence Classification Schema*, the use of CBT is recommended for practice.

The results of IPT will be presented next. A total of six studies were found that used IPT, including one systematic review and five individual trials.

Interpersonal Psychotherapy (IPT)

The results for IPT are displayed in Table 2. When IPT was considered separately, a systematic review found IPT is effective in decreasing depressive symptoms, improving interpersonal and social functioning (Brunstein, Zalsman, & Mufson, 2007). In addition, in a randomized controlled trial of IPT, the group receiving the intervention had less symptoms of depression and overall better functioning at the end of the study, as well as, at three and six-month follow up (Young, Mufson, & Davies, 2006). When anxiety was taken into consideration in an IPT study, results showed that patients with comorbid anxiety and higher depression scores at baseline benefitted less from IPT-A (Young et al., 2006). IPT has also been used successfully in schools. Three individual studies of IPT in schools were found in this literature search.

IPT in schools.

First, a trial carried out in three Catholic schools in New York City found that adolescents receiving IPT had lower depression scores and a higher improvement in level of functioning (Mufson et al., 2004). Second, IPT also had positive results in decreasing suicidal risk and presuicide behaviors (Tang, Jou, Ko, Huang, & Yen, 2009). Third, IPT was used in pregnant adolescents, and this treatment modality improved mood and quality of life in this population (Miller, Gur, Shanok, & Weissman, 2008).

Weight-of-Evidence Classification Schema (IPT)

IPT has shown to be effective in the treatment of adolescent depression in different clinical and school settings. According to the ONS/PEP *Weight-of- Evidence Classification Schema*, based on the results presented, IPT is recommended for practice.

In addition to CBT and IPT, other psychotherapy approaches have been used, such as supportive psychotherapy (ST). The results for three studies will be presented next.

Supportive Psychotherapy (ST)

The results for ST are found in Table 3. The studies found using supportive psychotherapy in this practice inquiry involved pregnant adolescents only, but different approaches have been used to treat depression in pregnant and post-partum adolescents (Logsdon, Ziegler, Hertweck, & Pinto-Foltz, 2008). Among the predictors for depression in pregnant adolescents are perceived stress followed by being the victim or witness of violence, low self-esteem and lack of social support. Furthermore, it is advised that the social support that adolescents receive be similar to their needs known as ecological congruence (Logsdon et al., 2008). In addition, a social support intervention to prevent depression in postpartum adolescents decreased depression and improved parenting and self esteem in both the intervention and control groups at six weeks postpartum (Logsdon, Birkimer, Simpson, & Looney, 2005). Also, researchers emphasized the importance of interventions to decrease depression in adolescents since depressive symptoms might be an independent risk factor for fast, second pregnancies in this population (Barnet, Liu, & Devoe, 2008).

Weight-of-Evidence Classification Schema (ST)

Even though the evidence found in these studies supporting ST did not originate from randomized controlled trials, results show a decrease in symptoms of depression. According to the ONS/PEP *Weight-of-Evidence Classification Schema*, the use of supportive therapy approaches are likely to be effective in practice when treating symptoms of depression in pregnant and post-partum adolescents. More research is needed.

Four studies that belonged to different psychotherapeutic modalities are included in the next section.

Other Psychotherapy Approaches

In addition to CBT, IPT and ST there are other types of therapy available. This practice inquiry also included two studies on motivational interview (MI), one in Skills Based Treatment and another one on Family Psychoeducation. These studies can be found in Table 4.

Motivational interview.

The first study included the use of the Internet in a randomized controlled trial of psychotherapy comparing motivational interview (MI) to brief advice. This trial found no difference between the two groups. However, the MI group exhibited a decrease in self-harm thoughts, hopelessness and risk of relapsing to depression. This intervention was also categorized as cost-effective (Voorhees et al., 2009).

Skills based treatment.

An intervention compared the "Skills Based Treatment" (SBT) modality to a "Supportive Relationship" following a suicide attempt. SBT is based on cognitive behavioral therapy. In this study SBT focused on problem solving and in affect management, such as relaxation techniques. No difference was found between groups since both groups reported decreased rates of depression and suicidal ideation (Donaldson, Spirito, Esposito, & Smythers, 2005).

Family psychoeducation.

A trial used family psychoeducation (FPE) as an adjunct to treatment for depressed adolescents. This intervention showed that the FPE group had significant improvement in the areas of social functioning and in adolescent and parent relationships (Sanford, Boyle, McCleary, Miler, & Steele, 2006).

Weight-of-Evidence Classification Schema (Other)

Even though two out of three trials in this category did not separate from placebo, the results for the studies presented in this section were effective in decreasing symptoms of depression. Following the recommendations by the ONS/PEP *Weight-of-Evidence Classification Schema*, it was determined that the effectiveness of these interventions (motivational interview, skills based treatment and family psychoeducation) was not established.

Summary

The results for CBT, IPT, ST and other psychotherapy approaches are presented in this section. After the results were reviewed, following the recommendations by the ONS/PEP *Weight-of-Evidence Classification Schema*, CBT and IPT were found to be recommended for practice; while ST interventions were determined to be likely effective in practice. Effectiveness of the other psychotherapy approaches was not established. Next, the results for pharmacological management are discussed. The tables presenting the studies on pharmacological management are found in Table 5.

Pharmacological Management

Table 5 displays the results of 28 studies involving pharmacological management approaches. Studies involving different antidepressant medications were found in the literature search conducted for this practice inquiry. These antidepressants belong to different classes of medications, such as the serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs) and tricyclic antidepressants (TCAs). There is also an older antidepressant category, the monoamine oxidase inhibitors (MAOIs), but no individual trials for these antidepressants were included in this practice inquiry.

Selective Serotonin Reuptake Inhibitors (SSRIs)

Evidence at the highest level, from seven meta-analyses (Dubicka, Hadley, & Roberts, 2006; Hetrick, Merry, McKenzie, Sindahl, & Proctor, 2007; Bridge, Iyengar, Salary, Barber, & Birmaher, 2007; Papanikolau, Richardson, Pehlivanidis, & Papadopoulos, 2006; Sharp & Hellings, 2006; Tsapakis, Soldani, Tondo, & Baldessarini, 2009; Usala, Zuddas, & Bonati, 2008) and from eight systematic reviews supported the effectiveness and safety of SSRI's for the treatment of depression in children and adolescents (Cheung, Emslie & Mayes, 2005; Cohen, Deniau, Maturana, Tanguy, & Bodeau, 2008; Hammad, Laughren, & Racoosin, 2006; Hazell, O'Connell, Heathcote, & Henry, 2009; Hetrick, Merry, McKenzie, Sindahl, & Proctor, 2007; Moreno, Arango, Parellada, Shaffer, & Bird, 2006; Posner, Oquendo, Gould, Stanley, & Davies 2007; Smith, 2009).

The results from 12 individual trials on medication management were also included (Berard, Fong, Carpenter, Thomason, & Wilknison, 2006; Cheung et al., 2008; Donnely et al., 2006; Emslie, Ventura, Korotzer, & Tourkodimitirs, 2009; Emslie et al, 2008; Emslie, Findling, Yeung, Kunz, & Yunfeng, 2007; Emslie, Wagner, Kutcher, Krulewicz, & Regan, 2006; Heiligenstein et al., 2006; Rynn et al., 2006; Shirazi & Alaghband-Rad, 2005; Von Knorring et al., 2006; Wagner, Jonas, Findling,Ventura, & Saikali, 2006).

Meta-analyses including SSRIs.

One meta-analysis revealed that paroxetine had the highest number of side effects which included: dry mouth, vomiting, nausea, diarrhea, somnolence, insomnia, dizziness, tremor and agitation (Sharp & Hellings, 2006). Moderate effectiveness was found for citalopram and sertraline (Usala et al., 2008); while fluoxetine was the medication with the stronger recommendations (Usala et al., 2008; Hetrick et al., 2007; Cheung et al., 2005).

Comparison of TCA's to SSRIs

Studies comparing TCA's to SSRI's are located in Table 5. The superiority of fluoxetine continued when it was compared to TCA's in a systematic review (Moreno et al., 2006). In a meta-analysis on TCA's involving the tricyclic antidepressants, (amitriptyline, clomipramine, desipramine, imipramine and nortriptyline) and the serotonin type agents, citalopram, fluoxetine, paroxetine, sertraline and venlafaxine found that 80% of the studies (24/30) failed to demonstrate superiority of antidepressant over placebo. Furthermore, of the six studies indicating benefit over placebo, five of these trials involved SSRI's with fluoxetine displaying a greater pooled efficacy (Tsapakis et al., 2009). The high placebo response found in studies involving children and adolescents was also addressed by Cohen et al. (2008) in a systematic review. In this study, the placebo response rate for major depressive disorder was higher than for anxiety disorders in children and adolescents (Cohen et al., 2008).

The negative results for TCA's and the significant results for SSRI's were also replicated in the meta-analysis by Papanikolau et al. (2006). When compared to placebo, TCA's were not found effective, and a subgroup analysis reported tricyclic drugs were more useful for adolescents than for children. However, TCA's were linked to significant side effects, such as vertigo, hypotension, tremor, dry mouth, tiredness, perspiration and micturation problems. Authors also discussed other risk factors associated with the use of tricyclic drugs such as their lethality in overdose and the possibility of cardio toxic effects even when used in therapeutic doses (Hazell et al., 2009).

Studies included in this practice inquiry not only address the effectiveness of antidepressants in children and adolescents, but the safety of these medications is also addressed. Results regarding the possibility of emergent suicidality will be presented next.

Suicidality

The FDA issued a black box warning on October 15, 2004 concerning the increased risk of suicidality in children and adolescents who are prescribed antidepressant medications following a finding that there was a 2-3% increased in suicidal ideation or behavior in patients taking antidepressants. However, no completed suicides were reported in the studies reviewed by the FDA (Bridge et al., 2005; Temple, 2004). Also, epidemiological reports have shown an inverse relationship between completed suicides and antidepressants (Cheung et al., 2005). In addition, the FDA has made recommendations for close monitoring of adolescents. A protocol issued by the FDA recommends observing for clinical worsening, suicidality and behavioral changes during face to face visits weekly for the first four weeks of treatment, then every other week for one month, and at 12 weeks (Emslie et al., 2006).

Meta-analyses have been conducted to determine the emergence of suicidality in patients treated with antidepressants. These meta-analyses can be found in Table 5. The pooled risk difference for suicidality was 1% in the meta-analysis by Bridge et al. (2007). Another meta-analysis explained that five in 100 children taking antidepressants could experience self-harm or suicidality when compared to three out of 100 children in a placebo group (Dubicka et al., 2006). Other authors reported a lower risk, the possibility that one or three adolescents taking antidepressants could experience an increase in suicidal behavior (Hammad et al., 2006). However, studies have failed to make clear differentiations between self-harm behaviors and suicidality. For example a meta-analysis by Columbia University reported that pharmaceutical companies tended to report self-harm behaviors as suicide attempts (Posner et al., 2007).

To explain the increased suicidal events found in adolescents taking antidepressants, researchers have examined the possible link between suicidal ideation and the half-life of

antidepressants. Increased suicidal ideation has been found in venlafaxine, a serotonin and norepinephrine reuptake inhibitor (SNRI), and this medication has the shortest half-life when compared to medications such as fluoxetine, the SSRI with the longest half-life (Smith, 2009).

Individual Medication Trials

The results included were obtained from 12 randomized trials and two open trials and can also be found in Table 5. Most of the medications included belong to the SSRI category (citalopram, escitalopram, fluoxetine, paroxetine, and sertraline). Also, two studies involve the use of venlafaxine XR, an SNRI. It has been reported that to obtain FDA approval for the treatment of depression of pediatric patients because the FDA Modernization Act requires two positive placebo-controlled trials (Cheung et al., 2005). At this time, fluoxetine is the only medication that is approved by the FDA for the treatment of depression in children and adolescents after two positive trials. However, Escitalopram (under the trademark {TM} Lexapro) is now approved for the treatment of adolescents only (Hitt, 2009). For example, one study involving escitalopram found a difference in favor of escitalopram when comparing baseline to endpoint treatment scores in the Children's Depression Rating Scale-Revised. Researchers noted differences in scores starting at Week 6 ($p=0.06$) and the greatest placebo response was at Week 4 ($p=0.001$) (Emslie et al., 2009). In addition, a study by Wagner et al., (2006); did not find a significant difference in favor of escitalopram, but after a post-hoc analysis was performed, it showed that escitalopram had positive effects in the treatment of adolescents (Findling, Bose, Aquino, Koretzer, Tourkodimitris, 2008).

As previously reported, fluoxetine was found to be a safe and effective medication in meta-analyses, but fluoxetine also has had positive results in preventing relapse of major depression after six months of treatment (Emslie et al, 2008). Also, a trial with a trial of

fluoxetine reported that 40-60 mg/day was more effective than fluoxetine 10-20 mg/day in achieving treatment response in patients who had failed to benefit from a nine-week trial of 20 mg a day of fluoxetine (Heiligenstein et al., 2006).

However, other medications have not shown positive results in two positive trials. For example, a study of citalopram did not reveal a statistical significant difference when compared to placebo (Von Knorring et al., 2006) but an open trial had positive results after six weeks of treatment (Shirazi & Alaghband-Rad, 2005). Paroxetine has had three failed trials (Berard et al., 2006; Cheung et al., 2005; Emslie et al., 2006). Also, two sertraline trials failed to find positive effects in two individual studies, but when the results were pooled, researchers noted a better response for adolescents than for children (Cheung et al., 2005). In addition, researchers tested time to first response among children and adolescents taking sertraline in an open trial and found that, when compared to placebo, sertraline had a faster time to first persistent response in adolescents (Rynn et al., 2006). Venlafaxine had two negative trials (Cheung et al., 2005). One of these studies reported that venlafaxine produced the most improvement in adolescents ages 12 to 17 years old, but this result was not significant (Emslie et al., 2007). Also, Nefazadone and mirtazapine each had one trial with negative results (Cheung et al., 2005).

Weight-of-Evidence Classification Schema (SSRIs)

Following the ONS/PEP *Weight-of-Evidence Classification Schema*, it is concluded that from the pharmacological approaches, SSRIs are an effective and safe treatment for depression in adolescents with the most supporting evidence found for fluoxetine. Escitalopram is also now approved for the treatment of adolescents, ages 13-17. SSRI's are recommended for practice

In the previous sections, the results for psychotherapy and for pharmacological management were presented. However, in certain cases, combination treatment is recommended.

Combination treatment consists of the use of psychotherapy in addition to pharmacological management.

Combination Treatment

The results of 27 studies in the combination treatment modality for adolescents with depression will be presented. These studies can be found in Table 6. Combination treatment involves the use of psychotherapy plus pharmacological management. Twelve of these studies were conducted as part of the Treatment for Adolescents with Depression Study (TADS), a randomized, controlled trial conducted in the United States. TADS lasted nine months and it is the largest controlled clinical trial of adolescent depression to date. It included 423 participants (Domino et al., 2009). The results of two other trials, the Treatment of Resistant Depression in Adolescents (TORDIA) trial and the Adolescent Depression Antidepressant and Psychotherapy Trial (ADAPT); as well as the results of three other individual trials is presented.

The TADS Trial

TADS strongly supported the used of combination therapy. After 12 weeks of treatment, TADS scores revealed response rates are higher for the combination (COMB) group consisting of fluoxetine (FLX) plus cognitive behavioral therapy, CBT (March et al., 2004). Patients in the COMB group also exhibited the largest improvement in quality of life (Vitiello et al., 2006), and the greatest reduction in suicidal ideation (March et al., 2004). Also, treatment with FLX was found to be more effective than CBT alone (March et al., 2004). Furthermore, TADS also found that physical and psychiatric adverse events were more common in the FLX group (Emslie et al., 2006). Suicidal ideation continued to be higher in the fluoxetine group, followed by COMB and CBT at the end of 36 weeks of treatment (March et al., 2007).

TADS addressed important factors that could impact the treatment of depression in adolescents. For example, TADS found that, even when patients responded favorably to treatment, 20% of these patients continue to have residual symptoms of depression (Kennard et al., 2006). However, adolescents in the combination groups had the highest response rate and the lesser incidents of relapse (Rohde et al., 2008). Combination therapy was also more effective in sustaining early response to treatment (Kratochvil et al., 2006). Even though patients in the combination and fluoxetine groups had a faster response rate in adolescents with moderate to severe depression by week 12 , the response rates were similar across the three treatment modalities (CBT, fluoxetine and combination) by week 36 (March et al., 2007; March et al., 2009). Furthermore, after the completion of TADS, at one year follow up, longer treatment duration was associated with sustained improvement even after the treatment was discontinued (March et al., 2009).

The use of combination treatment is also strongly supported by four studies describing results from the Treatment of Resistant Depression in Adolescents (TORDIA) trial. This randomized-controlled study lasted 12 weeks. It included 334 adolescents who had been resistant to treatment with a selective serotonin reuptake inhibitor (SSRI) (Asarnow et al., 2009).

The TORDIA Study

In the TORDIA study, patients who were switched to another SSRI or to the SNRI, venlafaxine, had a better response to treatment when CBT was added to a medication switch (Asarnow et al., 2009). No differences are found in response between SSRIs and venlafaxine, but this last medication was associated with more side effects (Brent et al., 2008). Another factor considered in the TORDIA trial is the emergence of suicidality during the treatment of adolescent depression.

Suicidality.

Regarding suicidality, the TORDIA researchers did not find statistical significant results across treatment modalities for suicidal and non-suicidal incidents, but the most important predictors of suicidal events reported were high suicidal ideation at baseline, family conflict and drug and alcohol use. In addition, patients with a history of suicidal behavior tend to repeat this behavior. The median time for a suicide event was three weeks. No protective effect was found for CBT monotherapy possibly because adolescents had not received enough sessions yet (Brent et al., 2009). In addition, TORDIA does not recommend the use of venlafaxine in patients with moderate to severe suicidal ideation at baseline because findings reveal an increase in self-harm behaviors in patients who were treated with this medication. Authors recommended that clinicians should target behaviors associated with poor response and increased adverse events that can interfere with treatment, among them high suicide ideation, family conflict, and alcohol and drug use (Brent et al., 2009). Furthermore, researchers have linked successful treatment to the duration of CBT treatment duration.

Duration of treatment.

As reported by TADS (March et al., 2009), longer treatment was also associated with better results in the combination approach in the TORDIA study. For example, a secondary analysis in patients participating in a continuation trial lasting 24 weeks, adolescents taking only antidepressants had an eight-fold possibility to relapse to depression (Kennard et al., 2008).

The ADAPT Trial

In addition to TADS and TORDIA, two articles describing the results for the Adolescent Depression Antidepressant and Psychotherapy Trial (ADAPT) were found. ADAPT was a

randomized controlled study conducted in England with a sample size of 208 adolescents (Goodyer et al., 2007; Goodyer, Dubicka, Wilkinson, Kelvin, Roberts & Byford, 2008; Table 6).

Contrary to TADS and TORDIA, the ADAPT trial concluded that, in the presence of routine specialist care, adding CBT to an SSRI in adolescents suffering from moderate to severe depression was not more beneficial than only receiving an SSRI (Goodyer et al., 2007). Furthermore, the addition of CBT to medication management improved safety because of its protective effect in suicidal ideation in the TADS trial (March et al., 2007), but this benefit was not found in the ADAPT study. Researchers reported that these results could be due to the ADAPT trial including very depressed subjects, and TADS not including adolescents with high acuity of symptoms. Also, all the subjects in the ADAPT trial received routine specialist care. This care included visits with a study psychiatrist for case management and medication monitoring (Goodyer et al., 2007) and the role of all participants being exposed to this type of intervention is not known.

Even though the ADAPT trial did not find combination treatment to be either more effective or cost-effective than the use of medication in addition to routine care, the guideline for the treatment of moderate or severe depression in the United Kingdom recommends that combination treatment is the only accepted management for this type of depression in adolescents (Byford et al., 2007). In addition, the lack of superiority of COMB treatment in the ADAPT trials could have been related to the number of sessions that the participants received.

Number of CBT sessions.

The ADAPT trial reported high rates of absenteeism to CBT sessions (Goodyer et al., 2008), and the TORDIA researchers linked CBT effectiveness to a larger number of therapy sessions (Asarnow et al., 2009). The average number of CBT sessions in the ADAPT trial was

6.2 sessions (Goodyer et al., 2008), eleven in TADS (March, et al., 2004), and nine in the TORDIA study (Brent et al., 2008). Another study observed that adolescents who received more than nine CBT sessions were 2.5 times more likely to be responsive to treatment (Kennard et al., 2009). The content of CBT sessions also appears to make a difference. For example, when problem-solving and social skills were addressed during their CBT sessions, adolescents were 2.3 to 2.6 times respectively more likely to respond to treatment (Kennard et al., 2009). In addition to response to treatment, the TADS and the ADAPT trials also reported cost-effectiveness.

Cost-effectiveness.

The TADS and the ADAPT trials also addressed cost-effectiveness. At the end of 12 weeks these two trials found that fluoxetine was the most cost-effective treatment modality (Domino et al., 2008; Goodyer et al., 2008; Goodyer et al., 2007). This cost-effectiveness continued for the duration of the ADAPT trial (Goodyer et al., 2008; Goodyer et al., 2007), but in TADS, this changed at 36 weeks. At this time, results favored combination therapy because patients, taking fluoxetine, without CBT, had the highest cost for psychiatric emergency room visits and hospitalizations. No differences in cost-effectiveness were found between CBT and fluoxetine monotherapy (Domino et al., 2009).

The above studies include adequate sample sizes. However, three other randomized trials with a sample size of less than 100 subjects also addressed the use of combination treatment.

Other Studies Using Combination Treatment

In one study, groups of adolescents receiving CBT, sertraline (SERT) and combination treatment all had high consumer satisfactions, but the participants who also received CBT had higher levels of skill acquisition than the patients treated with only sertraline (Dudley, Melvin,

Williams, Tonge, & King, 2005). Combination treatment has also been linked to less risk of relapsing to depression (Kennard et al., 2009). In contrast to these studies favoring COMB, another study reported that combination treatment was not superior to medication management or to CBT in a sample of 73 adolescents. This study also reported that in cases of mild to moderate depression, CBT is the most effective treatment modality (Melvin, Tonge, King, Heyne, Gordon, & Klinkeit, 2006). Combination treatment is also offered in primary care settings. Two articles were found in the literature search involving combination treatment in primary care.

Combination treatment in primary care.

A study conducted in primary care, the Youth Partners in Care Program, with a sample size of 418 participants, exhibited a statistically significant improvement in depressive symptoms and an improvement in quality of life in patients receiving Combination treatment when compared patients receiving usual care. There was also a decline in suicide attempts in both groups (Asarnow, Jaycox, Duan, LaBorde & Rea 2005). However, a follow-up study of this intervention found that the effect achieved after six months of treatment, was not statistically significant at 18-month follow-up (Asarnow, Jaycox, Duan, LaBorde & Rea, 2009).

In another study, the use of combination treatment in primary care reported that there was only weak evidence for the effectiveness of combination treatment. Authors credit that these results could have been influenced by the reduced number of CBT sessions received by the adolescents. They received a total of 5-9 sessions, while during TADS, the protocol, included 15 sessions during the acute phase (Clarke, Debar, Lynch, Powell, & Gale, 2005).

In addition to individual studies, a guideline and an algorithm, using a combination approach, are also part of this practice inquiry. These two documents endorse the use of combination treatment (Cheung et al., 2007; Hughes et al., 2007).

Guideline for the Treatment of Adolescent Depression

This guideline addresses the treatment of adolescent depression in primary care (Cheung, et al., 2007). In the case of primary care settings, psychotherapy, CBT and interpersonal therapy (IPT) are considered the first line of treatment for mild to moderate depression. However, the use of combination treatment, antidepressant medications, SSRIs plus psychotherapy, is also recommended in primary care (Cheung et al., 2007).

The Texas Children's Medication Algorithm

The purpose of this algorithm is to provide guidance to mental health specialists on determining the best treatment option for adolescents and their families (Hughes et al., 2007). The Texas Children's Medication Algorithm also recommends the use of cognitive behavioral therapy and interpersonal therapy for cases of mild to moderate depression. However, in cases when a patient is taking antidepressants, it is recommended that clinicians should evaluate for the addition of psychotherapy if the patient is not achieving treatment goals during any stage of treatment (Hughes et al., 2007).

Weight-of-Evidence Classification Schema (Combination)

The use of combination treatment was found to be an effective and safe treatment for adolescent depression. According to the ONS/PEP *Weight-of- Evidence Classification Schema*, the use of combination treatment has enough evidence to recommend its use for practice in adolescents suffering from depression in a variety of settings, including in primary care.

In addition to psychotherapy, medication management and combination treatment, other types of interventions have also been studied. The results for other types of interventions are presented in the following section.

Results for Other Types of Interventions

Even though other types of interventions might not be commonly employed, they remain an option for mental health specialists and for patients and their families. Among these interventions are the use of physical activity, complementary and alternative medicine, repetitive transcranial magnetic stimulation and electro convulsive therapy.

Physical Activity

Among the approaches used to increase physical activity are dance movement therapy (DMT) and jogging. Table 7 presents the results for physical activity. Three studies were found on physical activity on adolescent females. The first two studies include sample sizes of less than 100 subjects and examine the effects of physical activity on neurohormones. The first study used DMT, and the subjects, who participated in the intervention, displayed decreased depression, increased levels of serotonin and decreased dopamine; however, there were no significant changes in cortisol levels (Jeong, Hong, Lee, & Park, 2005).

The second trial included jogging. Authors found that mild level of jogging not only lowered levels of depression, but it also decreased the levels of cortisol and epinephrine levels (Nabkasorn et al., 2006).

The third study was part of the Trial of Activity for Adolescent Girls (TAGG), a randomized, multicenter trial (involving 36 schools) to evaluate the benefits of physical activity on heart disease. To conduct the present study, researchers evaluated 1397 girls in three cross-sectional measurements of depressive symptoms and physical activity. Authors concluded that

no significant association between depression and physical activity was observed in this study; however, the levels of physical activity in these girls were found to be lower than the current public health recommendations of 60 minutes of moderate to vigorous physical activity a day (Johnson et al., 2008).

Weight-of-Evidence Classification Schema (Physical Activity)

Even though the number of studies examining the relationship of physical activity to symptoms of depressions is limited, the results presented in this practice inquiry are supportive of this treatment modality. According to the ONS/PEP *Weight-of-Evidence Classification Schema*, this intervention is likely to be effective.

Complementary and Self-Help Treatments

Table 8 displays the results for this section. For example, a systematic review in children and adolescents found that results for Omega 3 fatty acids, light therapy and massage appear to show some benefit (Jorm et al., 2006). Authors also reviewed "psychological or lifestyle treatments." such as art therapy, bibliotherapy, distraction technique and relaxation therapy, but not enough evidence was found to support these modalities. Authors also reported that treatment with St. John's Wort could be effective in decreasing symptoms of depression, but they did not elaborate on this finding (Jorm et al., 2006).

A second study, an open label trial, evaluated the efficacy and safety of St. John's Wort (SJW), with an ending sample of 11 subjects. In this trial, authors reported that nine of the patients had a significant change in the Clinical Global Improvement scale (Simeon, Nixon, Millin, Jovanovic, & Walker, 2005).

Weight-of-Evidence Classification Schema (Complementary)

Since the evidence presented for complementary and self-help treatments consist of scarce, not well controlled studies with a small sample size, according to the ONS/PEP *Weight-of-Evidence Classification Schema*, it is concluded that the effectiveness for these types of interventions is not well established.

Repetitive Transcranial Magnetic Stimulation (rTMs)

Table 9 contains the two studies found for rTMs. One small trial and a case study involving the treatment for adolescents with resistant depression with rTMS were found. The first study had a sample of nine subjects. This study reported a significant decrease in depression levels at days seven through ten and these positive effects continued one month after finishing treatment. However, suicide ideation did not change with rTMS therapy (Bloch et al., 2008). The second study included two subjects. According to authors, the depression scores improved for both subjects and their symptoms of depression decreased (Loo, McFarquhar, & Walter, 2006).

Regarding memory test results, both studies report subjects did not suffer any change in their cognitive abilities (Bloch et al., 2008 ; Loo et al., 2006). In addition, the benefit of rTMs had persisted for three and four months after the treatment had ended in the second study (Loo et al., 2006).

Weight-of-Evidence Classification Schema (rTMs)

The evidence presented for rTMs is not considered rigorous because of the lack of randomized controlled trials. Also, the two studies included are of small sample size. In the first study, the sample size was 9 and the second study only had 2 subjects. Thus, the evidence presented is insufficient and following the ONS/PEP *Weight-of-Evidence Classification Schema*, it is concluded that the effectiveness for rTMs is not well established.

Electroconvulsive Therapy (ECT)

The evidence found for the use of ECT is presented in Table 10. The American Academy of Child and Adolescent Psychiatry (AACAP, 2005) recommends the use of ECT only for cases of severe, disabling and life-threatening symptoms, such as increased suicidality, refusal to eat or drink, extreme mania and psychotic symptoms. Patients also must have failed at least two trials of pharmacological agents in conjunction with other treatment modalities, such as psychotherapy, prior to considering ECT.

A literature review conducted by AACAP including 60 studies, with sample sizes ranging from 11 to 45 subjects, found a response rate of 60 – 100% among all these studies (Ghaziuddin et al., 2004). Adverse events reported included difficulty learning new material, seizures and the risks associated with general anesthesia. Because of the serious side effects involved, some clinicians still consider ECT to be an unethical and a controversial treatment; however, it has been documented that, at 8.5 ± 4.9 months after the last treatment, participants had completely recovered and had returned to their cognitive pre-ECT baseline (Ghaziuddin et al., 2004).

Authors concluded that ECT is an effective treatment during periods of high acuity, but it will not prevent relapse. At the time this article was written, there were no specific guidelines regarding the use maintenance ECT in adolescents; however, researchers advised for adolescents to be placed in a maintenance schedule to maintain treatment response (Ghaziuddin et al., 2004).

Weight-of-Evidence Classification Schema (ECT)

ECT is considered to be a safe and effective treatment for adolescent depression. However, based on the side effects discussed, as well as the risk involved with general anesthesia, following the ONS/PEP *Weight-of-Evidence Classification Schema*, it is concluded that benefits need to be balanced with harms prior to considering ECT.

The treatment modalities presented under Other Types of Interventions include the use of physical activity, complementary and self-help treatments, rTMs and ECT. Based on the ONS/ PEP *Weight-of-Evidence Classification Schema*, it is determined that physical activity is likely to be effective; while the effectiveness for complementary and self-help treatments and rTMS was not well established. In addition, when considering ECT, benefit needs to be balanced with harms.

The results presented provided the foundation for a guideline. The recommendations for practice in this guideline are made following the ONS/PEP *Weight-of-Evidence Classification Schema*.

Guideline for the Treatment of Unipolar Depression in Adolescents

The following practice guideline was developed based on the evidence found in the literature. It includes recommendations for practice for screening, and for the treatment of mild, moderate and severe depression.

Screening

It is recommended that primary care providers screen adolescents, 12 to 18 years old, only when there is a system in place for diagnosis, treatment and follow-up. Adolescents should especially be screened when they are positive for parental depression, comorbid mental health disorders, chronic physical health problems, and a history of having experienced a recent negative event (Raphael, 2009; USPSTF, 2009).

Two screening methods are recommended. The Patient Health Questionnaire for adolescents and the Beck Depression Inventory-Primary Care Version are the scales with the most evidence for the primary care setting (Raphael, 2009; USPSTF, 2009).

Mild to Moderate Depression

The interventions with the most supportive evidence for mild to moderate depression are cognitive behavioral therapy and interpersonal psychotherapy (Cheung et al., 2007; Hughes et al., 2007; Melvin et al., 2006).

Moderate to Severe Depression

Combined treatment had the most supporting evidence for moderate to severe depression. Combined treatment includes the use of antidepressants plus cognitive behavioral therapy. Even though the addition of CBT may decrease suicidal ideation and behaviors, antidepressants have a black box warning. The FDA has issued an antidepressant protocol to be used when an adolescent is prescribed an antidepressant (Cheung, et al., 2007; Emslie et al., 2006).

FDA Antidepressant Protocol

Mental health specialists must assess for clinical worsening, suicidality and behavioral changes during face-to face visits. These assessments should take place weekly for the first four weeks, followed by every other week for one month, and at 12 weeks (Cheung, et al., 2007; Emslie et al., 2006). However, adolescents should be assessed for suicidal ideation at every visit (Bridge et al., 2007; Cheung et al., 2005; Dubicka et al., 2006; Hammard et al., 2006).

Moderate to Severe Depression

If combined treatment is not an option because psychotherapy is not available, monotherapy with antidepressants is recommended with the implementation of the FDA antidepressant protocol (Asarnow et al., 2009). The antidepressants recommended, with or without psychotherapy are: 1) Fluoxetine, FDA approved since 2003, for the treatment of depression in children and adolescents. This antidepressant should be used first because it had the most supporting evidence (Hammard et al., 2006; Huges et al., 2007; Moreno et al., 2006); 2)

escitalopram was FDA approved in 2009 for the treatment of adolescents with depression, ages 13 to 17 (Findling et al., 2008; Hitt, 2009); and 3) citalopram and sertraline are considered second line options (Birmaher et al, 2007; Hughes et al., 2007; Posner et al, 2007)

Summary

Chapter 3 presented the results for psychotherapy, pharmacological management, combination treatment and for other types of interventions in the treatment of adolescent depression. After the results were reviewed, it was determined that, following the recommendations by the ONS/PEP *Weight-of-Evidence Classification Schema*, CBT and IPT are found to be recommended for practice; while ST interventions and other psychotherapy approaches are likely to be effective in practice. The use of pharmacological management and combination treatment are recommended for practice. For other types of interventions, physical activity is found likely to be effective in practice. The use of complementary and self-help treatment and rTMs were not well established. Finally, in the case of ECT, benefit needs to be balanced with harms.

Chapter 3 presented the results of the articles that are displayed on the different tables and recommendations for practice are made. Chapter 4 discusses the implications, the limitations, the need for future research and the conclusions of this synthesis of the literature on the treatment of adolescents with depression.

CHAPTER FOUR: IMPLICATIONS

All articles included in this practice inquiry document the need for the treatment of depression in adolescents (Birmaher, et al., 2007). If left untreated, depression not only affects the individual, and their families, but it also raises health care costs (Kuyken et al., 2006; Lynch et al., 2005). Untreated depression also impacts the future of the adolescents suffering from it since it profoundly affects all aspects of their lives (Lewis, 2002; Lynch, 2005; Melin, 2002). School performance, relationships with peers and parents and physical health can be affected if depression is not addressed (Byford et al., 2007; Lewis, 2002). In addition, untreated depression in adolescents has been linked to substance abuse, pregnancy, early parenthood, adult depression, suicidal ideation and suicide attempts (Meredith et al., 2009).

In order for adolescents to receive appropriate care, parents, teachers and primary care providers should be aware of the prevalence of depression in adolescents and of the need to screen, diagnose and treat this mental health problem (United States Preventive Services Task Force, 2009). In addition, primary care providers must know when to refer patients to mental health specialists (Raphael, 2009; Williams et al., 2009), such as doctor of nursing practice psychiatric and mental health providers. Thus, mental health specialists must have the knowledge for providing treatments based on evidence-based practice to their patients and their families.

Recommendations for Practice

Psychotherapy

Cognitive behavioral therapy and interpersonal psychotherapy are effective in the management of depression in adolescents in individual, family, in group approaches, and in school settings. The use of psychotherapy is considered the first approach in cases of mild depression to moderate depression (Cheung et al., 2007; Hughes et al., 2007; Melvin et al.,

2006). However, CBT has shown only a "modest" effect in acute cases (Klein, 2007). In TADS, the treatment response tended to be slower for CBT, but this treatment modality was as effective as combined treatment and fluoxetine monotherapy at the end of weeks 18 and 36 (Rohde et al., 2008). However, rapid response to treatment is crucial in cases of moderate to severe depression.

Pharmacological Management

The highest level of evidence was found for the use of selective serotonin reuptake inhibitors (SSRI's), specifically for the use of fluoxetine (Cheung et al., 2005; Hetrick et al., 2007; March et al., 2004; Moreno et al., 2006; Usala et al., 2008). Fluoxetine is FDA approved for the use in the treatment of depression in children and adolescents (Hammard et al., 2006), and escitalopram is now also FDA approved for the treatment of adolescents with depression (Findling et al., 2008; Hitt, 2009). Other SSRI's, citalopram and sertraline, are considered second line options (Hugues et al. 2007; Posner & Birmaher, 2007) even though they are not FDA approved.

Since there is a warning about a possible emergence of suicide ideation in behavior in patients taking antidepressant medications, it is recommended to assess for these symptoms at baseline and at every visit (Bridge et al., 2007; Cheung et al., 2005; Dubicka et al., 2006; Hammad et al., 2006). In addition, the FDA protocol recommends observing for clinical worsening, suicidality and behavioral changes during weekly for the first four weeks of treatment, then every other week for one month, and at 12 weeks (Emslie et al., 2006).

Combination Treatment

Newer studies support the use of combined treatment over monotherapy with psychotherapy or with antidepressant medications for the treatment of moderate to severe depression. For example, the benefit of two large studies, TADS (March et al., 2004; Vitiello et

al., 2006) and TORDIA (Asarnow et al., 2009) supported the use of combined treatment (medication plus psychotherapy). In addition, in the United Kingdom, the use combination treatment is the only recommended treatment for adolescents with moderate to severe depression (Byford et al., 2007).

Because of inaccessibility and high cost of psychotherapy, SSRIs are usually the first used alternative and, even though adding CBT to antidepressants might be beneficial in patients not responding to treatment, there are instances in which medication monotherapy could be as effective as combination treatment (Asarnow et al., 2009). Thus, the use of combined treatment has also been found safer due to a protective effect provided by CBT to decrease suicidal ideation and behavior (March et al., 2007).

Although other interventions were found likely to be effective, they are not recommended in this practice inquiry without additional research.

Limitations

The limitations of this practice inquiry are related to the quality of the studies reviewed. One of the most important observations made was the lack of RCT's in the adolescent population (Hughes et al, 2007). Researchers also found that conducting meta-analysis and systematic reviews were difficult because of the lack of methodological consistency (Dubicka et al., 2006). For example, when examining the incidence of suicidality in trials, different methodologies also influenced results since some studies did not distinguish between self-harm, suicidal thoughts and suicidal attempts (Dubicka, et al., 2006; Hammard et al., 2006; Posner et al., 2007). There was also a lack of consistency when reporting efficacy because researchers reported that studies used different criteria to define response and remission (Hetrick et al., 2007; Kennard, 2006; Moreno et al., 2006). Also, side effects were reported differently (Emslie et al., 2006).

Researchers also report that studies of small sample size and of limited rigor could hinder results (Cuipjers et al., 2006). For example, sample size was also a limitation for other authors to determine intervention effects (Donaldson et al., 2005; Hammard et al., 2006; Heiligenstein et al., 2006; Lewis et al., 2009; Trowell, 2007).

Other limitations found include lack of consistency in studies carried out in multiple sites (Berard, et al., 2006; Emslie et al., 2006; Von Knorring et al., 2006), high attrition problems (Hetrick et al., 2007; Miller, 2008), and a high response to placebo could alter the results (Cohen, et al., 2008; Donnelly et al., 2006;. Emslie et al, 2006). Other researchers indicated the lack of a placebo group (Kennard et al., 2008; Rynn, 2006; Trowell 2007 ; Goodyer et al., 2007; March et al., 2009; Melvin, 2006). The lack of blinding was also a limitation in the Waddell et al., 2007 study.

Authors also indicated that the short duration of trials might not allow determining efficacy and/or side effects (Papanikolau, 2006). In cases of psychotherapy, researchers were concerned about the different levels of skill in the staff delivering the intervention (Horowitz et al, 2007; Weisz, 2009).

Researchers also reported difficulty in determining the efficacy of interventions. For instance, Berard et al. (2006) used a scale that has not been validated in adolescents with major depression. In addition, some studies include children and adolescents and most of them did not analyze results separately for these two groups (Bridge et al., 2007; Cuipjers et al., 2006; Emslie et al., 2008; Emslie et al., 2007; Emslie et al., 2006; Heilingstein et al., 2006; Hetrick, et al., 2007; Stice et al., 2009; Watanabe et al., 2007; Weisz et al., 2006). For example, Watanabe et al. (2007) separated results for children and adolescents receiving psychotherapy and found a significant effect for adolescents, but not for children.

Emergent suicidality is a concern when using pharmacological approaches. The results found on the incidence of suicidality in the studies reviewed might be limited. For example, when reviewing the incidence of suicidality, the subjects included were ages six to 17 (Posner et al., 2007). Also, the incidence for major depressive disorder could be higher than reported in some antidepressant trials. It is known that subjects with major depression are at higher risk for suicide (Centers for Disease Control, 2008). However, when determining the rate of suicidality, studies have included both children and adolescents taking antidepressant medications, and reviews have included studies that included not only major depressive disorder, but also participants with other disorders, such as obsessive compulsive disorder and attention deficit hyperactivity disorder (Posner, et al., 2007).

Need for Future Research

Further research is needed, using rigorous methodological approaches and instruments, to address the use of psychotherapy, pharmacological management, combination treatment, other treatment modalities and the implementation of EBP. These interventions have the potential of devising new treatment modalities that will improve the life of adolescents, their families and their communities.

Psychotherapy

Future research is needed to study how to make psychotherapy more accessible since this treatment modality is difficult to obtain because of the lack of providers and also because of its associated costs. Further studies on group therapy and on psychotherapy in schools might help more adolescents obtain this treatment modality at a lower cost. For example, in a study by Rosello et al., (2008) group therapy was almost as effective as individual therapy. Also, trials involving the most effective modalities to deliver psychotherapy to groups of adolescents should

be explored as a way of providing this intervention to a large group of adolescents since psychotherapy delivered in school settings has been proved to be effective in preventing and treating symptoms of depression (Cuijpers, et al., 2006; Horowitz, 2006; Shetfield et al., 2006; Spence et al., 2005). In addition to psychotherapy, the use of newer pharmacological approaches could provide relief for adolescent depression.

Pharmacological Management

Research addressing pharmacological approaches to target the stage of brain development in adolescents, rates of medication metabolism, pharmokinetics and toxicity in this population are needed (Moreno et al., 2006). Newer approaches are also required since, even when subjects respond to antidepressant medications, 30-40% still suffer from subsyndromal symptoms (Moreno et al., 2006), and also because of the link between increased suicidality and antidepressants.

Pharmacological approaches used with children and adolescents were first designed for adults, and there is a need for antidepressant medications that are developed to fit their biological needs. The differences found in children and adolescents when using antidepressant medications are not only related to their psychological development, but also to their physical development. For example, researchers have reported that, in children and adolescents, SSRI medications are effective because the serotonergic neurotransmitter system is similar to an adult by ages five or six, while the noradrenergic system, where TCA's and the SNRI's supposedly work, are not completely built until adulthood (Hazell et al., 2009; Moreno, et al., 2006).

Longitudinal studies involving the treatment of adolescent depression are needed to understand long term effects of antidepressants in adolescents (Hazell et al., 2009). For example, researchers have expressed concerns because short term studies are not designed to identify side

effects, such as the emergence of manic symptoms or the long-term effect of antidepressants in mood. For instance, excess of serotonin in the brain has been associated with emotional problems in adulthood (Papanikolau et al., 2006). Longitudinal trials would also help determine the safety and efficacy of maintenance treatment since, at this time, only adult studies exist on this topic (Hughes et al., 2007).

In addition to psychotherapy and pharmacological management, researcher involving other approaches has been planned for adults, but this type of research is also needed in adolescents. It has been documented that, in adults, one in five patients need more than one treatment approach to respond to treatment and that only 50% of these patients are considered remitters (Garcia-Toro et al., 2010). To address this need, other interventions: Exercise, diet, sunlight exposure and sleep-control will be examined, as an adjunctive treatment for depression in adults, in a future trial by Garcia-Toro et al., (2010).

Exercise was chosen since regular moderate physical activity has shown to produce antidepressant effects (Garcia-Toro, 2010). Authors also included diet because a Mediterranean diet, containing vegetables and fish, and the addition of vitamins and omega acids, have been found to be helpful in the prevention and treatment of depression. In addition, the use of sunlight exposure will be studied because this treatment has been found to have a positive effect in seasonal and in non-seasonal depression. Lastly, authors will include sleep control because of the associations between decreased quality and quantity of sleep, and increased depression (Garcia-Toro, 2010).

In addition to studies including psychotherapy, pharmacological, and other adjunctive possibilities, such as exercise, diet, sunlight exposure and sleep-control, future research is also needed to address the use of EBP in the delivery of care for children and adolescents. Because

most of this population depends on their families and in other entities to obtain treatment, the use of research using evidence-based practice taking into consideration different systems has been proposed to facilitate the process of determining the best treatment modality for adolescents (Kazak, Hoagwood, Weisz, Hood, Kratochvil, Vargas & Banez, 2010).

Evidence-Based Practice (EBP)

Research for evidence-based practice from a meta-systems approach is currently being planned by Kazak et al., 2010. The gap between the care patients receive and current research recommendations has been recognized; as well as, the need for a more efficient coordination of care for children and adolescents who receive treatment from different facilities. This proposed meta-systems approach includes first the children and their families, school systems, pediatric health care systems, specialty mental health systems, juvenile justice systems, child protection systems and substance abuse systems (Kazak et al., 2010).

Kazak et al., (2010) report that the use of EBP for children differs from adults because evidence-based treatment in children needs to align with the child's developmental stage. Children need to be evaluated as the child grows to address their social, emotional and behavioral growth. Next, the child's family is considered a key component because families will decide whether or not a child will receive mental health treatment based on their resources, culture, beliefs, stressors and resiliencies (Kazak et al., 2010).

Schools are also part of this framework because of the amount of time children spend at these facilities and also because family members may also participate in school activities. Pediatric health care systems are included since primary care clinicians might be the first ones to identify behavioral health problems. Researchers also indentified specialty mental health systems as part of facilitating the use of EBP. These systems include the child welfare system (foster care

and adoptive services), substance abuse, general health and the juvenile justice system (Kazak et al., 2010). In summary, research including not only established treatment modalities, but also research in new interventions and in EBP can benefit the treatment of adolescents.

Conclusions

The purpose of the practice inquiry was to conduct a critical review and synthesis of the literature on evidence-based treatment of unipolar depression and to make recommendations for practice. Adolescent depression can remain undetected and the lack of treatment can have devastating effects in the lives of adolescents and their families (Birmaher et al., 2006). Parents, teachers and mental health specialists may benefit from the information provided in this practice inquiry to learn about adolescent depression and also educate adolescents and their families about their options for treatment. Informed adolescents and families will be more likely to follow up a treatment plan they agree on and feel comfortable with. Compliance with treatment of depression is important because it will allow adolescents to reach their full potential in a safe manner while improving relationships with their families, peers and communities. Doctor of nursing practice professionals are prepared to educate adolescents and their families about options to manage depression and also to provide evidence-based recommendations for the treatment of depression taking into consideration the needs and preferences of the adolescents and their families.

TABLE 1

INTERVENTIONS FOR THE TREATMENT OF DEPRESSION IN ADOLESCENTS –

PSYCHOTHERAPY –

COGNITIVE BEHAVIORAL THERAPY (CBT)

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY – Cognitive Behavioral Therapy (CBT)						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Bridge, J.A., Barbe, R.P., Birmaher, B., Kolko, D., & Brent, D.A. (2005). Emergent Suicidality in a Clinical Psychotherapy Trail for Adolescent Depression.	The purpose of this study was to examine the incidence and predictors of emergent suicidality during a psychotherapy trial for depressed adolescents. This study focuses in the active phase which consisted of 12 to 16 sessions of weekly psychotherapy. The outcome variable was the emergence of suicidality. Researchers also had a booster phase, during which patient received 2 to 4 monthly therapy sessions.	Sample consisted of 88 adolescents who denied suicidality, during an interview, at the time of intake. In order to participate, subjects had to be fee from taking psychotropic medications, ages 13 to 18 with a DSM-III diagnosis of major depressive disorder with a baseline Beck Depression Inventory (BID) of ≥ 13. Intervention consisted of 12 to 16 weeks of psychotherapy. (75%) of the subjects were female. Subjects were randomly assigned to three treatment arms: cognitive behavioral therapy, systemic behavioral family therapy or nondirective supportive therapy.	For the interview, adolescents were evaluated with the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) and the Suicide Circumstances Schedule, a semi-structured interview to assess for the precipitants, suicidal intent, and lethality of a previous suicidal episode.	There were no completed suicides during this trial, but out of the 88 patients, who denied suicidality during an interview at baseline, 11 (12.5%) develop suicidality during treatment. 10 of these subjects develop suicidal ideation and one made a suicide attempt. Eight of these incidents took place within three weeks of starting this study. 10 of these patients had marked Item 9 in the BID reporting thoughts of wanting to kill themselves prior to starting treatment.	The incidence of suicidality was the same for this trial, which included only psychotherapy, as for trials using pharmacotherapy. Researchers recommend the use of specific and systematic assessment to detect suicidality at baseline since previous studies have relied only on patients reporting adverse events or on the observation by study investigators. In this study, self-reported suicidal thoughts at baseline, marking Item 9 on the BID, were better predictors of emergent suicidality than interview-rated suicidality, type of treatment received, cognitive distortions and degree of depression.	In October 15, 2004, the FDA issued a black box warning regarding the increased risk of suicidal thinking and behavior in children and adolescents who are prescribed antidepressant medications. **Level of Evidence** Recommended for practice **I** (3) - Randomized trial with < 100 sample size.

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY/Schools -CBT/Schools						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Cuijpers, P., Van Straten, A. Smits, N., & Smit, F. (2006) Screening and early psychological intervention for depression in schools: a systematic review and meta-analysis	Researchers conducted a meta-analysis by first searching Pubmed, PsychINFO, Embase and the Cochrane Central Register of Controlled Trials from 1966 to 2005. Eight studies met inclusion criteria. These studies examined the effect of screening and the early treatment of depression in school settings. Six studies used cognitive behavior therapy (CBT) and two relaxation training.	Authors included randomized controlled trials only. 413 subjects were included. They were between the ages of 7 and 19. Subjects participated in 6 to 8 sessions. Only two studies included follow-up at longer than three months (follow-up was not included in this meta-analysis. Authors estimated effect sizes by comparing pre and post test scores. Another purpose for this score was to find out the numbers need to treat (in this case the number of students that needed to be screened to generate one case of depression treated with success.	The Children's Depression Inventory (CDI) was used in five studies as a screening instrument, while the Reynolds Adolescent Depression Scale (RADS) was used in three studies (one trial used both the CDI and the RADS).	The mean effect size was 0.55 (95% CI: 0.35–0.76). This mean effect size can be considered "moderate to high". The 'numbers-needed-to-screen' was 31 (95% CI: 27–32), Drop-out rate was at 21% in the studies included.	Even though researchers recognize that screening and eerily intervention are effective, they recognize that there are concerns about this type intervention need to be addressed prior to implementing these interventions on a routine basis, such as possible negative effects. For example, a screening tool may indicate that a subject is depressed equivocally and this may lead to unnecessary stigmatization. Other areas that need to be explores are the cost-effectiveness of the intervention and more research is needed to determine long-term effects. The number of studies in this meta-analysis was small and their quality was described as "limited." Concealment strategies were not explained in the studies using a waiting list control group Also, assessors were only blinded in three studies. It was not clear if the results in this meta-analysis were due to the intervention or if it was because the subjects were not suffering from clinical depression. Only one study used an interview to determine if the subjects were depressed. The other trials used a self-rating tool.	**Level of Evidence**: Recommended for practice **I** (1) - Systematic Review and meta-analysis of RCT's.

Interventions for the Treatment of Depression in Adolescents – PSYCHOTHERAPY - CBT						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Garber, J., Clarke, G.N., Weersing, R., Beardslee, W.R., Brent, D.A., Gladstone, T. R., . . . , Yyengar, S. (2009). Prevention of Depression in At-Risk Adolescents: A Randomized Trial.	4-site, multicenter Randomized-controlled trial comparing Cognitive behavioral (CB) to "usual care." CB was a prevention program consisting of 8 week-sessions lasting 90-min. followed by 6 monthly sessions. Usual care was mental health or other health care services the youth was involved with prior to the study. 159 subjects were randomized to the CB Group and 157 to "usual care."	316 adolescents, ages 13-17 years, recruited from Aug/2003 to Fe/2006. Admission Criteria: Participants were required to have had a history of depression, but they needed to be in remission for at least 2 months., and/or current subthreshold depression determined by an entry score of 20 or higher in the Center for Epidemiological Studies Depression Scale (CES-D). Also, to be included, one parent or caretaker had to have had a major depressive episode in the past 3 years or 3 or more episodes of major depression or dysthymia during the participant's lifetime.	Longitudinal Interval Follow-up Evaluation (LIFE) Structural Clinical Interview for DSM-IV Axis I Disorders (SCID-I) The Schedule for Affective Disorders and Schizophrenia for School-Age Children, Epidemiological Version (K-SADS) was taken by child and caregivers to determine the subject's diagnoses according to the DSM-IV. Child and Adolescent Service Assessment (CASA).	After the 6-month f/u, the rate and hazard ratio of depressive episodes was lower for the adolescents in the CB group, and the subjects in this group also had less self-reported symptoms. Baseline depression in parents affected the results of some results. Adolescents whose parents were currently depressed CB was not more effective than the "usual care" intervention in preventing onset of depression In Adolescents whose parents were not actively depressed. CB prevention program prevented onset of depression more effectively than usual care.	Sample was middle class with access to health insurance. Training: Most evaluators had a mental health master's degree; only three had a bachelor's degree. Evaluators received training about all the measures used. 15% of the interviews were rerated.	Authors recommend more studies with a diversity of economic and ethnic backgrounds since it is already known that CB is effective in participants of higher incomes. Authors state that this study proves that the use of CB can be generalized to different settings. It is also important to note that CB can reduce future depressive episode. as seen in this study in the group of children receiving CB whose parents were not actively depressed. The preventive effect of the CB program had a similar response as treatment with medications. **Level of Evidence** Recommended for practice **I** (2) - Well-controlled, randomized clinical trial with adequate sample size.

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY - CBT & IPT						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Horowitz, J.L., Garber, J., Ciesla, J. G. Young, J. F., & Mufson, L. (2007). Prevention of depressive symptoms in adolescents: a randomized trial of cognitive-behavioral and interpersonal prevention programs.	Researchers examined the efficacy of two psychotherapy approaches: Cognitive Behavioral Therapy (CB) and Interpersonal Therapy-Adolescent skills training (IPT-AST) for the prevention of depressive symptoms in adolescents. and compared them to a No Intervention (Control Group).	380 students attending wellness classes in three high schools were enrolled. The average age was 14.43 years. 94% of them were freshmen and 54% were female. Subjects were 79% Caucasian, 13% African American, 2% Latino, 1% Asian, 1% Native American, and 3% of mixed ethnicity. Students were randomly assigned to 3 groups n= 112 students were allocated to CB, n= 99 to IPT (AST) and n=169 in the No Intervention groups. Participants were divided into 9 groups to receive CBT and IPT (AST). These two interventions were provided once a week in 90-min. sessions.	Subjects were evaluated at baseline, post intervention and tat 6 month follow-up Outcome measurements: Children's Depression Inventory (CDI). Center for Epidemiologic al Studies Depression scale (CES–D). Sociotropy–Achievement Scale for Children (SASC): to test affiliation and achievement orientation. Children's Attributional Style Questionnaire (CASQ–R) – lower scores reflect poorer attributional style.	At post-intervention, there was a small effect for CB (d=0.37) and IPT-AST (d=0.26). When taking into consideration the levels of depression among the intervention groups, the "high risk" subjects, because of their elevated depressive symptoms, had strong effects when compared to the No Intervention Group: CB (d=0.89) and IPT-AST (d=0.84). These results were not detected at 6 month follow-up. No differences were found in results for boys and girls. Increased depression was present in the No Intervention Group post-intervention, but not at follow-up.	Limitations, reported by researchers, included that the interventions were done by teachers, and not by outside providers. Students might have felt uncomfortable discussing their personal problems. Also, part of IPT-AST included pre-group sessions, and this was not carried out. Thus interfering with the students' ability to discuss their specific concerns. Another possible limitation was that students reported fewer symptoms because they knew they were receiving an intervention. The researchers explained the reduced in depressive symptoms at 6-month follow-up by explaining that the students with the highest post-intervention scores also had increased attrition rates. Authors stated that due to the large number of participants, diagnostic interviews were not conducted; instead, symptoms were used as an outcome. Researchers reported that subclinical depressive symptoms are predictors of subsequent depressive disorders.	Even though universal programs are associated with less stigma, selective depression programs produce a higher effect size than universal interventions possibly because universal interventions require large sample sizes. **Level of Evidence** Recommended for practice **I** (2) - Well-controlled, randomized clinical trial with adequate sample size.

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY - Schools						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Horowitz, J. L. & Garber, J. (2006). The prevention of depressive symptoms in children and adolescents: a meta-analytic review.	This meta-analysis included 30 studies addressing the prevention of depression in children and adolescents in schools. Studies were obtained from a computer search of PsycINFO since its beginning, as well as from other sources, such as dissertations, from references found in studies, and from a manual search, starting in 1971, of all the journals that had published any of the chosen studies.	Inclusion criteria were: Studies had to address the prevention of depressive symptoms or other depressive disorders. Subjects had to be randomly assigned to a treatment or to a placebo group. Studies had to have used an accepted outcome measurement, and the subjects had to be under age 21. In this meta-analysis, the mean ages varied between 6. 3 and 15.4 years old. Number of subjects were between n=41 to n=1500. Interventions included: education, behavioral training, problem solving, and anxiety management. The aim of some studies was to improve interpersonal relationships and social skills. Some used lectures and videotapes as teaching tools.	Effect sizes were calculated.	Effect sizes post intervention and at 6 month-follow up showed small to moderate effects in selective and indicated prevention programs. Positive effect sizes indicate a decrease in symptoms. Six of the 30 studies indicated negative results. Greater effect sizes were found in older participants and with higher number of females. Clinical site, the number of months after follow-up or the number of sessions received did not affect results.	Universal interventions are conducted in school presentations to large groups. This type of intervention is linked to a decrease in stigma and to lower drop-out rates. Selective interventions are usually delivered in small groups and it targets family stressors, such as divorce, parental death, parental depression and parental alcoholism. Indicated interventions are designed for the individuals who already have signs and symptoms of depression.	Selective and indicated treatments had higher effect sizes than universal programs. Based on the results of this meta-analysis, researchers found that it is premature to no longer use universal programs, but at the same time, focusing in populations at high risk for developing depression might be more helpful. **Level of Evidence** Recommended for practice **I**(1) Meta-analysis of multiple well-designed, randomized, controlled clinical trials

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY - CBT						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Klein, Rachel, Jacobs, & Reinecke, (2007) Cognitive-behavioral therapy for adolescent depression: a meta-analytic investigation of changes in effect-size estimates	A meta-analysis which included a literature review from January 1980 to September 2006. Medical and psychological databases, such as Psych INFO and Medline were used. The words guiding this search were depression, dysthymia and major depression and limited to youth populations. The studies included were limited to subjects with diagnoses of depressive disorders according to the DSM-III or later, the Research Diagnostic Criteria or the Bellevue Index of Depression. Studies had to have a CBT group and a control or alternative psychotherapy group. Inclusion criteria for the studies also included reported pre and posttests for both groups. Studies had to be written in English.	There were 809 subjects from 11 RCTS. The population included students, outpatients, and youths in the juvenile justice system. Mean age ranged from 12.7 to 16.2 years, and the hours of received treatment average 17.60 hours.	The CONSORT (Consolidated Standards of Reporting Trials) criteria for the reporting of RCTs was used as an index of methodological rigor. The studies included met 17 of the 22 criteria established by the CONSORT committee. Studies ranged from 14 to 21 CONSORT criteria points. To deter power, a retrospective power analysis was conducted. Cohen's effect size was used to detect ES differences (small=0.2, medium 0.5 and large 0.8). To calculate if the ES (Effect size) for each study was statistically different from zero, the researchers used z tests. The z tests results were obtained by dividing each ES by its SE (Standard Error of the mean).	In this meta-analysis, The mean weighted post -treatment ES found was .53 significantly different from zero ($z = 3.58$; $p < .01$) for CBT. The investigators were interested in finding reasons for the lower effects of CBT for adolescent depression in newer RCTs when compared to larger effects found in the past. Authors became interested in the topic after Weisz et al. (2006) found an effect size, ES= 0.34 in 31 RCTs of CBT adolescents. The effect size reported by Weisz was smaller than previous findings. For example, Lewinsohn and Clarke, 1999 found an ES = 1.02, and in a meta-analysis by Reinecke, et al. (1998), the ES=1.27.	These results indicate that CBT may be effective for the acute treatment of depression among adolescents, although treatment effects may be more modest in clinical settings than previously thought. Authors recognized that one of the limitations in the present meta-analysis was the small number of studies. They also reported that studies in nonclinical settings had a decreased effect side. The possible explanation given by the researchers is the shift from an emphasis on the efficacy of treatment in a controlled research setting to demonstrating the effectiveness of the intervention. As well as, the increased statistical and methodological rigor applied in research studies. Authors recognize the importance of reporting moderators that could influence results. In the studies included, the literature was inconsistent in reporting factors, such as comorbidities, socioeconomic status and other demographical information.	Authors concluded that the differences in effect size may be due to differences in methodology used in previous studies when compared to recent ones. **Level of Evidence** Recommended for practice **I** (1) - Meta-analysis of well-designed, randomized, controlled clinical trials

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY - GROUP CBT						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Lynch, F.L., Hornbrook, M., Clarke, G.N. Perrin, N., Polen, M.R. et al. (2005). Cost – effectiveness of an intervention to prevent depression in at-risk teens	Kaiser Permanente Norwest, a Health Maintenance Organization, HMO, used the results of a previously conducted randomized trial to test the cost-effectiveness of a group intervention in at-risk adolescents. In their original study, performed in 2001, this HMO used their database to identify parents who had a diagnosis and/or symptoms of depression, and 2995 letters were mailed. Researchers ended with a sample of 123 eligible youths, but only 94 agreed to participate.	94 subjects ages 13 to 18 years old, who were at risk for depression, agreed to participate. In addition to parents with a history of depression, subjects also had to have a history of a previous episode of depression that did not meet criteria for a DSM-III-R diagnosis. Participants were randomized to: N=49 to usual care, and N=45 to usual care plus a cognitive therapy prevention program consisting of (15) one-hour sessions. Sessions were delivered to a group of 6-10 adolescents. Usual care was defined as any type of treatment adolescents were already receiving, including mental health services and antidepressants.	Parents were assessed with the Family Schedule for Affective Disorders and Schizophrenia (SADS). Adolescents were placed in groups according to their symptoms and DSM-III-R diagnoses. Subjects included had a Center for Epidemiologic Studies Depression Scale (CESD-S) score of ≥24 (medium depression).	The results for cost-effectiveness when comparing groups were not statistically significant. The average cost of the intervention, CBT, was $1632 per youth, and intervention subjects had an increase in direct and indirect costs of $610. One year after the intervention, participants in the intervention group had 53 fewer depressed days in the year following intake (p=0.01). This showed a Significant increase in Quality Adjusted Years (QALYs); p = 0.059 for the intervention group compared with controls. After one year, intervention subjects had used less services (p=0.05) in 7 of 13 areas of service.	The cost of identification and recruitment of subjects was 65% of the cost of the intervention. The cost of CBT was $1632 per subject. According to guidelines, a new intervention is effective, cost effective and it should be adopted if they cost less than $20,000, $50,000, or $100 000 per QALY. Researcher indicated that, according to their base-case analysis the cost of the intervention was 9275 per QALY. When they conducted a base-case and sensitivity analyses, authors concluded that their intervention was cost effective because it me the criterion of $50,000 per QALY or less Researchers recommend comparing these results to other studies, but they are not aware of any other study that has examined the cost-effectiveness of prevention of depression in adolescents in a randomized clinical trial.	**Level of Evidence** Recommended for practice I (3) well-controlled, randomized clinical trials with less < 100 participants.

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY - CBT						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
O'Kearney, R., Kang, K., Christensen, H., & Griffiths, K. (2009). A controlled trial of a school-based Internet program for reducing depressive symptoms in adolescent girls	The purpose of this study was to examine the effectiveness of Internet delivery of self-directed cognitive behavioral therapy (CBT), MoodGYM version, in the reduction of depression and for improving attributional style in adolescent females. Authors also studied the secondary outcomes of knowledge about depression, depression literacy, and their attitudes to depression.	157 girls, attending 10th grade in Canberra, Australia were eligible to participate. Adolescents were ages 15 to 16. They were assigned to two groups, MoodGYM (n=67) and (n=90) to a control (usual curriculum) group. Girls were assigned according to their class assignment. Three classes were chosen for the intervention because of computer access. The intervention was delivered, as part of a school curriculum, over the course of 6 weeks.	Authors separated levels of depression as low, <24, and high, >24, by using the Centre for Epidemiological Studies Depression Scale (CESD). Secondary Outcomes were measured with: Attributional style was measured with the Revised Children's Attributional Style Questionnaire (CASQ-R), depression knowledge with the Depression Literacy Scale (DLS), and the attitudes to depression, with a nine (4)-point Likert scale.	Immediate results were non-significant for MoodGYM, but the decline of self-reported depressive symptoms was faster in the Mood GYM group. At 20 –week follow up, there was a moderate effect for MoodGYM, and a moderate to high effect in the group with highest baseline scores. There were no differences post intervention or at follow-up in the secondary outcomes.	No costs were reported about the cost of this Internet program. Authors reported that the low levels of adherence seen in this study may provide information on problems completing Internet programs for depression.	CESD was used due to its validity and reliability. Cutoff for detection of depression in adolescents has been suggested as a score of 16, while other authors recommended a score of 22 for boys and 24 for girls. 30%, 20/67, students completed three or more modules of MoodGYM, and those who did less than three modules had the highest level of depression at baseline. **Level of Evidence** Recommended for Practice **I**(3) - well-controlled trial without randomization

Interventions for the Treatment of Depression in Adolescents - CBT & IPT						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Rosello, Bernal, & Rivera-Medina, (2008). Individual and group CBT and IPT for Puerto Rican adolescents with depressive symptoms	112 subjects were randomized to 4 groups: 1) individual cognitive behavioral therapy ((CBT) (2) group CBT (3) individual Interpersonal Psychotherapy (IPT) (4) group IPT Individual and group therapy was delivered once weekly over the course of 12 weeks. The individual sessions lasted 1 hours and the group treatment met for 2 hours. CBT and IPT were developed to meet the needs of Puerto Rican adolescents	112 adolescents' ages 12 to 18 met the inclusion criteria from a number of 322 who were referred. Subjects were students attending 6^{th} to 12^{th} grade, and 50% were in public schools. Also, 55.4% of the sample was female. To be included, the adolescents had to meet DSM-III R Criteria for MDD or to be identified by an evaluator as suffering from depression. Also participants with more than 13 score on the CDI were included. Exclusion criteria: adolescents who were actively suicidal, with psychotic symptoms, mental retardation, bipolar disorder, history of fights, conduct disorder and drug use. In addition, adolescents already receiving psychotherapy or medications were not included.	Pretreatment and post-treatment evaluation after 12 weeks using the: 1) Children's Depression Inventory (CDI). 2) Child Behavior Checklist, Adolescent and Parent version (CBCL-A and CBCL-P). 3) Social Adjustment Scale for Children and Adolescents (SASCA). 4) Diagnostic Interview Schedule for Children (DISC-2.1).	All treatment modalities decreased depression symptoms, but CBT was the most effective one according to the CDI scores (p= .016]. CBT also produced the highest changes in self-concept, as measured by the PHCSCS p = 0.006]. CBT also was more effective in decreasing internalizing behaviors: p=.037, as well as externalizing behaviors: p =.035. The efficacy of individual over group therapy was small (.10).	Study was limited to adolescents in San Juan Puerto Rico. Researchers reported that the present results could be related to CBT having a higher fidelity than IPT in this study. They also stated that the more structured delivery of CBT could be more culturally appropriate for Latinos due to the "respeto" factor which looks for figures of authority for guidance. Another explanation was that CBT may be a better choice for the acute treatment of depression. Due to the small efficacy for individual therapy, researchers suggest to consider the group format due to its cost-effectiveness.	**Level of Evidence** Recommended for practice **I** (2) - **w**ell-controlled, randomized clinical trial with adequate sample size, > 100.

Interventions for the Treatment of Depression in Adolescents – PSYCHOTHERAPY - CBT/School						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Sheffield, J. K., Spencer, S. H., Rapee, R. M., Kowalenko, N., Wignall, N. Davis, A. & McLoone, J. (2006). Evaluation of universal, indicated, and combined behavioral approaches to the prevention of depression among adolescents	Researchers designed randomized, controlled trial with a 12-month follow up. This trial was conducted in Australia. The purpose of this study was to compare two preventative approaches in relation to each other and also to a control group, receiving no intervention. Researchers also evaluated the impact of a 12-montth indicated intervention for at risk adolescents following a universal approach. The rational for this last intervention was that the usual 8 to 12 weeks of universal intervention might not be enough and that adolescents will benefit from extra therapy sessions to consolidate what they had learned during the universal intervention.	At the beginning of the study, there were 2,479 male and 1,347 female participants. These students were attending the equivalent of 9th grade in the United States. Their mean age was 14.34 years. From the original sample, 521, or 21%, were identified as "high symptom." In the high risk group, 163 (31%) were male and 358 (69%) female. Their mean age was 14.34 years. Authors were interested in this subset of the sample because of the link between subclinical levels of depression and the development of depressive episodes in the future.	Children's Depression Inventory (CDI) and the Center for Epidemiologic Studies—Depression Scale (CES-D) The Beck Hopelessness Scale (BHS) Anxiety Disorders Interview Schedule for Children (ADIS-C). This is a semi-structured diagnostic interview based on the of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). Longitudinal Interval Follow-Up Evaluation (LIFE) was used to asses for depressive symptoms at 12-month follow-up	Researchers compared: 1). A combined, universal, classroom intervention followed by an indicated approach to prevent the development of depression in at risk teenagers. 2) Then they compared the above combined approach to an indicated intervention alone, 3) to a universal intervention 4) or to no intervention. No differences were found across all the prevention treatment modalities.	Researchers compared the results in these preventive interventions with the results of March et al., 2004, which did not find a positive result for cognitive behavioral therapy (CBT) when compared to placebo. Also, since the March et al., 2004 study showed that the combined treatment of psychotherapy plus medications was statistically significant, the authors wonder if CBT alone is enough to decrease symptoms of depression. Authors mentioned the possibility of stigma in indicated interventions.	Interventions to prevent the development of depression in adolescents have been divided into three categories: universal, selective and indicated preventive approaches. Universal approaches involve whole populations regardless of their risk level. On the contrary, selective interventions are directed at youths who are at risk due to a trigger in the environment, such as family relationship problems, divorce of parents, death of a parent. Indicated actions are aimed at adolescents who already have mild to moderate symptoms of depression and are deemed to be candidates to suffer a mood disorder in the future. **Level of Evidence** Recommended for practice I (2) - Randomized trial with adequate sample size.

Interventions for the Treatment of Depression in Adolescents - PSYCHOTERAPY - School Based						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Spence, S. H., Shetfield, J. K., & Donovan, C. L. (2005). Long-term outcome of a school-based, universal approach to prevention of depression in adolescents	In a cluster, stratified randomized design, researchers examined the effect of a universal, school-based, cognitive behavioral intervention at 2, 3 and at 4 year follow up. The purpose of the intervention was to prevent the development of depression in youths. Schools were matched according to demographic characteristics and randomly assigned to a universal prevention program, the Problem Solving for Life (PSFL), delivered by teachers or to a monitoring control condition.	This study consisted of 1,500/eighth grade students, attending 16 coeducational high schools in Queensland, Australia. Participants were also divided into two depression groups: high risk and low risk according to scores on the Beck Depression Inventory (BDI). For the intervention group, mean age was 12.82 years, 47% were males and 52.0 male. In the control group the mean age 12.90, and 49.4% of the sample was male and 50.6% female. Intervention consisted of eight weekly sessions. Each session lasted 45-50 minutes.	Beck Depression Inventory (BDI). Social Problem-Solving Inventory—Revised Short Form (SPSI–R) Children's Attributional Style Questionnaire-Revised (CASQ–R). Child and Adolescent Social and Adaptive Functioning Scale (CASAFS) Youth Self-Report (YSR) Anxiety Disorders Interview Schedule for Children (ADIS–C).	Adolescents with the higher degree of depression, assigned to the intervention group, had the greater increase in problem-solving scores at the end of the 8 week-intervention phase, but these effects were not present at 12-month follow up and at all evaluation points during the 4-year follow up. The lack of benefit at follow-up meant that researchers failed to find a delayed or "sleeper" effect in this intervention. There were no significant differences between the students who completed the PSFL intervention and the students who did not. Researchers found that the patients in the high risk group had a lower level of functioning over time showing the prolonged effects of depression.	Authors had difficulty contacting students throughout this study, and at the end of 4 years, they were able to retain 60.4% of the original sample. There were more missing students in the intervention group. Authors also reported higher dropout rates in the high risk group. No costs related to training were reported, but teachers attended training sessions for approx. 6 hours. One of the limitations of this study was the teachers were not observed when delivering this intervention and that teachers may have lacked the necessary skills to deliver the intervention. Another reported limitation was that the intervention was delivered to high numbers of students and not to individuals. Participants were also not interviewed at the time of enrollment due to financial problems.	PSFL consisted of teaching cognitive-re-structuring and problem-solving skills to students. Researchers emphasize the need for long-term follow-up to evaluate programs to prevent adolescent depression to find the programs that will work in retaining its original benefit. **Level of Evidence**: Recommended for Practice **I**(2) well-controlled, randomized trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY - School						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Stice, E., Shaw, H., Bohon, C., Marti, C.N., & Rohde, P. (2009). A meta-analytic review of depression prevention programs for children and adolescents: factors that predict magnitude of intervention effects.	This meta-analysis was designed on the premise that depression programs in schools would be more effective, by showing larger effects, when the interventions targeted older adolescents while focusing on the following interventions: reduction of negative thinking (cognitions), changes in behavior (promoting enjoyable activities, and the development of problem-solving skills, and of social skills. Researchers were interested at examining moderators that will make the intervention more effective.	To find relevant randomized controlled trials a search was done for the years 1980 to 2008 in PsychINFO, Medline, and Dissertation Abstracts databases. Authors also searched the table of contents for journals that publish on this topic, as wells as narrative reviews and previous reviews of meta-analysis, reference sections of articles, and unpublished articles in the process of being reviewed or in press. Authors found 47 trials evaluating 32 prevention programs. 11 trials included more than 1 prevention program, 9 programs were evaluated in 2-8 trials, with a resulting 60 effect sizes.	Effect sizes were calculated	Results for the reduction of depression were small when comparing pre-treatment to post-treatment results: Correlation coefficient: (r = .15). From post-treatment to follow-up: r = .11. Looking at results individually: 13 (41%) prevention programs showed a significant reductions in symptoms of depression. 4 (13%) reported a significant decrease in depressive symptoms in at- risk adolescents at follow up.	The costs associated with the interventions were not reported. Other limitations: inability to detect the moderator effects due to the lack of data, such as the type and length of training received by facilitators. No data were found on social functioning, days of school absenteeism. From the results presented in this meta-analysis, researchers found that the programs with the higher intervention effects included females, older adolescents, participating in shorter programs (longer programs had smaller intervention effects because subjects might lose interest which may lead to a higher attrition rate.). Youths who were assigned homework with exercises as part of the intervention had higher intervention effects. Follow-up effects sizes were higher for programs that had been delivered by "dedicated interventionists" rater that by classroom teachers. Younger participants had a men age of 12.1 years old. The mean age for lager effect sizes was detected in adolescents with a mean age of 15.1 years.	**Level of Evidence**: Recommended for practice **I** (1) - Meta-analysis of multiple well-designed randomized controlled trials.

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY - CBT						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Stice, E., Rhode, P., Seeley, J. R., & Gau, J. M. (2008). Brief cognitive-behavioral depression program for high-risk adolescents outperforms two alternative intervention: a randomized efficacy trial	The aims of this study were: First, to compare a Brief group cognitive intervention (CB) to an assessment-only control group. Second, to compare CB to two active control conditions: CB skills in bibliotherapy, and in supportive-expressive group. Third, to study if CB had an effect in improvements in social adjustment and reductions in binge eating and substance abuse.	341 participants from six high schools, ages 14 to 19, were recruited between 2004 and 2007. Subjects consisted of 2% Asians, 9% African Americans, 46% Caucasians, 33% Hispanics and 10% of mixed race. Subjects were randomly assigned to: CB group (n=89), supportive expressive group (n=88), bibliotherapy (n=80), and to assessment control group (n=88). A survey and diagnostic interview was completed at pretest, posttest, and 6-month follow-up.	Subjects with a score of 20 or above in the Center for Epidemiologic Studies–Depression scale (CES-D) were asked to fill out a baseline assessment (pretest). Other measurements: Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) Beck Depression Inventory (BDI Social Adjustment Scale–Self Report for Youth 10 Item substance use Questionnaire	Attendance was similar across groups. CB participants had a significant decrease in depressive symptoms at baseline and at 6 months when compared to assessment-only control group. CB subjects showed more improvement than supportive-expressive and bibliotherapy participants at post-test only (not at 6-month follow up). The CB group had better scores in social adjustment than supportive-expressive, bibliotherapy and assessment-only groups at 6 month-follow up (social adjustment was not measured at posttest). Bibliotherapy and support-expressive intervention had significant effects when compared to the control group at posttest, but not at 6-month follow-up.	Training of staff was discussed. No expenses were included, but researchers reported that bibliotherapy is a good alternative to CB because is less expensive and easier to disseminate. CB focused on building group rapport, involvement in pleasant activities, and on replacement of negative thoughts. Support-Expressive Group, a supportive psychotherapy modality, was designed to build rapport, give support and teaching how to identify and expresses feelings, and on discussing safe environments. Bibliotherapy consisted of giving subjects a copy of the book, “Feeling Good,” a self-help book for the treatment and prevention of depression. Topics discussed included understanding feelings, increasing self-esteem and how to deal with stress and hopelessness. Assessment-only subjects received a brochure only educating youths about major depression, “Let’s Talk about Depression” and completed assessments of the outcome measures.	This study consisted of 6 CB sessions when the usual average for CB is 11 meetings. Researchers found that CB could be a useful modality in clinical settings since it showed more improvement in decreasing depression when compared to other treatment modalities. **Level of Evidence** Recommended for Practice **I** (2) – Well-controlled randomized clinical trial with adequate sample size, >100.

Interventions for the Treatment of Depression in Adolescents - PSYCHOTERAPY - CBT						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Trowell, J., Joffe, I., Campbell, J., Almqvist, F., Soinenen, M. Koskenranta-Alto, U., . . . Tsiantis (2007). Childhood depression: A place for psychotherapy	Researchers conducted a randomized controlled trial to examine the effectiveness of Individual and Family Therapy in adolescents suffering from moderate to severe depression. This trial took place in different countries: London, Helsinki and Athens. The duration of this intervention lasted 9 months. Family therapy included 8-14 (90) minute sessions, mean number of family session was 11. Individual therapy provided 16 to 39 (50) minute sessions (mean 24.7).	72 patients were randomized to either Individual therapy or to Family therapy. There was no placebo group. Age range was 12 to 15. Mean age: 12 years old. 62% of the participants were male and of diverse economic backgrounds. Most of the adolescents were white and 62% lived with both parents. 76% had been depressed for more than 6 months.	Subjects were evaluated at baseline and also at the end of the study. Childhood Depression Inventory (CDI) Children's Global Assessment Scale (C-GAS). The Demographic Interview, a semi-structured interview Moods & Feelings Questionnaire (MFQ)	At baseline, 90% of the patients had a diagnosis of major depressive disorder. At the end of the study, 6(17.1%) still had this diagnosis. **Individual Therapy** 74.3% of the participants did not meet criteria for a depressive disorder at the end of this study, and after 6 months none of the patients was depressed. **Family Therapy** 75.7% of the cases was no longer clinically depressed at the end of this trial, and this number improved to 81% six months later.	No cost was reported. At the beginning of therapy, 48% of the participants in Individual therapy and 45.9% in the Family Therapy group were diagnosed with Major Depressive Disorder and Dysthymia. Since all cases of depression had resolved at 6 months follow-up, this was attributed to an ongoing response to therapy, "the sleeper effect." Researcher reported 4 cases who did not complete trial, all these cases were in family therapy. Individual and Family therapy are considered to be effective in treating moderate to severe depression in children and adolescents. Limitations include small sample size, lack of a placebo group. This study obtained similar, positive results even though the intervention was conducted in different countries where the protocol for these two therapy modalities could vary.	**Level of Evidence** Recommended for practice **I**(3) – Randomized study without a placebo group of small sample size, <100 s.

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY - Group CBT						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Waddell, C., Hua, J.M., Garland, O.M. Peters, R.D., & McEwan, K. (2007). Preventing mental disorders in children: a systematic review to inform policy-making.	Authors searched for RCTs related to programs on preventing conduct disorder, anxiety and depression in children 0-18 years old.	Two reviewers conducted the search for this systematic review by searching Medline, PsychINFO, Cochrane Database of Systematic Reviews, and hand searching for known systematic reviews. Search was limited to the English language and by articles published between 1981and 2003. These two reviewers evaluated all abstracts and obtained relevant articles. They were also in charge of applying the inclusion criteria, The studies evaluated, included four trials were on the topic of depression and one study included all three disorders.	CES-D Center for Epidemiologic Studies (Depressive symptoms) HAM-D Hamilton Depression Rating Scale (Depressive symptoms) K-SADS-E** Schedule Affective Disorders & Schizophrenia Epidemiologic Version (any depressive disorder/ Suicide symptoms) CBCL Child Behavior Checklist (Internalizing symptoms) BDI: Beck Depression Inventory (Depressive Symptoms) CDI Children's Depression Inventory.	**Depression** **(**2) Trials were conducted in the United States, called: "Coping with Stress) in children 13-18 years old using Group CBT as treatment modality delivered by Clinicians. Magnitudes of effect: 11% and a 17% respectively reduction in diagnostic measures and a Hazard Ratio of: 2.2. These results were considered a "modest" effect by authors. (2) Other programs took place in Australia. One program called "Penn Prevention," delivered by clinicians (for children ages 11-13) and the second program "Problem solving for Life," (for 13 y/o children) was delivered by teachers. These two programs did not show a benefit. (1) Study originated in the United Kingdom, "Help Starts Here" for subjects ages 11-12. This study used group child drama therapy. It was delivered by teachers. This study did not show a significant reduction in any of the three disorders.	Limitations: the studies included were considered "moderately" rigorous, with a lack of blinding, and not reporting outcome measures at all points of the study. Also, most studies failed to report magnitudes of effect. Authors were also concerned that studies had a tendency to rely on assessment tools for symptoms rather than in diagnostic measurements. Cost of interventions was not reported.	**Level of Evidence:** Recommended for practice **I**(1): Systematic review of multiple, randomized controlled trials

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY – Mostly CBT						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Watanabe, N., Hunot, V., Omori, I.M. Churchill, R.,& Furukawa, T.A. (2007). Psychotherapy for depression among children and adolescents: a systematic review	27 studies which contained 35 comparisons were selected after a search in the Cochrane Depression, Anxiety and Neurosis Registers on December 17, 2004. Researchers also conducted a hand search of psychiatric, medical and conference articles.	27 studies including 1744 participants in 35 randomized comparisons were included in this review. Subjects were between ages 6 and 18 who had a diagnosis of major depression, minor depression or dysthymia. 81% of subjects were adolescents, ages 12-18. Studies with a comparison group of no treatment, waiting-list control, attention-placebo, and TAU (treatment as usual) were accepted. Only two studies had a sample size of ≥100. Some studies had <10 subjects in the control or placebo arms.	Three independent evaluators and assessed the quality of the data using the Quality Rating Scale (max. score: 46).	Patients had an RR of 1.39 (95% CI [1.18–1.65], p = 0.0001), indicating a benefit for psychotherapy (Cognitive Behavioral Therapy and Interpersonal Therapy). Number needed to treat= 4.3. Researchers found a small sample effects and a publication bias in these studies. There was no evidence of the benefit of psychotherapy at 6-month follow-up in 18 comparisons that reported follow-up RR 1.18 [0.94–1.47], p = 0.15). Dropout at post-treatment was significantly increased for psychotherapy during follow up.	No adverse effects and no costs for these interventions were reported. Dropout rates were the same for placebo and treatment groups CBT was the most used psychotherapy used in these studies. In children no differences in benefit were detected. In adolescents, there was a significant response to psychotherapy (1.35 [1.10–1.66], P = 0.004, NNT 4.2). CBT and IPT provided more benefit in subjects with moderate to severe depression than for mild to moderate depression. Number of sessions varied treatment 4 – 19 weeks. .	Researchers caution that the results of this meta-analysis might lack generalizability since the subjects in this review were recruited in schools. **Level of Evidence** Recommended for practice **I** (1) - Well conducted systematic review.

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY - CBT						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Weisz, J.R., Southam-Gerow, M.A., Gordis, E.B. Connor-Smith, J.K. Chu, B.C., Langer, D.A., . . . Weiss, B. (2009). Cognitive-behavioral therapy (CBT) versus clinical care for youth depression: an initial test of transportability to community clinics and clinician.	The purpose of this study was to bridge the knowledge acquired from CBT clinical trials to public, outpatient community mental health clinics. The CBT program in the present study used the Primary and Secondary Control Enhancement Training (PASCET) system (in this method children can learn coping skills through videotaped cases and group discussion). This study used double randomization. Therapists, as well as youths, were randomized to CBT or to Usual Care (UC). Subjects were assessed at the start and at the end of the intervention by staff blinded to the intervention.	The sample of 57 adolescents was recruited by referrals to seven public, urban clinics. Subjects were ages 8 – 15 years with a median age of 11.77 years and 56% were female. Regarding race, subjects were 33% Caucasian, 26% African American, 26% Latino/Latina, 11% "mixed/other," and 4% did not specify race. 26 therapists delivered CBT and 28 UC. They were master's prepared or higher. Their average age was 32 years. 43% were Caucasian, 34% were Latino/Latina, 13% were Asian/Pacific, 6% were of mixed ethnicity, and 4% were African American. They averaged 4.3 years of experience with 2.4 years of additional professional training.	Diagnostic Interview Schedule for Children (DISC 4.0) Children's Depression Inventory (CDI). Children's Depression Inventory—Parent Form (CDI-P). Child Behavior Checklist (CBCL). Expectations of Therapy Outcome Scale (ETOS) Post-treatment only Therapeutic Alliance Scale for Children (TASC) .	CBT and UC results did not differ, and 75% of youths had no reported depressive symptoms at the time of termination. Authors reported that youth in CBT needed fewer sessions. Also CBT participants did not incur in additional expenses, such as medications.	Authors reported a possible decreased in costs for CBT because youths in the CBT groups had used fewer resources, such as in medications and in other modalities not specified. The number of patients who attained remission was larger in the CBT/PASCET. Youths were treated to "normal" termination which was until the therapists detected improvement. However, testing was not done during the course of treatment. Average number of sessions for CBT was 24 and for UC: 39 weeks, 4 months longer than CBT. Also, according to videotaped sessions, therapists had different levels of skill in delivering the CBT/PASCET method. Also CBT/PASCET therapists were unfamiliar with this system while the UC providers chose a method they felt more comfortable with. Therapists delivering PASCET only had a 6-hour training.	The enrollment for this study seems very broad especially when the target population was age 8 to 15. from 1998 to 2003. Assessments were finished in 2005. It is difficult to assess the efficacy of the interventions since there was no set time of duration. **Level of Evidence**: Recommended for practice **I** (3) randomized trial with < 100 sample size

Interventions for the Treatment of Depression in Adolescents: PSYCHOTHERAPY - Mostly CBT						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Weisz, J. R., McCarty, C.A., & Valeri, S. M. (2006). Effects of psycho-therapy for depression n children and adolescents: a meta-analysis	This meta-analysis included 35 studies. They were obtained by database searches for PsycINFO from 1887-2004, Dissertation Abstracts International (1861-2004), and MEDLINE, 1994-2004. They also examined references from studies, hand searched for journals that had published at least five of the articles in their computer search, and contacted authors to identify relevant studies.	Children < 13 years and adolescents > 13. Samples included in this meta-analysis were: Child: 20 Adolescent: 60 Mixed: 20 Studies included had to be the result of a treatment outcome, a clinical trial, single-blind or double blind design. Researchers reported that only 13 of the 35 studies provided information on race and ethnicity.	ES= Effect size to report results	This meta-analysis found that their men effect of psychotherapy was 0.34 (small effect 0.20 and 0.50 medium by Cohen's scale). Because of the concern about SSRIs raising the possibility of suicidality, investigators looked at 6 studies which took into consideration this variable and found a small reduction of suicidality: mean ES of 0.18 (slightly better than zero).	Researchers found that in these studies, the subjects tended to report better outcomes, but not their parents. The length of treatment was different in these studies: from 4 to 32 sessions, but the outcomes were not related to the number of sessions. Authors advocated for the need of follow up assessment since more than one third of the studies they included lacked that type of data. only 6 of the studies considered moderators that could impact the results. Another problem indicated by researchers was that 20 of the 35 studies used passive control systems, such as waitlist and no treatment. Authors find that this type of approach is not acceptable because it not only the weakest, but also difficult to maintain during a waitlist period due to ethical and humane reasons. Researchers were concerned that since psychotherapy did not show a strong result, this could be discouraging for subjects looking for an alternative to medication.	Researchers thought the low response of psychotherapy in some studies was because of the low potency of the intervention. Meta-analyses might be difficult to perform since they include studies that have included different types of subjects, methods, varied doses of medications and outcome measures. In this case, 33 of the 44 treatments included CBT, cognitive changes, authors advise to study all noncognitive types of psychotherapy in this age group. **Level of Evidence**: Recommended for Practice **I** (1) Meta-analysis

TABLE 2

INTERVENTIONS FOR THE TREATMENT OF DEPRESSION IN ADOLESCENTS –

PSYCHOTHERAPY –

INTERPERSONAL PSYCHOTHERAPY (IPT)

Interventions for the Treatment of Depression in Adolescents – PSYCHOTHERAPY - IPT - Systematic Review (SR)						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Brunstein, A., Zalsman, G., & Mufson, L. (2007). Interpersonal psychotherapy for depressed adolescents (IPT-A).	This article offered a timeline of the development of Interpersonal Psychotherapy (IPT). Researchers also reviewed the efficacy and effectiveness of IPT-A in four studies.	Subjects included in this review ranged from ages 12-18. Study 1 (Mufson and colleagues (1994). Sample consisted of 14 adolescents who participated in a 12-week open clinical trial of IPT. Study 2: (Mufson, et al, 1999). Adolescents received either IPT or clinical monitoring. Study 3: (Rosello & Bernal, 1999) Comparison of cognitive behavioral therapy (CBT) and IPT-A. Only mentioned that the intervention included adolescents. Study 4: (Mufson, 2004). Study compared treatment as usual (TAU) with IPT-A in adolescents in a school setting (no other information was provided).	Information about measures was only mentioned for study 1. This study used a Semi-structured interview, self-report and clinic-administered instruments (not specified).	Study 1: Authors reported a decrease in depressive symptoms and improved interpersonal functioning. Study 2: IPT showed improvement in social functioning. Study 3: Reported that 82% of youths in the IPT group compared to 52% in the CBT had met recovery criteria. Improvements in self-esteem and social adaptation were mentioned. Study 4: showed that IPT-A was more effective in improving overall functioning and in decreasing depression.	Clinicians interested in providing IPT to adolescents will need training. Authors reported that Study 1modified the treatment to the needs of adolescents and that Study 3 used modified the Adult version. No costs about treatment were given, but authors stated that the group interventions in IPT-A could also be effective for depressed adolescents and that this approach could be cost effective.	Information in this article is useful to gain an understanding on IPT, even though information was not all from randomized-controlled trials. **Level of Evidence** Recommended for practice **II** (4) Systematic review including non-experimental design studies.

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY - IPT						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Miller, L., Gur, M., Shanok, A., & Weissman, M. (2008). Interpersonal psychotherapy with pregnant adolescents: two pilot studies	Authors developed two open clinical trials based on their awareness of the risk of morbidity in children of depressed parents and because of lack of evidence on the use of psychotherapy in pregnant adolescents suffering from depression. In these two studies, researchers used school-based, group Interpersonal psychotherapy (IPT). The first clinical trial consisted of a sample of 14 adolescents with a varying degree of depressive symptoms. The second clinical trial had a sample of 11 youths.	First study: Adolescents were ages 13 to 17 (mean age: 14.7 years) attending a high school for pregnant and parenting females in Harlem, New York. Average gestational age was 2-8 months, with a mean of 4.9 months. 14 participants, ten were Hispanic, three African American and one of mixed race (Hispanic and African American). The second study included 11 youths. who had a diagnosis of depressive disorder according to the DSM-IV. In this sample, eight youths were African American, 1 Hispanic and 2 were biracial. Mean age was 16.5 years.	STUDY 1: Adolescents were evaluated at baseline and at 12 weeks (end on intervention, with the Beck Depression Inventory Beck (BDI) Edinburgh Depression Scale (EDS). STUDY 2 In addition to assessments at baseline and 12 weeks, participants were also evaluated at week 20 (8 weeks after IPT ended).	STUDY 1: Subjects attended 8.8 of the 12 sessions offered. Decreased scores in the BDI and the ESD scores were Statistically significant (p=0.05) at the end of the 12-week intervention. A decrease of about half in all symptoms of depression was observed in 13 of the 14 adolescent. STUDY 2 Youths attended 6.1/12 sessions. At the end of 12 weeks, participants had a 40% decrease of depression symptoms. 8 of 11 girls no longer met criteria for DSM-IV diagnosis, two of the participants had decreased severity of symptoms (per DSM criteria). Overall, participants showed a moderate to high effect size (.7 to 1.2) in measures of depression and global functioning. These results were maintained at week 20.	The cost for this intervention was not reported. The first study consisted of a sample of 14 adolescents. 10 girls lived with their mother, one lived with both parents, and three of them resided with older relatives. IPT was conducted during health class. In the second study, IPT was delivered after school. Attendance was better for IPT delivered during school hours possibly due to need to attend medical appointments at the end of the school day. Authors found that pregnant adolescents with depression in low socioeconomic had a positive response to IPT. However, these results belong to girls who remained in school throughout these interventions. Authors reported the high number of drop outs in this school due to homelessness, and relocation. The rate of absenteeism was also elevated, and only 25 – 35% of the students attend school on a routine day.	More research is needed to address the need for treatment in adolescents who attend school (there are 3,000 schools for pregnant girls in the United States). IPT in this group might have led to subjects making better choices about safer living environments that could benefit prenatal and neonatal health. **Level of Evidence** Recommended for practice I (3) Well-designed trials without randomization

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY - IPT						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Mufson, L., Dorta, K. P., Wickramaratme, P., Nomura, Y., Olfson, M., & Weissman, M. M. (2004). A randomized effectiveness trial of interpersonal psychotherapy for depressed adolescents.	For this study, five school-based clinics in New York City were sponsored by 3 hospitals. Patients were randomly assigned to receive IPT-A = n=34 or TAU = n=29 TAU = treatment as usual	Sample consisted of 63 subjects, 12-18 years old. Mean age: 15.1 years. Sample consisted mostly of females and Hispanics of low socio-economic status. 71% female 84% Hispanic To be eligible, they had to meet DSM-IV criteria for major depression, dysthymia, depressive disorder not otherwise specified, or adjustment disorder with depressed mood. They also need a Hamilton Depression Rating Scale score of 18.6 (SD, 5.5) and a mean Children's Global Assessment Scale score of 52.6 (SD, 5.5).	The Hamilton Depression Rating Scale, Beck Depression Inventory, Children's Global Assessment Scale, Clinical Global Impressions Scale. Social Adjustment Scale–Self-Report.	.Subjects in the IPT-A group had decreased points on the Hamilton Depression Rating Scale (p= 0.04), the Global Assessment Scale (p=0.04). They also had a higher improvement on the Social Adjustment Scale-Self Report (p=0.01, significant greater clinical improvement: p= 0.03. On the Clinical Global Impressions scale they also had lower severity of symptoms p=0.03.	No information on cost was provided. Authors find that this study represents an important step to closing the gap between previous research conducted in a laboratory to a community setting. They also concluded that Interpersonal psychotherapy received in school-based clinics is an effective treatment for adolescents suffering from depression.	**Level of Evidence** Recommended for practice **I** (3) Well-designed trial with < 100 sample size

Interventions for the Treatment of Depression in Adolescents - PSYCHOTERAPY - IPT-A						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Tang, T.C., Jou, S.H., Ko, C.H., Huang, S.Y., & Yen, C.F. (2009). Randomized study of school-based intensive interpersonal psychotherapy for depressed adolescents with suicidal risk and presuicide behaviors	Researchers studied the impact of interpersonal psychotherapy for depressed adolescents with suicidal risk (IPT-A-IN) by comparison with treatment as usual (TAU). The intervention lasted 6 weeks. Subjects participated in two sessions per week due to suicidal concerns. The most commonly identified themes in the interpersonal group were: Interpersonal conflicts, 90% Grief and loss response 8%, Interpersonal sensitivity and role transition, 2%.	347 students, or one fifth of all students, ages 12 to 18, were recruited from schools in Taiwan. Students were assessed for suicidal ideation, and 73 depressed students were randomly assigned to two groups. One group of 35 subjects, 12 boys and 23 girls received interpersonal psychotherapy for depressed adolescents with suicidal risk (IPT-A-IN), and 38 students (13 boys and 25 girls) were assigned to treatment as usual (TAU). Mean age for the IPT - A-IN arm was 15.26 and for the TAU group 15.24. Evaluators who assessed the subjects at post-treatment were blinded to the pre-intervention results.	Beck Depression Inventory-II (BDI) Beck Scale for Suicide Ideation (BSS) Beck Anxiety Inventory (BAI) Beck Hopelessness Scale (BHS) were used for Screenings of suicidal risk. A psychiatrist interviewed the chosen students to clarify the diagnosis and to assess the degree of depression and the severity of suicidal risk.	Researchers found that IPT-A-IN was significant, $P<0.01$, in the measurements of BSS and BHS. Also, $p<0.001$in measurements of BDI and BAI.	Researchers did not report the cost of this intervention. Eight school teachers were trained and they delivered the TAU intervention (supportive counseling and psychoeducation). IPT-A-IN was delivered by trained IPT-A therapists. Suicide is ranked as the second cause of death in subjects ages 15 to 24. Depressed adolescents are usually not treated, and researchers stated that bringing the interventions to school will be helpful since many refuse treatment in hospitals (outpatient treatment in community clinics was not mentioned as an option). In this intervention adolescents declined the participation of their parents, or the parents did not have time to attend the sessions, however, part of IPT-A is the involvement of family members. Researchers recommend further research to assess the long term benefits of similar interventions. They also advised the use of IPT-A-IN in various types of interpersonal difficulties.	The post-intervention assessments were conducted by the evaluators who were blind to the results of pre-intervention assessments. **Level of Evidence** Recommended for practice **I (**3) - Well-controlled randomized clinical trials with sample size <100.

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY - IPT						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Young, J. F., Mufson, L., & Davies, M. (2006). Efficacy of Interpersonal Psychotherapy -Adolescent Skills Training: an indicated preventive intervention for depression.	Researcher conducted a prevention, randomized trial to compare Interpersonal Psychotherapy-Adolescent Skills Training (IPT-AST), a school-based group intervention, to School Counseling (SC). To be eligible to participate, subjects had to have 2 subthreshold symptoms or subthreshold depression symptoms without meeting criteria for a current depression episode. Depressed mood, irritability or anhedonia were required. IPT-AST is known to students as, "Teen Talk."	365 adolescents were screened at 3 Catholic schools in New York City. From this number, researchers randomized 41 students to either IPT-AST or SC. Twenty-six adolescents were in the IPT-AST group and n=15 in the SC group. Subjects were 85% female, 92.7% were Hispanic, ages 11 to 16, mean age 13.4. Subjects were attending the 7th to 10th grade. 66% of the participants lived in a single-parent household with an annual income of $25,000 or less. 75% of the sample had sub threshold depression.	Adolescents were assessed at baseline, right after the intervention ended and at 3to 6 months after the study was completed. Scales used were the : CESD-R and the CGI-I	At the end of the intervention, none of the IPT-AST participants met diagnosis criteria for depression, while 3 members of the SC group did. Adolescents in the IPT-AST group had fewer symptoms of depression and overall better functioning at termination and at 3 and 6-month follow up.	The generalizability of this study was difficult not only because of the small sample size, but also due to high refusal rates. Less than half of the eligible adolescents accepting to participate. Another limitation was the higher number of participants in the IPT-AST treatment arm. Also, the sample was mainly female and Hispanic.	Authors recommended future research for IPT-AST in a larger and more diverse sample to study its preventive capability to decrease the development of a depressive episode. **Level of Evidence** Recommended for practice **I**(3) - Well-controlled, randomized trial with <100 sample size

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY - IPT						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Young, J.F., Mufson, L., & Davies, M. (2006). Impact of comorbid anxiety in an effectiveness study of interpersonal psychotherapy for depressed adolescents	This was a randomized trial conducted from April 1, 1999 to July 31, 2002. Researchers wanted to study the impact of anxiety in depressed adolescent in an effectiveness trial by comparing interpersonal psychotherapy (IPT-A) to treatment as usual (TAU). Trial was carried out at three middle schools and two high schools.	63 adolescents ages 12 to 18 who had a diagnosis according to DSM-IV criteria for major depression entered this study. Average age was 15.9 years, 84.1% female and 71% Latino. Inclusion criteria entailed a score of ≥10 in the Hamilton Rating Scale for Depression (HRSD), and a score of ≤ 65 on the Children's Global Assessment Scale (CGAS).	Outcome measurements were: The Hamilton Rating Scale for Depression (HRSD) and the Children's Global Assessment Scale (CGAS). Assessments were carried out by psychologists or social workers who were blind to the treatment condition. Co-morbidity with anxiety was determined by the Diagnostic Interview Schedule for Children Predictive Scales (DPS), a self-report screening questionnaire containing DSM-IV questions about different disorders.	Patients with comorbid anxiety had higher depression scores at baseline $p<0.01$. Anxious participant also benefitted less from treatment, $p= 0.05$. IPT-A was not significant in the treatment of depressed adolescents with comorbid anxiety, $p= 0.07$, but in patients whose depression and level of functioning improved, their anxiety level decreased.	Authors reported limitations in determining comorbid diagnosis. They used the DPS in this study, but they recommended future studies to use more detailed diagnostic instruments. Researchers suggested that for patients with mild to moderate anxiety, patients may benefit from the therapy provided for depression without accommodating the therapy to anxiety. The inability to find a statistical significant result in favor of IPT-A may be related to the difficult anxious patients may have in establishing a therapeutic relationship with a clinician.	Comorbid disorders present in 15% to 60% of patients with depression, and there is a possibility that anxiety may interfere on recovery from depression. **Level of Evidence** Recommended for practice **I**(3) - well-controlled, randomized trial with < 100 sample size

TABLE 3

INTERVENTIONS FOR THE TREATMENT OF DEPRESSION IN ADOLESCENTS –

PSYCHOTHERAPY –

SUPPORTIVE THERAPY

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY - Pregnant & Post-Partum Adolescents						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Barnet, B., Liu, J. & Devoe, M. (2008). Double Jeopardy: depressive symptoms and rapid subsequent pregnancies in adolescent mothers	Authors conducted a secondary analysis of data from pregnant and parenting adolescents participating in 2 longitudinal risk-reduction interventions in Baltimore, Maryland. The aim of the study was to examine the effect of depression on repeat pregnancies. Participants were enrolled from February 2001 to April 29, 2005.	Eligible participants had to be between 12-18 years old and ≥ 24 weeks pregnant receiving prenatal care at 5 prenatal clinics. 96% of the sample was African American. Data from 245 adolescents who had follow-up data at 2 years postpartum were used. Youths filled out questionnaires at baseline (during pregnancy) and at either 1 or 2 years postpartum.	Center for Epidemiological Studies Depression Scale (a score of ≥ 16 was used as a cutoff for defining depressive symptoms).	Baseline symptoms of depression were present in 46% of the adolescents. At two year follow-up, 49% of these adolescents had experienced a second pregnancy. Authors concluded that depressive symptoms might be an independent risk factor for fast, second pregnancies in this population, African American adolescents.	Intervention in the original study was delivered by trained paraprofessionals. Intervention included parenting instruction, case management and motivational interviewing. Limitations include the lack of a clinical diagnosis of depression and also not having a measurement of symptoms of depression in the first weeks following delivery.	Adolescent mothers have twice the incidence of depression when compared to adult mothers, and African American girls have double the risk for depression than white teens. Authors recommend identification and treatment of depression in pregnant and parenting mothers. **Level of Evidence** Likely to be effective **I** (3) - well-designed, longitudinal trial without randomization

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY – Pregnant & Post-Partum Adolescents						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Logsdon, M.C., Ziegler, C., Hertweck,, P., & Pinto-Foltz, M. (2008). Testing a bioecological model to examine social support in postpartum adolescents	Researchers used a bioecological model as a framework to: 1). Describe social support in postpartum adolescents. 2). To determine the relationship between social support and symptoms of depression.	Cross-sectional study with convenience sample. This study included 85 adolescents, recruited at two community hospitals in Louisville, KY. Participants were ages 13 to 18, mean age 16, which had had a baby within 4-6 weeks.	Center for Epidemiologic Studies for Depression (CES-D Scale). Instruments to measure support at the macro, meso and micro levels were conducted during home visits.	Researchers found that perceived stress was the most significant predictor for depression followed by being the victim or witness of violence, low self-esteem or mastery and decreased social support. 37% of the sample had symptoms of depression, but only 7% had received mental heal services and were taking antidepressants. Being a victim of violence may play a bigger role than witnessing violence in the development of depressive symptoms.	Authors recommend screening adolescents for perceived stress. They also advocate for the development of adequate nursing interventions to avoid the negative effects of postpartum depression. Limitations included the use of a small, convenient sample. Researchers stated that the sample used had been small due to not all eligible youths entering the study. Authors also reported that the results might lack generalizability since they only included subjects of low-socio-economic status. Perceived levels of perceived stress could be related to the early adjustment period to motherhood. Even though researchers acknowledged limitations, they also reported that the present study advanced the science related to postpartum care in adolescents.	Birth rates for adolescents remain high. In 2005, 400,000 infants were born to adolescents. Outcomes in this population improve when they receive social support that is similar to their needs (ecological congruence). Mental health and support are controlled by social networks, and personal and environmental variables. Personal variables include mastery, self-esteem and perceived stress. Environmental factors are related to socioeconomic status and exposure to violence. **Level of Evidence** Likely to be effective **I** (3) - well-designed trial without randomization

Interventions for the Treatment of Depression in Adolescents - PSYCHOTHERAPY– Pregnant & Post-Partum Adolescents						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Logsdon, M. C., Birkimer, J. C., Simpson, T., & Looney, S. (2005). Postpartum depression and social support in adolescents	The purpose of this repeated measures design was to examine the effectiveness of a social support intervention in preventing depression in postpartum adolescents attending an alternative school for pregnant and parenting youths. Hypothesis predicted that the biggest improvement in rates of depression will be found in adolescents receiving both a written and a videotaped social support intervention. The information was provided by a 16-page pamphlet, and a videotape lasting 8 minutes.	Adolescents were randomly assigned to three treatment modalities: pamphlet, video, and to pamphlet plus video. Sample consisted of 128 participants, 32 to 36 weeks pregnant, 13 to 18 years old, mean age 16 years attending a school that usually enrolls 700 students a year. Adolescents were 56% African American, 38% White, and 6% were of other race/ethnicity. 74% lived with her parents, 13% with other family members, 5% lived with her partner and 8% had other living arrangements.	The following three questionnaires were filled out by the participants, first, at 32 to 36 weeks of pregnancy; and second, at 6 weeks postpartum. The Center for Epidemiological Studies of Depression (CES-D) The Postpartum Support Questionnaire (PSQ) Rosenberg's Self-Esteem instrument	The research hypothesis was not supported. No statistical differences were found among groups at 6 week postpartum. However, all groups had decreased levels of depression and improved parenting and self esteem. This study found that that an isolated intervention in pregnancy to strengthen social support is not sufficient to prevent symptoms of postpartum depression.	No costs regarding printing the pamphlet or production of the video were reported. Authors stated that the small effect size could be related to the reduced sample size.	Previous research indicates that adolescents with limited social support perceive that they not have adequate resources and tend to feel isolated. The lack of support might originate from places where they live, peers, school and family. **Level of Evidence** Likely to be effective **I**(3) - Well designed trial without a placebo group

TABLE 4

INTERVENTIONS FOR THE TREATMENT OF DEPRESSION IN ADOLESCENTS –

PSYCHOTHERAPY –

OTHER PSYCHOTHERAPY APPROACHES

Interventions for the Treatment of Depression in Adolescents – PSYCHOTHERAPY – Other Approaches						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Donaldson, D., Spirito, A., & Esposito-Smythers, C. (2005). Treatment for adolescents following a suicide attempt: results of a pilot trial	Study to examine the efficacy of a Skills based treatment (SBT), and to compare it to supportive relationship treatment (SRT). SRT consisted of unstructured meetings. This study had and active and maintenance treatment phases. The active phase was delivered in 3 months and consisted of six individual sessions and one family session. During the maintenance phase, participants received 3 monthly sessions. The therapists had the option of offering two additional family sessions and two crisis sessions.	Sample consisted of 39 adolescents, ages 12-17, mean age: 15 years old, following a suicide attempt in the Northeast, United States. 84% of the sample had attempted suicide by overdose, and seven (18%) were males and 32 (82%) were females. Subjects were 33(85%) white, four (10%) as Hispanic, and two (5%) African American. Youths were randomized to two treatment groups: SBT, and to supportive relationship treatment SRT. During individual sessions with the subjects, the adolescent's parents were contacted for collateral information, a model followed in community settings.	Outcome measures: Diagnostic Interview Schedule for Children (DISC). Suicide Ideation Questionnaire (SIQ) The Center for Epidemiologic Studies-Depression Scale (CES-D). The State-Trait Anger Expression Inventory (STAXI) Social Problem Solving Inventor-Revised (SPSI-R).	31 (80%) of the original sample finished treatment and were available for evaluations 6 months after completing the active phase. Decreased rates of depression and suicidal ideation were detected throughout this study, but there was no difference between the two treatment groups on any of the study outcomes at any time. There were six suicide attempts at 6-month follow up: 4/15 in SBT and 2/16 in SRT. Researchers reported that there was no difference in groups regarding taking prescribed psychotropic medications.	Limitations included small sample size and lack of control over prescribed medications. Authors were concerned that medications might have influenced results, and it was reported that all re-attempters were taking a serotonin reuptake inhibitor (SSRI) antidepressant. Researchers reported that the lack of difference between groups could be related to the maintenance of a therapeutic relationship with the therapists regardless of treatment content.	Suicide attempt was defined as any intentional self-injury, despite medical lethality, as long as intent to die was present. Two areas have been identified as deficient in adolescents with a history of suicide attempt, problem solving and affect management skills. These two areas were addressed in the SBT sessions. **Level of Evidence** Likely to be effective **I (**3) Well designed randomized trial of <100

Interventions for the Treatment of Depression in Adolescents – PSYCHOTHERAPY – Family – Other Approaches						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Sanford, M., Boyle, M., McCleary, L., Miller, J., Steele, M. (2006). A pilot study of adjunctive family psychoeducation in adolescent major depression: feasibility and treatment effect	The objectives of this study were to examine the feasibility of using Family Psychoeducation (FPE) and second to investigate the efficacy of FPE as an adjunct treatment in depressed adolescents.	This study was an unblinded, randomized, controlled trial. Sample consisted of 41 adolescents, ages 13 to 18 referred from outpatient clinics in Hamilton and London, Ontario (a region with a population of 500,000). About 2/3 of the sample was female, mean age 15.9. To be included, subjects had to meet DSM-IV criteria for major depressive disorder in the past 6 months. 31 participants were recruited in Hamilton and 10 in Ontario. Participants were randomly assigned to: FPE plus usual care or to usual care only.	Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present Episode Version (K-SADS-P) Children's Global Assessment Scale (CGAS). Outcome measures took place at baseline, 2 weeks, 3 months (mid-treatment)m 6 months (end of treatment), and at 9 months (3-month, follow up).	The London site had to be dropped from the study because of difficulty with participant retention and the results are from the Hamilton site. 31 subjects were randomized, 16 to FPE and 15 to the control group. FPE group had greater improvement at post treatment and at 3-month follow-up in the areas of social functioning, and in adolescent-parent relationships ($p<0.05$), parents in this group were also more satisfied.	Limitations include the small sample size. Other factors that might lead to biases are: (1) participants were not blinded to treatment assignment, (2) CGAS ratings were performed by the primary clinician and not by an independent evaluator, (3) the fidelity of the intervention was a self-rated by the therapists and not by an independent evaluator, and (4) the lack of standardization regarding the psychosocial interventions and psychotropic medications that patients in this study were receiving. A prior trial of FPE did not show benefit for this intervention. Based on their experience regarding the discontinuation of a treatment site, researchers stated that even if FPE is proven to be effective, it might be difficult to transfer it to clinical settings.	FPE consisted of 12 sessions of 90 minutes each in the home. It involved all family members who agreed to participate for the first 6 months of treatment and in booster-session three months later, at a follow-up visit. Main comorbid disorders in this study were generalized anxiety disorder, social phobia and use of alcohol and of illicit substances including marijuana and hallucinogens. **Level of Evidence** Likely to be Effective I (3) - Randomized trial with < 100 sample size

Interventions for the Treatment of Depression in Adolescents – PSYCHOTHERAPY / Motivational Interview in Primary Care – Other Approaches						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Van Voorhees, Bemjamin, W., ,Fogel, J., Reinecke,, M. A., Gladstone, T., Stuart, S., . . . Bell, C., (2009). Randomized clinical trial of an Internet-based depression prevention program for adolescents (Project CATCH-IT) in primary care: 12-week outcomes	Randomized-controlled trial based on 2 approaches to prevent depression in adolescents in primary care. 1. Motivational Interview (MI) lasting 5-10 minutes + Internet Program . Approach 2. Brief Advise (BA) lasting (1-2 minutes) + Internet Program. Researchers hypothesized that the MI group participants were going to participate more in the Internet program, and that the MI group were going to have less symptoms of depression.	84 subjects, ages 14 to 21, were randomized to either group (MI or BA) after they were found to have subthreshold depression for 3-4 weeks. 5 primary care sites participated in recruiting adolescents who presented with at least one core symptom of depression for at least two weeks. Recruitment took place from February 1, 2007 to November 31, 2007. The 14 Internet modules were based on cognitive behavioral therapy (CBT), interpersonal psychotherapy (IT) and a community resilience concept model (Project CATCH-IT: Competent Adulthood Transition with Cognitive-behavioral and Interpersonal Training).	Patient Health Questionnaire-Adolescent and Center for Epidemiologic Studies Depression Scale (CES–D). Measures were compared at baseline, and at 6 and 12 weeks.	Authors found that there was no difference in engaging in the Internet site in the MI, 90.7%, and BA, 77.5%, groups. CES-D -10 scores decreased in both groups (MI, 24.0 to 17.0, $p < .001$; BA, 25.2 to 15.5, $p < .001$). Even though there was no statistical difference between the MI and the BA groups, the MI group had less self-harm thoughts and subjects were less likely to experience a depressive episode (4.65% to 22.5% p=.023. The MI group also reported less hopelessness at the end of the intervention.	Primary care providers received training on delivering either the MI or the BA. This program was identified by researchers as cost-effective.	**Level of Evidence:** Likely to be effective **I** (3) well-controlled, randomized trial with <100 participants

TABLE 5

INTERVENTIONS FOR THE TREATMENT OF DEPRESSION IN ADOLESCENTS – PHARMACOLOGICAL MANAGEMENT

Interventions for the Treatment of Depression in Adolescents - PHARMACOLOGICAL						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Berard, R., Fong, R. Carpenter, D., Thomason, C., & Wilkinson, C. (2006). An international, multicenter, placebo controlled trial of paroxetine in adolescents with major depressive disorder	Researchers tested the efficacy, safety and tolerability of paroxetine in patients suffering from unipolar major depression during a 12-week, double-blind treatment phase.	This was a 12-week study of 275 adolescents who were randomized to receive active treatment with paroxetine or to a placebo group. 196 (71.3%) of the participants finished twelve weeks of treatment. This study included 10 different countries in 5 continents. Centers in Belgium and South African recruited the most subjects, 61 (22.7%) and 100 (30.8%) .	This study defined responder as at least a 50% decrease in these two scales: The Montgomery Asberg Depression Rating Scale. The Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS-L). Secondary outcome measure: Clinical Global Impression-Improvement (CGI-I).	Response rates for both group was not statistically different for the paroxetine group when MADRS scores were compared (baseline to treatment completion), p=0.702. No difference was found in and K-SADS- L scores either. Only the CGI-I scale showed a response to the paroxetine treated group (69% for paroxetine and 57.3% for the placebo group, p=0.045. Patient older than age 16 had a greater response to treatment.	Limitations included having no control over patient receiving outside therapy treatment, the study was conducted in different countries and researchers noted greater response in some countries. Because this study was a multicenter trial, the sample at each facility was small. Another possible limitation was that the MADRS has not been validated in adolescents with major depression. Researchers reported that patients taking paroxetine had tolerated it well. Adverse events were more commons in patients older than 16 years old. More subjects discontinued treatment related to adverse events in the paroxetine group: 11% versus 7% in the placebo group. Authors performed a post hoc analysis of suicidal behavior. Even though the difference was not statistically significant, (odds ratio, 2.15, 95% confidence interval= 0.45, 10.33; p = 0.502), the paroxetine group showed more suicide related events, 4.4% when compared to the placebo group, 2.1%.	Authors concluded that paroxetine had been well tolerated. **Level of Evidence** Benefit is balanced with harms **I**(3) - well-controlled, randomized trial with > 100 sample size

Interventions for the Treatment of Depression in Adolescents - PHARMACOLOGICAL						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Bridge, J. A., Iyengar, S., Salary, C. B., Barber, R. P, Birmaher, B., Pincus, H.A., . , .Brent, D.A. (2007). Clinical Response and risk for reported suicidal ideation and suicide attempts in pediatric antidepressant treatment: a meta-analysis of randomized control trials	A meta-analysis to assess the efficacy and risk of suicidal ideation in subjects taking antidepressant medications for major depressive disorder (MDD) obsessive compulsive disorder (OCD) and non-OCD anxiety disorders. Researchers conducted a search in PubMed from January 1988 to July 2006. They also obtained data from other agencies, such as: the FDA and British Medicines and Healthcare Products Regulatory Agency and the American Academy of Child and Adolescent Psychiatry	Researchers found 27 SSRI randomized, placebo-controlled trials in children and adolescent < 19 years old. From the total of 27 trials: 15 were on Major Depressive Disorder (MDD) with a total of n=343. Response rates were available for all but 2 MDD trials. Most of the trials were conducted in several sites, median number of sites: 21.	Authors used the DerSimonian and Laird random-effects model43 to obtain a pooled estimate of the risk difference. In 8 of the MDD trials the Clinical Global Improvement scales were used, and in 11 of the trials the Children's Depression Rating Scale-Revised was utilized.	A larger number of sites and longer duration of the episode was associated with less antidepressant efficacy. Children showed a higher placebo response rate. Response rate was 61% for patients on antidepressants and 50% for subjects receiving a placebo. Trials of SSRI's yielded larger efficacy effect sizes. The pooled risk differences in the (3) disorders studied did not reach statistical significance.	Authors stated that this meta-analysis encounter difficulties with the quality and quantity of the available data. They also mentioned that the number of trials was small in all of the (3) categories and this limits their results about treatment response and suicidal ideation or attempt. They also recognize that other factors could have an impact in the differences in the results of trials, such as t not having data on the subjects' baseline differences, protocol for dosing medications, and compliance with treatment Results for the risk difference estimates were lower in this study than the reported by the FDA estimates possibly because this meta-analysis included other studies; three of them were not available at the time of the FDA analysis	This meta-analysis included children and adolescents. It also studied data from OCD and other non-OCD anxiety disorders. Participants with MDD had a higher rate of suicide attempts in the placebo groups. **Level of Evidence** Recommended for practice **I(**1) - Meta-analysis of multiple, well-designed randomized controlled trials

Interventions for the Treatment of Depression in Adolescents – PHARMACOLOGICAL						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Cheung, A,H., Emslie, G.J., & Mayes, T.L. (2005). Review of the efficacy and safety of antidepressants in youth depression	Due to concern about the efficacy and safety of antidepressant medications, the authors conducted a review of published and unpublished randomized controlled trials, as well as of meeting abstracts. Studies in older antidepressants were not included because of the lack of data from clinical trials on Monoamine Oxidase Inhibitors (MAOI's) and the lack of efficacy reported for tricyclic antidepressants (TCAs).	Data from the studies reported by the FDA in 2004 regarding the safety of antidepressants were reviewed. Authors also searched MEDLINE and PSYCH Info for studies not reported to the FDA from the beginning until December 2004. A total of 17 studies were included in this review. 8 reports were published studies and 9 were unpublished.	Effect sizes were not calculated because of the missing data. Most of the studies used the Clinical Global Improvement (CGI) scale as their main outcome measure: (1=much improved & 2= very much improved).	**Fluoxetine:** (3) Trials. The first trial, children ages 7-17) by Emslie, et al., 1997, had positive results for fluoxetine. Second trial, (Emslie, et al, 2002 did not favor fluoxetine over placebo. The third trial was conducted by March et al. (2004), confirmed the efficacy of fluoxetine alone or in combination with psychotherapy. **Paroxetine:** (3) Trials. None of these trials has shown that paroxetine is more effective than placebo. **Sertraline**: (2) Identical trials. When data was analyzed separately there was no difference for active treatment, when results were pooled, adolescents had a better response than children, but the studies were not powered to detect a difference between groups. **Citalopram**: (1). Study by Wagner et al., 2004 showed benefit for Citalopram, while and an unpublished study (MHRA website) did not separate from placebo. **Venlafaxine**: (2). Studies, children ages 7-17, found no difference between medication and placebo. **Nefazadone**: One trial that failed to show significance at week 8. **Mirtazapine:** No differences were found in one trial.	Adverse Events: No deaths were reported in any of these trials. Lethality or intent of attempting was not reported in this study. Authors cited the FDA re-classification which reports a 2-3% increased in suicidal ideation or behavior in patients taking antidepressants. However, epidemiological reports have shown an inverse relationship between completed suicides and antidepressant use.	To obtain FDA approval for the treatment of depression of pediatric patients the FDA Modernization Act requires 2 positive placebo-controlled trials. **Level of Evidence** Recommended for Practice **I**(1) - systematic review of multiple well-designed, randomized, controlled clinical trials

Interventions for the Treatment of Depression in Adolescents - PHARMACOLOGICAL						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Cheung, A., Kusumakar, V., Kutcher, S., Dubo, E., Garland, J., Weiss, M., . . . , Levitt, A. (2008). Maintenance Study for Adolescent Depression. Brief Report	Researchers wanted to find out the efficacy of sertraline after the acute phase of treatment in depressed adolescents. Authors reported that the literature is increasing in regards to the acute phase of treatment, but they found a lack of evidence originated from randomized controlled trials about the risks or benefits in long-term treatment with antidepressants.	This was a randomized placebo controlled, discontinuation trial conducted in multiple sites. The initial 93 subjects were recruited between 1997-2000 in three clinics in Canada. Sample for the present study consisted of 22 adolescents ages 13-19 years diagnosed with major depression who had had a positive response to sertraline and who had not relapse during the open-label continuation treatment, which lasted 24 weeks. After 24 weeks, 13 subjects were randomized to sertraline and 9 to placebo. This maintenance phase lasted 52 weeks. Sertraline was tapered by 25% of the dose every week for the first 4 233ks of the maintenance phase.	Patients were assessed every two weeks. Inclusion criteria for the continuation phase was two consecutive Hamilton Rating Scale for Depression (HAMD-D) scores <9 and a decrease of > 50% in the HAM-D within 12 weeks of treatment. However, relapse during the maintenance period was determined by the clinical judgment of the treating clinician and not by HAM-D scores. Adverse events were monitored every 4 weeks during the continuation and maintenance phases by the Common Adverse and Side Effects Scale (CASES). CASES did not include measures for suicide.	38% of the patients in sertraline continued response to treatment, while in the placebo group, all 9 patients relapsed. No differences between the sertraline and placebo group in the areas of gender, comorbid anxiety and number of previous depressive episodes were found.	The major limitation in this study was its small sample size, but researchers found that this was a first step for future research in determining the efficacy of antidepressants to prevent recurrence of symptoms following acute treatment. The small size in this study was related to the low retention rate in the open-label treatment phase. Researchers discussed that, in this study, the efficacy of sertraline, a selective serotonin reuptake inhibitor, was examined and that these results might not be applicable to other medications within this group.	Three phases are recognized in the treatment of depression. The first phase, or acute period, lasts 8-12 weeks. The second phase, recovery, consists of treatment for 6 months, and treatment after 6 months is maintenance therapy. During the 12 week acute phase and 24-week continuation phase, >5% of subjects in the sertraline group complained of fatigue, drowsiness, dizziness, tremor, weight gain, headache, irritability, sweating and sexual dysfunction. **Level of Evidence** Recommended for practice **I** (3) – Well-controlled randomized clinical trial with <100 sample size

Interventions for the Treatment of Depression in Adolescents - PHARMACOLOGICAL						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Cohen, D. Deniau, E., Maturana. A., Tanguy, M. L., Bodeau, N., Labelle, R., . . . , Guile, J. M. (2008). Are child and adolescent responses to placebo higher in major-depression than in anxiety disorders? A systematic review of placebo-controlled trials.	Researchers conducted a search on the Medline database for randomized placebo controlled trials of medication for children and adolescents with diagnosis of Major depressive disorder (MDD), obsessive compulsive disorder (OCD), and anxiety disorder, AD, non OCD. The studies were published between January 1972 and October 2007.	From 70 studies, researchers found 23 trials that were relevant, with a total of 2533 patients. 1528 diagnosed with MDD, 371 with OCD and 634 with AD. 567 children, <12 years of age, and 1171 adolescents, ≥ 12 years old were included in this study.	ANOVA tests were performed to test response rates between groups.	The placebo response rates were for MDD: 49.6% (range: 17–90%) For OCD 31% (range: 4–41%) AD, non OCD 39.6% (range: 9–53%) The response rate to placebo was higher for children in all groups, but this was not statistically significant.	Therapeutic relationships and the regular meetings present in studies may help children and adolescents to improve their mood and this could be responsible for the placebo effect. Researchers reported that the studies used different methodologies especially in studies conducted before the late 90s. Other limitations included that the inclusion criteria was not strict, and in some trials there were children with depression in the anxiety trials and vice versa.	SSRIS have been prescribed since the 1980s and this type of medications have less reported side effects than previous antidepressants, such as monoamine oxidase inhibitors and tricyclic medications. Some argue that the use of SSRIs increased in the 1990s at a higher rate than the prevalence of depression in youths The efficacy of medications has been difficult to prove due to high placebo responses. **Level of Evidence** Recommended for practice **I**(1) - Systematic review

Interventions for the Treatment of Depression in Adolescents - PHARMACOLOGICAL						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Donnelly, C.L., Wagner, K.D., Rynn, M., Ambrosini, P., Landau, P., Yang, R., & Wohlberg, C. (2006) Sertraline in Children and Adolescents with Major Depressive Disorder	This study included the data of two (ten-week studies) placebo controlled, double blind trials followed by a 24-week open label study, an extension study for patients who finished one of the two previous studies. Researchers conducted a post hoc analysis using the CDRS-R and the CGI scales as improvement predefined criteria The purpose of this study was to compare time to first response and first persistent response among children and adolescents. . . .	This analysis included 62 children, 6-11 years old and 76 adolescents (ages 12 to 17) fished the open-label study. 13 sites were involved. Studies were conducted in the United States.	Children's Depression Rating Scale (CDRS-R) and the Clinical Global Impressions-Improvement (CGI-I).	Placebo response was high in both groups, especially in children. In children, CDRS-R. Response rate was 72.6% for sertraline and 66.7% in placebo, p=.387. On the CGI, the response rate was 65.5% for sertraline and 59.8% for placebo, p= .365. In adolescents, the CDRS-R showed a response rate for sertraline: 65.4%, placebo, 51.1%, p=0.37. In the CGI-I: response for sertraline was 60.4%, and for placebo 45.7, p= .043. First response: Regardless of being treated with sertraline or placebo, children had a faster time to first response than adolescents, but this response did not persist. When compared to placebo, sertraline had a faster time to first persistent response in adolescents.	In subjects taking sertraline, there were five suicide related incidents. Three occurred in children(two suicidal ideation and one suicide attempt) and two in the adolescent group (one suicidal ideation and a suicide attempt). In the placebo assignment, there were no incidents in the children's group. In adolescents, there were two suicide attempts (a paitent who attempted suicide twice). Adverse side effects, such as vomiting, were more common in children than adolescents. One adolescent discontinued the study due to "moderately" increased in liver function tests attributed to sertraline. One of the limitations in this study was the high response to placebo.	**Level of Evidence** Recommended for practice **I**(3) well-designed trial without randomization

Interventions for the Treatment of Depression in Adolescents - PHARMACOLOGICAL						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Dubicka, B., Hadley, S., & Roberts, C. (2006). Suicidal behavior in youths with depression treated with new-generation anti-depressants meta-analysis	This meta-analysis re-examined the data used by the Committee on Safety of Medicines (CSM) on children and adolescents. The CSM meta-analysis presented all self-harm and suicide-related events. In this meta-analysis, data on suicidal ideation and attempts were analyzed separately to distinguish between risks for behaviors and thoughts. The data was divided into 3 levels of detail. Number 3 was used for the most detailed on suicide related events. Researchers also did a literature review to find newer information by searching Medline, PsychINFO for the period January 2004 to August 2005, but no pertinent medication trials were found.	Subjects were ages 6-18 years. Most trials did not separate children from adolescents. Only Citalopram divided the data for children and adolescents. The studies included were published and unpublished, randomized, placebo-controlled clinical trials lasting 8-12 weeks. Fluoxetine had three published trials, one unpublished and one for the treatment of obsessive compulsive disorder. Sertraline had two trials which were published in one article. Citalopran had two trials, Authors found three trials for paroxetine, two for venlafaxine and two for mirtazapine. Researchers state that these types of studies are powered to detect therapeutic effect and not adverse effects.	The data were analyzed by a user-written stata procedure. Tests of homogeneity were performed to see if the treatment effect showed differences between medications, and no difference was found for all self-harm and suicide-related events.	Self-harm or suicide-related events presented in 71 of 1487 or 4.8 % of youths treated with antidepressants and in 38 of 1254 (3.0%) of the ones in the placebo groups. If reported in terms of the number needed to treat (NNT), 57 adolescents would need to be treated for one of them to experience an event involving suicidality. Thoughts of suicide presented in 9 of 738 (1.2%) of patients taking citalopram, mirtazapine, sertraline and venlafaxine. Self-harm occurred in 19 of 569 (3.3%) of youths treated with citalopram, mirtazapine, and Sertraline. Suicide attempts presented in 19 of 992 (1.9%) youths on mirtazapine, fluoxetine, paroxetine and Sertraline, compared to 9 of 773 or 1.2% on placebo.	No suicides were reported in any of the arms of the studies included. The results of this meta-analysis showed that youths treated with antidepressants had a higher risk for suicidal thoughts, self-harm or suicide attempts, with odds ratio of 1.70% defined as a small, but statistically significant finding. This was explained as 5 in 100 children taking antidepressants could experience self-harm or suicidality when compared to 3 out of 100 children in a placebo group. Researchers advise that results of individual studies because they are based on small number of participants. Limitations cited were the inclusion of unpublished studies whose methodological approaches were not always available. Also, studies used different methodology and this makes it difficult to obtain the needed data. Researchers cautioned that suicide completion and suicidal behavior is part of depression in adolescents, and that a British study found that 41.2 % of adolescents with depression had attempted to harm, hurt or kill themselves, and because studies exclude patients with a history of suicide attempts, their results may not be applicable to clinical practice. Future studies should be designed to measure and distinguish between self-harm, suicidal thoughts and attempts. Researchers also advise to include children with severe depression in studies.	The results of this meta-analysis were compared to results from an FDA report issued in 2005. In this report, the risk ratio for "definite suicide", excluded non-suicidal self harm. When the FDA report took into consideration all the trials for major depression, the risk ratio, for all youths being prescribed antidepressants, was 1.7 (95% CI 1.05–2.77). When all suicidal events were taken into consideration, the relative risk was slightly elevated, 1.81 (95% CI 1.19–2.77). **Level of Evidence** Recommended for Practice **I** (1) Meta-analysis of multiple, well-designed, randomized trials

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Emslie, G. J., Ventura, D., Korotzer, A., & Tourkodi-mitris, S. (2009). Escitalopram in the treatment of adolescent depression: a randomized placebo-controlled multisite trial	Authors conducted a double-blind, placebo-controlled trial from April 2005, to May, 2007 in 40 sites in the United States. This study was sponsored by the maker of escitalopram, Forrest Pharmaceuticals. Patients were started with Escitalopram 10 mg. a day. This dose could be increased at the end of 3 weeks to 20 mg/day. Patients were evaluated at the end of weeks 1, 2, 3, 4, 6 and 8.	316 were randomly assigned to the escitalopram (n=158) or to the placebo group (n=158. Youths were 12 to 17 years. In the placebo group, 58.6% were female and 78.3% were Caucasian. In the escitalopram group 72.9% were Caucasian. All participants had to met a diagnosis of major depressive disorder (MDD) according to DSM-IV criteria for at least 12 weeks at the time of screening. This intervention lasted 8 weeks. 52 participants had taken medications in the past, and 32 of this patient were considered non-responders to medications, 16/23 of these patients were in the placebo group and 16/29 were in the escitalopram group.	Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children--Present and Lifetime version Children's Depression Rating Scale-Revised (CDRS-R) Clinical Global Impressions Severity Children's Global Assessment Scale (CGAS) Clinical Global Impressions-Improvement; (CGI-I)	259 participants finished this trial. 133(84.7%) in the placebo group and 126 (81.3%) were in the medication group Authors reported a difference in favor of escitalopram when comparing baseline to endpoint treatment scores in CDRS-R (p=.022). When response was defined as at 40% in the CDRS-R score, response rate was 59.1% for escitalopram and 48.4% for placebo (p=0.06). Difference in scores were noticed starting at Week 6, p=0.06. Greatest placebo response was at Week 4 (p=0.001). Responders according to the CGI-S scores were significantly in favor of escitalopram (p=0.03). There were no post-treatment differences in CGAS scores.	The rate for exiting this trial prior to completion due to adverse effects was the same for placebo and for escitalopram (118 subjects, or 75.2%), were in the placebo group and 121, 78.1%, were in the medication group. The only adverse effect that had a double presentation in the escitalopram group was influenza-like symptoms (3.2% placebo and 7.1% for Escitalopram). The most common side effects were headache, menstrual cramps, insomnia, nausea, abdominal pain, inflicted injury, pharyngitis, fatigue, influenza-like symptoms, rhinitis, vomiting, diarrhea, and upper respiratory tract infections. In the case of "inflicted injury", most of them were determined to be accidental. There were two cases considered as "serious adverse events.' One patient in the placebo group had "suicidal tendency" and one in the escitalopram group presented with self-injurious behavior.	Because of the concerns about antidepressants and suicidality in adolescents with depression, these authors used the following scales to monitor this possible adverse event by using the: 1) The Clinician and rated suicidal behavior (MC-SSRS) 2) Patient rated scales measured changes in suicidal ideation (SIQ-JR) **Level of Evidence**: Recommended for practice **I(**2) – Well-controlled, randomized clinical trial with adequate sample size NOTE: Because of the results favoring escitalopram in CDR-R scores in this and in another unpublished study, escitalopram was approved by the FDA for the acute and maintenance treatment of adolescent major depression in 05/23/09 (Hitt, E. 2009). Fluoxetine used to be the only FDA approved medication for this age group.

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Emslie, G.J., Kennard, B. D., Mayes, T.L., Nightingale, J., Carmody, T., Hughes, C.W., . . . , Rintelman, J. W. . (2008) Fluoxetine versus placebo in preventing relapse of major depression in children and adolescents	The purpose of this study was to evaluate continuation of treatment with fluoxetine to prevent relapse to major depression. This trial was carried out at one site only and it spanned for 36 weeks. Double-blind randomized discontinuation trial, from August 2000 to July 2006. Patients were assessed by a psychiatrist weekly during 1-4 weeks of treatment and then bi-weekly until the end of the acute phase of treatment at week 12. According to authors, in 2003, the FDA recommended to include 12 years old in the adolescent group.	102 subjects, mean age 11.5 ears, entered continuation treatment (50 were randomized to fluoxetine and 52 to placebo). To be included in the continuation phase, participants had to be in remission or to have responded to treatment. This study include n=28 children ages 7-11, and n=24, adolescents ages 12-18 years. 75% of participants were Caucasian. No differences were reported for age, gender, baseline scores, and duration and number of previous episodes. Subjects taking medications for ADHD on the acute phase were allowed to continue taking them. Patients were evaluated by a psychiatrist biweekly during weeks 12-16, and monthly for weeks 16 to 36.	Primary measures were relapse and time to relapse. Researchers defined relapse as a score of ≥40 in the CDRS-D for at least two weeks. However, even if the CDRS was <40, relapse could also be determined by clinical assessment. Secondary CGI measures were used to assess for severity.	Subjects in the placebo group had higher rates of relapse, n = 36 (69.2%) in the placebo group and n=21 (42%) in the fluoxetine group. Patients who had no residual symptoms at the time of randomization were six more times likely to relapse when placed in the placebo group. Median time to relapse was 8 weeks in the placebo group after fluoxetine discontinuation. Researchers also reported a median time of 14 weeks for "full relapse" for the placebo group. Authors were not able to determine the time to relapse for the fluoxetine group, but it was reported it was greater than 24 weeks.	No costs were reported for this intervention. After week 12, patients entered the continuation phase if they had achieved remission (CGI score of 1 or 2, much or much improved), and a decrease of at least 50% in the Children's Depression Rating Scale- Revised (CDRS-R), or if they had achieved remission (CDRS-R score ≤ 28). Subjects were then randomized to continue the same dose of fluoxetine they were receiving during the acute phase or to placebo. Assessments also included evaluation for adverse events, which may include incidents leading to death, and failed suicide attempts among others. Authors reported that this is the first randomized, placebo-controlled trial assessing the efficacy of continuation treatment with fluoxetine in children ages 7-18 with a diagnosis of major depressive disorder. Researchers addressed safety concerns regarding stopping fluoxetine by excluding patients with a history of severe suicide attempts (as recommended by the National Institute of Mental Health). Consent was obtained separately for the continuation phase.	Researchers recommend future studies to examine different treatment alternatives that could increase remission rates and prevent relapse. **Level of Evidence** Recommended for practice **I** (2) – well-controlled randomized clinical trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - PHARMACOLOGICAL						
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Emslie, G.J., Findling, R.L., Yeung, P.P., Kunz, N.R., & Yunfeng, L.I. (2007). Venlafaxine ER for the treatment of pediatric subjects with depression: Results of Two Placebo-Controlled Trials	Researchers evaluated the safety, efficacy and tolerability of venlafaxine extended release (ER) in two multicenter, randomized, double-blind, and placebo controlled trials. These studies took place from October 1997 to August 2001 in 50 sites in the United States. Study 1 was carried out at 14 academic sites and Study 2 at 37 facilities.	Subjects were ages 7 to 17 years old who met the criteria for major depressive disorder (MDD) randomized to two treatment arms: Venlafaxine and placebo for 8 weeks. There were 158 participants in Study 1 and 124 in Study 2. A total of 48/179 subjects in the placebo-groups, and 59/182 in the venlafaxine ER trials withdrew from study.	Childhood Depression Rating Scale-Revised (CDRS-R) Hamilton Rating Scale for Depression (HAM-D) Montgomery-Asberg Depression Rating Scale (MADRS) Clinical Global Impression Severity (CGI-S)	Adolescents, ages 12 to 17 years old, had the most important decrease in CDRS-R when taking venlafaxine, but this result was not significant (effect size was 0.28136). In children, subjects ≤ 11 showed no significant differences on any outcome variable (researchers reported that a high placebo response might have made difficult to detect a treatment difference). Presence of adverse effects, including suicidal ideation, which were higher in the venlafaxine treated, groups 7 of 11 subjects. One patient withdrew from the venlafaxine group due to a seizure.	Increased heart rate of at least 4 beats per minute (bpm) was observed with venlafaxine. This change was statistically significant. A decrease in weight of 0.5 kg was reported in the venlafaxine ER group. Increases in blood pressure were also reported for the venlafaxine ER group, 2-3 mmHG at some points. Limitations included the short duration of treatment, 8 weeks. Results of this study might not be applicable to clinical practice due to not including patients with comorbidities.	>0.6 effect size is needed to reflect clinical relevant differences between treatment modalities. **Level of Evidence** Benefit is balanced with harms **I**(2) - well-controlled, randomized trial with adequate sample size

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Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Emslie, G.J., Yeung, P.P., & Kunz, N. (2007). Long-term, open-label venlafaxine extended-release treatment in children and adolescents with major depressive disorder	This was an open-label study conducted in 13 clinical facilities from April 2000 to September 2001. It included children (7-12 years of age) and adolescents, 13-17 years old. This trial consisted of a 6-week acute treatment followed by a continuation period of up to 6 months with venlafaxine ER, a norepinephrine reuptake inhibitor (SNRI).	From the original sample of 86 participants, 69 (80.2%) received treatment for 6 weeks, and only 36(42%) continued treatment for 6 months. Participants were predominantly white, 69%, and almost half of them were female. Subjects had do have depressive symptoms for one month prior to entering the study, including a CDRS-R score of >40 and a score ≥4 in the Clinical Global Impressions-Severity (CGI-S) at the screening and baseline visits. Open label trials limit the possibility of evaluating the effectiveness and safety and long term treatment (6 months).	The primary outcome measure was the Children's Depression Rating Scale-Revised (CDRS-R).	The most improvement took place at 6 weeks of treatment. **Response** At week 6, 45% of the subjects had responded to treatment. At the end of 6 months, 55% had responded to treatment. **Remission** At week 6, the rate of remission was 32%, followed by 36% at Week 8, and at the end of the study, 6 months, it was 45% (38/85).	The costs incurred were not reported. Main side effects included headache, nausea, infection, abdominal pain, vomiting and pharyngitis. There were no suicide in these studies, but two participants had a suicide attempt and two experienced hallucinations. Authors reported a high dropout rate, 20% of the sample left the study in the first 6 weeks of treatment, and less than half of the patients finished the six months of treatment, n=36. Authors reported a significant increase on mean heart rate at the end of 6 months (5.77 beats per minute); (p=.001). Important raises in blood pressure occurred in two patients and one patient had a significant elevated pulse. One subject had a significant weight gain (≤ 7%of body weight) and 5 patients experienced a clinical significant weight loss (≥7% of body weight). An increase in baseline chloride and a decrease in alkaline phosphate has been reported in patients taking venlafaxine.	Two venlafaxine ER studies, lasting 8 weeks, showed modest response in adolescents, but not in children. Venlafaxine is considered a third-line treatment for the treatment of depression according to the Texas Children's Medication Algorithm Project. Treatments with selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs) have been linked to a risk for hostility. 15% of the subjects were enrolled in this study while receiving psychotherapy. **Level of Evidence** Benefit is balanced with harms **I**(3) well designed trial without randomization with < 100 sample size

Interventions for the Treatment of Depression in Adolescents - PHARMACOLOGICAL						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Emslie, G.J., Wagner, K.D., Kutcher, S., Krulewicz, S., Fong, R., Carpenter, D.J., . . . , Wilkinson, C. (2006). Paroxetine treatment in children and adolescents with major depressive disorder: a randomized multicenter, double-blind, placebo-controlled trial	The purpose of this study was to examine the effectiveness and side effects of paroxetine in the treatment of depression in children and adolescents in an 8-week trial.	Study was a prospective, multicenter, randomized, double-blind, placebo controlled trial conducted at 40 centers in the United States and one center in Canada from March 2000 to January 2001. Sample consisted of 206 subjects: male and female children (ages 7-11) and adolescents (12-17 years old). 104 participants were randomized to the paroxetine group and 102 to the placebo group. Only 73.4% 149/203 of patients completed the 8-week study. Patients in the paroxetine group had a higher rate of withdrawal from this study. In the 7-11 year old group, the withdrawal rate was larger, 38.8%, 19/49, while in the adolescent group, the rate was 12/8%, (6/47) participants.	Outcome measure was changes from baseline in the Children's Depression rating scale-Revised-(CRSD) Mean score at baseline was 61.7, moderate to severe depression. Researchers also used the Clinical Global Impressions Item (CGI-I) as a secondary measure. Safety was assessed by subjects reporting suicidal and/or homicidal ideation by spontaneous report	At the end of 8 weeks, paroxetine failed to show to be more effective than placebo in the treatment of depression in children and in adolescents. 22.7% of the participants had a comorbid psychiatric disorder; attention deficit hyperactivity disorder was the most common one. Side effects, cough, dyspepsia, vomiting and dizziness, were twice more likely to present in the paroxetine group than in the placebo group. Suicidal behavior occurred in (2) of the patients in the paroxetine group and in (1) of the placebo group.	Each site was responsible for training the raters. Authors consider that the high placebo effect in this study, could be related to the short duration of the study and also to raters not being familiar with the rating scales and to receiving training only once. Another limitation is the high number of sites used in this study.	At the time of this study, fluoxetine was the only medication approved by the FDA for the treatment of depression in patients younger than 18 years old because only fluoxetine has more than one RCT with positive results. Two previous studies on adolescents using paroxetine yielded unclear results. **Level of Evidence** Benefit is balanced with harms **I**(2) well-controlled, randomized trial with adequate sample size

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Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Hammard, T.A., Laughren, T., & Racoosin, J. (2006). Suicidality in pediatric patients treated with antidepressant drugs.	Data were obtained from 24 randomized controlled trials, 23 of them were carried out by 9 pharmaceutical companies. An additional trial was funded by the National Institute of Health (NIH), the Treatment for Adolescents with Depression Study (TADS). There were 16 trials for major depressive disorder, 8 trials for obsessive compulsive disorder, 2 trials for attention deficit hyperactivity disorder and 1 trial for social anxiety included in this meta-analysis.	Data from 4582 subjects was used in this analysis. 20 trials were used in the risk analysis for suicidality because 4 trials did not show any suicidal incidents in the placebo or control groups. After reviewing all suicide related adverse events (SREs), 109 events plus 11 from TADS were considered relevant, and they were grouped in: n=89: primary outcome was suicidal behavior or ideation and n= 120 possible suicidal ideation.	"Worsening Suicidality" was determined by an increase of 2 or more points in item 13 of the Children's Depression Rating Scale-Revised, or on item 10 of the Montgomery Asberg Rating Scale, or an increase of 3 points in the Hamilton Depression Rating Scale.	TADS was the only trials that showed a statistically significant risk for suicidal ideation and behavior in the fluoxetine treated group. Risk ratio 4.62% (95% confidence interval 1.02-20.92. The overall risk ratio for selective serotonin reuptake inhibitors in this meta-analysis was 1.66 (95% CI, 1.02-2.68) for major depressive disorder. For all antidepressants , including all diagnosis, the risk ratio was 1.95 (95% CI, 1.28-2.98). The Risk Difference indicated that in 100 patients taking antidepressants: 1 or 3 may experience an increase in suicidality.	The FDA has approved fluoxetine for use in pediatric MDD and obsessive-compulsive disorder, and fluvoxamine and sertraline have indications for pediatric obsessive-compulsive disorder. Authors suggested that the results need to be taken with caution since some of the databases for the drugs studied were small and were not adequately powered. There were also differences on how adverse events were recognized. Researchers mentioned that the broad approach to find SREs may explain how SREs were excluded from previous analysis.	**Level of Evidence** Recommended for practice **I** (1) Meta-analysis of multiple, well-designed, randomized trials

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Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Hazell, P., O'Connell, D., Heathcote, D., & Henry, D.A. (2009). Tricyclic drugs for depression in children and adolescents	Authors conducted this systematic review because of the need for effective and safe treatments for depression in children and adolescents. To be included, studies had to be randomized controlled trials comparing oral tricyclic medications to placebo in the treatment of depression in children and adolescents, ages 6-18.	Authors searched for studies in the CCDAN and the CCDANCTR on 12/2/2008. They also contacted authors who had pertinent abstracts in conferences of the American Academy of Child and Adolescent Psychiatry, and hand searched the Journal of the American Academy of Child and Adolescent Psychiatry. Authors included 12 studies published between 1981 to 1998. Total number of subjects was, n=506. 7 studies were done in outpatient settings and five in inpatient facilities. Seven studies included children ages 12 and over, and two trials incorporated children and adolescents.	Outcome measures used by the studies included were: 1. Schedule for Affective Disorders and Schizophrenia for School-Age Children (Kiddie-SADS), combined child and parent report. 2. Children's Depression Rating Scale (CDRS). (4) 3. Bellevue Index of Depression (BID) 4. Children's Depression Inventory (CDI) 5. Hamilton Depression Rating Scale (HAM-D) 6. Depressive Adjective Checklist (DACL)	13 studies were chosen, but authors reported only 12 met criteria for a meta-analytic analysis. Medications studied were compared to inactive placebo in the following studies: imipramine in (5) trials, amitriptyline in (4) trials desipramine in two trials and nortriptyline in two other trials. These data did not show that tricyclic drugs were more effective when compared to placebo. A subgroup analysis reported tricyclic drugs were more effective for adolescents than for children (effect size=0.47).	Only 5 studies reported side effects consistently. Significant side effects were vertigo, hypotension, tremor, and dry mouth. Other adverse events most commonly reported in the treatment groups were tiredness, perspiration and micturation problems. Authors discussed other risk factors associated with the use of tricyclic drugs such as their lethality in overdose and the possibility of cardio toxic effects even when used in therapeutic doses. There was also a concern for the possible "switch" to mania and in the induction of rapid cycling bipolar disorder. Researchers discussed that the small effect size of these medications could also be related to shorter duration of the studies, 4 to 10 weeks. Other possibilities discussed for the lack of efficacy of these medications in this population, was that these drugs affect the adrenergic system and this neural pathways do not fully develop until adulthood. Based on this pharmacological theory, selective serotonin reuptake inhibitors, like fluoxetine, might be more effective in children and adolescents because the serotonergic system develops earlier in life, ages 5 to 6.	Researchers suggested that new research should be directed towards new medication approaches and to non-pharmacological treatments, such as psychotherapy. Authors also stated that there could be a possible use of tricyclic drugs in the management of adolescent depression, but the effects are likely to only be modest. **Level of Evidence** Effectiveness not established **I**(1) - Meta-analysis of multiple, randomized, controlled clinical trials

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Heiligenstein, J. H., Hoog, S .L., Wagner, K. D., Findling, R .L. Galil, N., Kaplan, S., . . . Jacobson, J. G. (2006). Fluoxetine 40-60 mg versus fluoxetine 20 mg in the treatment of children and adolescents with a less-than-complete response to nine-week treatment with fluoxetine 10-20 mg: a pilot study.	The purpose of this study was to examine if the titration of fluoxetine to 40-60 mg/day was more effective than fluoxetine 10-20 mg/day to achieve treatment response in patients who had failed to benefit from a 9 –week trial of fluoxetine.	After a 9 weeks of acute treatment al with fluoxetine, subjects who had not responded to treatment were randomly assigned to two groups. Group 1: continuation of 20 mg/d of fluoxetine. Group 2: Raise the dose of fluoxetine to 40 mgs/day (n=15). If patients were still not responding to treatment after 4 weeks, subjects had the option of increasing dose to 60 mg/day (n=14).	Response in this study was measured as a ≤ 30% decrease in the Children's Depression Rating Scale-Revised (CDRS-R) score.	At the end of this trial,, 10/14 patients (71%) on 40-60 mgs/day became responsive to treatment compared to 5/14 patients (36%) on the 20 mg/day group (p=0.128). Both groups had a decrease in CDRS scores. Fluoxetine 40-60 mg/day: -9.4. Fluoxetine 20 mg/day: - 1.5 (p= 0.099). .	Authors recognized that this study did not have an adequate sample size to detect differences between the two groups.	**Level of Evidence** Recommended for practice **I (**3) - Randomized trial with < 100 sample size

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Hetrick, S., Merry, S., McKenzie, J., Sindahl, P., & Proctor, M. (2007) Selective serotonin reuptake inhibitors (SSRIs) for depressive disorders in children and adolescents (Review)	Authors conducted a Search on different databases: MEDLINE (1966-October 2005) • PSYCINFO (1886-October 2005) • CENTRAL in the Cochrane Library Out of 12 published and unpublished randomized controlled trials that met inclusion criteria, only 10 had data that could be used in this systematic review. Studies were conducted in multiple centers. They also took place in many countries. Three reviewers determined the eligibility of the studies. In case of disagreement, the decision was made by a 4th reviewer. SSRIs included were fluoxetine, fluvoxamine, paroxetine, citalopram, escitalopram and sertraline.	The risk of bias was addressed by using quality ratings by Moncrieff and colleagues. The Cochrane Colloquium, Media advertisement was also used to determine the risk for bias. Subjects were treated in outpatient settings and were 6 to 18 years old who met criteria for a diagnosis of depressive disorder according to the DSM or ICD. Children were defined as subjects between the ages of 6-12 and adolescents: 13-18 years old. This systematic review included subjects between the ages of 6-18 years old.	Schedule for Affective Disorders and Schizophrenia For School-Age Children (Kiddie-SADS). 2. Children's Depression Rating Scale (CDRS) 3. Bellevue Index of Depression (BID) 4. Children's Depression Inventory (CDI) 5. Hamilton Depression Rating Scale (HAM-D) (3) 6. Depressive Adjective Checklist (DACL)	After 8 to 12 weeks of treatment children had "responded "to SSRIs (RR 1.28, 95% CI 1.17 to 1.41). However, there was also an increased for suicidal ideation and behavior on the subjects taking SSRIs (RR 1.80, 95% CI 1.19 to 2.72). Fluoxetine was the only medication that showed effectiveness in three studies in by improving symptoms in both children and adolescents (CDRS-R treatment effect -5.63, 95% CI -7.38 to -3.88).	No information on cost was provided. Researchers identified different areas that could interfere with the results in these studies, such as the high attrition rate, 19% to 38% of participants. The definition of response and remission was not the same across studies. For example, the parameters set by an escitalopram study to define response were used to define remission in two fluoxetine studies.	There were no completed suicides in these studies, and this was assessed by using the Medicines and Healthcare Products Regulatory Agency (MHRA) report **Level of Evidence** Recommended for practice **I (**1) - Systematic review of multiple well-designed, randomized, controlled clinical trials

Interventions for the Treatment of Depression in Adolescents - PHARMACOLOGICAL						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training and Cost Training Needs and Costs	Level of Evidence and Comments
Hughes, C.W., Emslie, G.J., Crismon, L., Posner, K. Birmaher, B., Jensen, P., . . . Trivedi, M. H. (2007). Texas Children's Medication Algorithm Project: Update from Texas Consensus Conference Panel on Medication Treatment of Childhood Major Depressive Disorder	The purpose of a conference held on January 14 and January 15 in Dallas Texas was to update consensus guidelines for the use of medications in the treatment of depression in children and adolescents. This conference included the opinions of clinicians, researchers, administrators and patients and their families.	Algorithms for major depression, with and without psychotic features, as well as for depression and comorbid attention deficit hyperactivity disorders were updated. Other symptoms, such as suicidality, aggression and irritability were also addressed. This algorithm is addressed to subjects ages 6 to 17. Due to the high placebo response rate found in studies, a waiting period is recommended prior to starting medication, especially in young children. However no specific time has been reported.	This guideline cited multiple studies using a variety of outcome measures. Data was classified as A if it was originated from randomized controlled trials. B = open label and large epidemiological studies. C= case series and expert consensus.	Stages of Treatment: **Stage 0**: This stage consists of diagnostic assessment and monitoring. Clinicians, informed parents and patient decide treatment. This may include "watchful waiting" or the initiation of medication if needed. Information from parents and school are needed to make this decision. **Stage 1:** SSRIs are recommended as monotherapy are fluoxetine, sertraline and Citalopram. Fluoxetine remains as first choice unless contraindicated. **Stage 2**: If the patient did not have adequate improvement, switch to another SSRI. Paroxetine and Escitalopram are included in Stage 2. **Stage 2A**. Augmentation with bupropion or mirtazapine. **Stage 3.** Switch to Alternate Antidepressant Monotherapy (Bupropion, Venlafaxine, Mirtazapine and Duloxetine). Nefazadone was not included in Stage 3 due to adverse side effects including hepatotoxicity. No trials in this population have been conducted with duloxetine. For depression with psychotic symptoms, add a second generation antipsychotic. In antidepressants, dose titration should be considered every 4-6 weeks in cases of weak improvement. Clinicians are advised to wait 8 to 10 weeks prior to deciding medication was a failure. Electroconvulsive Therapy is recommended for severe cases. Clinicians should also evaluate for the addition of psychotherapy if patient is not achieving treatment goals during any stage of treatment.	Even though the FDA has issued concerns about suicidality in children and adolescents treated with antidepressants, an inverse relationship has been found between prescriptions written and suicides in the communities. Centers for Disease Control reported a 14% increase in suicide rates in 5 to 19 year olds since the FDA issued their concerns about suicidality and antidepressants. Clinicians should be trained to assess suicide at baseline because higher rates of suicide have been found one month prior to treatment. Knowledge about past suicide attempts, family history, current stressors and medical problems are important information as well as assessment of emerging suicidality. Limitation cited by authors was the reduced number of RCTs found in this population.	Treatment of depression is subdivided into three phases: acute, continuation and maintenance. Options for treatment modality should be discussed with patient and their families. Cognitive behavioral therapy (CBT) and interpersonal therapy have shown to be effective treatments in mild to moderate depression. Authors explain that guidelines do not limit clinical judgment, but that it does provide a framework to facilitate clinical decisions. **Level of Evidence** Recommended for practice **I** (1) - Systematic review

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Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Moreno, C., Arango, G., Parellada, M., Shaffer, D., & Bird H. (2006). Antidepressants in child and adolescent depression: where are the bugs?	Authors performed a literature search which included hand retrieval of studies, including online trials. Authors reviewed evidence on antidepressant in adults first to offer possible differences between response in children and adolescents. Researchers focused on efficacy and not on safety in this review. Data was obtained from published and unpublished randomized controlled trials. Databases explored were: Medline and the Cochrane Database of Systematic, including all articles until September 2006.	32 trials addressing pediatric depression were found relevant. These trials consisted of 13 trials looking at tricyclic antidepressants (TCAS), 12 at SSRIs, and seven at "newer" antidepressants (venlafaxine, mirtazapine, and nefazodone). These newer medications did not show statistically significant results in favor of antidepressants.	Diagnostic criteria for depression vary slightly in the DSM-IV and ICD-10.	Most of the trials with TCA's have not shown significance. About two thirds of published unpublished trials with SSRIs have also not shown a difference. Citalopram separated from placebo in one of two trials. Sertraline showed a positive result when two studies were analyzed together, but not when assessed individually. One study for escitalopram did not show significance. Three trials with venlafaxine did not separate from placebo. Remission was higher in patients taking medications, (41.3% for fluoxetine, 36% for citalopram and 63.3 for paroxetine).	No information regarding costs was provided. Authors found difficult to compare data of the studies used for this systematic review because improvement between drug and placebo was determined by different outcome criteria for all the studies. The FDA issued a requirement for a black box warning in 2003 regarding the possibility of SSRIs increasing the risk for suicidal behavior in children and adolescents. Researchers reported that the lack of efficacy for most of the medications, in addition to methodological disparity, could be due to differences in neurotransmitter systems because the serotonin structure is very similar to the adult neurons by ages 5 or 6 while the noradrenergic system (TCAs) is not completely built until adulthood. Need for newer medication approaches were recognized because in patients taking an SSRI, 30-40% of the subjects continue to experience subsyndromal symptoms.	Due to positive results in two randomized trials for fluoxetine, it is recommended to start treatment in children and adolescents with this medication. It is important to note that the response by children and adolescent varies from results in adults possibly to due differences in developmental stages, antidepressant metabolism, pharmacokinetics, and toxicity. Young children may have higher response to placebo because they tend to respond to therapeutic contact. Also, the variety of symptoms of depression in this population may interfere with studies not showing a positive effect. **Level of Evidence**: Recommended for practice **I (**1) Meta-analysis of multiple, well-designed, randomized controlled trials.

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Papanikolau, K., Richardson, C., Pehlivanidis, A., & Papadopoulos, D.Z. (2006). Efficacy of antidepressants in child and adolescent depression: a meta-analytic study.	Authors conducted a computerized and manual search of the literature starting in 1966 for controlled and uncontrolled trials on children and adolescents who had a diagnosis of depression and had been treated with pharmacological management. Databases used were MEDLINE and the Cochrane Database Systematic Reviews. The purpose of this meta-analysis was to determine if tricyclic (TCA's), selective serotonin reuptake inhibitors (SSRIs) and all kinds of antidepressants are superior to placebo.	18 controlled and 23 uncontrolled studies were included in this meta-analysis. 1405 subjects were part of this meta-analysis. Authors pooled the results for the controlled and uncontrolled trials separately and also combined them.	Studies were assessed using a modified version of the Chalmers method for randomized controlled trials. This method uses a scale of 0-100 (0-60 for the study protocol; 0-30 for statistical analysis and 0-10 for the presentation of results. Authors found a quality score for the controlled trials between 0.31 and 0.91. Correlation between two raters was 0.887.	Even though authors included data from uncontrolled studies to increase the sample size, this did not change previous negative results for tricyclic (TCAs) antidepressants. Age also did not make a difference for TCAs. Conversely, SSRI trials for controlled and uncontrolled trials yielded significant statistical results for children and adolescents. (odds ratio 1.83, 95% CI 1.40–2.40) and for adolescents alone (odds ratio 1.78, 95% CI 1.03–3.04). In five controlled SSRI trials the odds ratio was 1.84 (95% CI 1.35–2.50) for children and adolescents, and for adolescents only: the odds ratio was 1.78, 95% CI 1.03–3.04. All controlled trials of antidepressants were superior to placebo (odds ratio 1.52, 95% CI 1.16–1.98). Uncontrolled trials showed positive results for children and adolescents (odds ratio 1.59, 95% CI 1.29–1.96) and for only adolescents (odds ratio 1.45, 95% CI 1.06–1.98).	Researchers found the lowest response to antidepressants in the children only group. They also state that the lack of efficacy for TCAs could be related to the heterogeneity of small samples, the diversity of outcome measures, the lack of validity of the diagnostic instruments used, the differences in dosing of the medication and the duration of trials. Authors mention the short term of trials and how this does not allow for the observance of adverse effects such as a switch to mania and changes in neural development in the brains of youths exposed to SSRIs. Studies in the mice with excessive serotonin in their brains have exhibited abnormal emotional behaviors in adulthood.	This meta-analysis addressed only the efficacy, but not the safety of antidepressants. Clinicians need to take into consideration possible adverse effects with non-treatment. **Level of Evidence**: Recommended for Practice **I (**1) Meta-analysis of multiple, well-designed, randomized controlled trials.

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Posner, Oquendo, Gould, Stanley, & Davies (2007) Columbia Classification Algorithm of Suicide Assessment (C-CASA): Classification of suicidal Events in the FDA's Pediatric Suicidal Risk Analysis of Antidepressants	This article reports a meta-analysis to evaluate the possibility of a link between suicidality and antidepressants. The FDA gave Columbia University the task of improving ways to interpret data regarding suicidality from previous clinical trials sponsored by pharmaceutical companies. Authors analyzed data from 15 studies for major depression,5 for obsessive compulsive disorder, 2 for generalized anxiety, 2 for attention deficit hyperactivity disorder ADHD) and (1) one for social phobia were found.	23 randomized and 2 non randomized trials were included in this meta-analysis. These trials had a total sample of 4562, ages 6 to 17; trials lasted 4 to 16 weeks. This meta-analysis used 9 expert raters on suicide and suicide assessment. Pharmaceutical companies reported 427 adverse events in these 25 pediatric trials. 24 of these trials were sponsored by pharmaceutical companies and one by the National Institute of Mental Health (NIMH), the TADS. For this meta-analysis, raters were blinded to name of medication and to possible biased information. Each adverse event was rated by 3 experts who had not been part of the original trials and who were not employed by Columbia University.	C-CASA system consists of 8 categories to differentiate suicidal from nonsuicidal events, including vague or potential suicidal events. The infraclass correlation coefficient for the C-CASA ratings are considered highly reliable: ICC=0.89.	In cases where the (3) raters did not reach unanimous, consensus conversations were held by teleconference. Agreement in 366 of the 427 events was unanimous. Fifty-nine events (13.8%) had agreement between two of three raters. Only two events (0.47%) had no agreement. The C-CASA found 38 discrepancies: 26 cases that were considered suicidal that had been previously labeled nonsuicidal. It also changed 12 incidents from suicidal to nonsuicidal. This reduced the rate of suicide attempts by 50%. Authors found that pharmaceutical companies tended to label more events as suicidal, such as a case of "slap in the face" been categorized as suicide attempt.	Cost was not reported. Raters received training by teleconference to review categories, definitions and case exampled. Raters also had training reliability and these exercises were reviewed for inclusion in the C-CASA definition. Disagreements were discussed with raters. Inconsistent methodologies and nomenclatures when defining events were limitations in this study. Researchers also discussed of possible increase in suicidal events in subjects taking medications because they tend to have increased contact with providers, thus having more opportunities to report events than those in the placebo groups.	Future studies with a systematic method of reporting occurrence and emergence of suicidality would be useful when determining the risk and benefits of antidepressant medications. **Level of Evidence**: **Level of Evidence** Recommended for practice **I** (1) Meta-analysis of multiple, well-designed, randomized trials

Interventions for the Treatment of Depression in Adolescents - PHARMACOLOGICAL						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Rynn, M., Wagner, K.D., Donnelly, C., Ambrosini, P., Wohlberg, C.J, Landau, P., & Yang, R. (2006). Long-term sertraline treatment of children and adolescents with major depressive disorder	The purpose of this study was to examine the safety and tolerability of sertraline. It was an open-label study which lasted 24-weeks. This study followed two identical separate, 10-week, double-blind placebo controlled studies. Patients, who took a placebo pill during these trials, were switched to 50 mg of sertraline at the beginning of this trial.	107 children and 114 adolescents completed the 24-week follow up. Children 6-11 years old Adolescents 12-18 y/o with a diagnosis of major depressive disorder according to DSM-IV criteria. The mean daily dose of sertraline was 109.9 mgs in the children's group and 120.8 in adolescents. Patients, who took sertraline during the initial trials, took this medication of a total of 34 weeks, while the eligible patients in the placebo group took it for 24 months.	The primary efficacy measure was the Children's Rating Scale Revised (CDRS-R). Authors also utilized the Children's Global Impression-Severity (CGI-S). The tolerability was assessed at every week. Adverse events were evaluated according to the World Health Organization recommendations .	A mean decrease of 34.8 points was found ($p= 0.001$). 86% of the patients met CDRS-R criteria for responders and 58% were classified as remitters at the end of this study. 61% of the subjects, who were non-remitters at the end of the 10-week trials, had achieved this status at the end of this trial. There were 18 discontinuations related to sertraline, 9 adverse events, 1 laboratory abnormality, (increased liver function tests) and 8 for lack of efficacy. One patient age 9, taking 200 mg/day of sertraline, discontinued the study due to suicidal ideation, unrelated to sertraline, after he developed gender identity disorder and was teased at school.	Limitations included lack of a placebo group.	Cognitive behavioral therapy was not permitted during this 24-week trial. The duration of episodes of major depressive disorder is usually 7-9 months. This disorder is related with future relapses. Remission defined as a CDRS $\leq$ 28. Responders were those who had at least a 40% decrease in the CDRS-R score from baseline. Sertraline was well tolerated and it continued to decrease symptoms of depression during the 34-weeks of treatment. **Level of Evidence** Recommended for practice **I** (3) well-designed, cross-sectional trial without randomization

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Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Sharp, S.C. & Hellings, J.A. (2006). Efficacy and Safety of Selective Serotonin Reuptake Inhibitors in the Treatment of Depression in Children and Adolescents	The purpose of this article was to present a review and a discussion about the safety and efficacy of selective serotonin reuptake inhibitors (SSRIs) in children and adolescents. Researchers performed a literature search for published and unpublished trials in MEDLINE, from 1990-2004. Authors also included information on 2 studies of paroxetine retrieved from the Glaxo Smith Kline website). The FDA website was also reviewed. Inclusion criteria: randomized, placebo-controlled trials.	Subjects in these studies were 6 to 18 years old who meet criteria for major depression. Total sample included diverse ethnic backgrounds and countries. Authors included 10 studies in this review. Seven were randomized, placebo-controlled trials. Five of the studies were conducted in multiple settings and two of them were conducted internationally. Sample size in the trials varied from 40 to 439 participants.	The chosen studies used the following outcome measures: The Clinical Global Impressions scale The Children's Depression Rating Scale-Revised The Hamilton Rating Scale for Depression, The depression subscales of the Kiddie Schedule for Affective Disorders and Schizophrenia for Adolescents-Lifetime version The Montgomery and Asberg Depression Rating Scale.	**Fluoxetine** Emslie et al. (2002) = positive for fluoxetine Emslie et al. (1997) = positive for fluoxetine March et al. (2004) = Fluoxetine PLUS psychotherapy was the most effective treatment **Paroxetine** Unpublished study (1998) No statistical difference Keller et al. (2001) + for 2 measures (-) for imipramine Emslie et al. (2001) = no significant differences **Sertraline** Wagner et al.(2003) = (+) for sertraline **Citalopram** Wagner et al.(2004) = (+) for Citalopram Simeon et al. (1990) = no significant difference MHRA Report (2003) = negative for Citalopram	SSRIs were overall well tolerated and showed some level of efficacy when treating adolescent depression. Withdrawal rates due to adverse effects ranged from 0% to 9.75%, Paroxetine had the highest number of incidents. Common physical side effects were: dry mouth, vomiting, nausea, diarrhea, somnolence, insomnia, dizziness, tremor and agitation. The only side effect that was statistical significant was somnolence in the paroxetine group.	Increased use of SSRI's has been observed over the past ten years, especially for adolescents who have severe symptoms or have not responded to psychotherapy. Researchers, who have taken into consideration published and unpublished studies, have reported that the published studies have found certain SSRIs to be effective, while the unpublished studies showed that the risks of most SSRIs, with the exception of fluoxetine, outweigh the benefits because of lack of evidence regarding their efficacy. **Level of Evidence** Recommended for practice **I**(1) Systematic review of multiple well-designed, randomized, controlled clinical trials

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Shirazi, E. & Alaghband-Rad, J. (2005). An open trial of citalopram in children and adolescents with depression	The purpose of this study was to examine the magnitude of effect and tolerability of citalopram in adolescents in six-week, open-label trial.	30 subjects, diagnosed with major depression disorder (MDD), ages 8-17, mean age 13.57, were treated with 10-40 mgs of citalopram. 53.3% were female subjects, and 24/30 subjects finished the study.	Outcome measures were: The Hamilton Depression Rating Scale (HDRS) The Children Global Assessment Scale (CGAS) The New York State Psychiatric Institute side-effect form.	Citalopram decreased early-onset depressive symptoms. Differences between baseline and 6 weeks were statistically significant on both scales. Moderate to large effect was observed in the HDRS and CGAS (p= <0.000) for both outcome measures. One participant (3.3%) discontinued the study because of nausea and vomiting. Five, or 16.7%, of the patients in this study switched to mania. No suicidal thoughts or behaviors were reported.	Authors did not report a cost for this intervention, but they had concerns about adverse side effects and recommended future prospective, double-blind, placebo controlled trials with larger samples especially for the high incidence of mania in this study. However, researchers reported that they did not evaluate for psychiatric comorbidity. It is documented that 20% to 40% of children and adolescents diagnosed with MDD will develop bipolar I disorder within 5 years following the onset of depression.	The prevalence of depression in adolescents has been found to be between 0.4% and 8.3%. and it often recurs in adulthood. **Level of Evidence** Recommended for Practice **I**(3) Well designed trial, without randomization and with a small sample size

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Smith, E. G. (2009). Association between antidepressant half-life and the risk of suicidal ideation or behavior among children and adolescents: confirmatory analysis and research implications	Authors used relative risks for 7 antidepressant for suicidal ideation, attempt or preparation from the FDA meta-analysis (Hammand, 2004) and from the FDA –Revised (which included the TADS (March 2004). Researchers also contacted authors of unpublished articles. Adult information was utilized because researchers were unable to find half-(½) life data for children. Researchers also indicated that ½ life of medications could be decreased in children, when compared to adults, because of a higher drug clearance rates.	Authors added ½ life information to the **(1) ORIGINAL FDA** risk ratio studies by Hammand (2004) and Weiss & Gorman (2005) and compared it to: the ½ life of antidepressants in the **(2) REVISED FDA data** (Hammand, et al., 2006).	The Spearman's rho test was used to find the correlation between the relative risk for suicidality and antidepressant half-life. Authors were looking to confirm the results in the Weiss and Gorman study. The risk ratio showed a stronger correlation between medication and suicidality when results from the TADS study were included in the Revised FDA Study.	Venlafaxine had a ½ life of 5.2 h and RR 2 in **(1**) and (**2**). Fluvoxamine had a ½ life of 15.6 hr RR=1 in (**1**) and (**2**). Paroxetine had a half-life of 21hr. RR=3 in **(1**) and **(2).** Sertraline: ½ life= 26hr RR 5 (in (**1**) and 6 (in **2**). Mirtazapine ½ life 30.5 hours. RR= 4 (**in 1)** and in **(2).** Citalopram: ½ life: 35 h. RR= 6 for **(1**) and 7 in **(2).** Fluoxetine: ½ life 96-144 h; RR = 7 **(in 1)** and 5 in (**2)** The lowest relative risks for suicidal ideation were found in medications with the longest half-life.	Author gave credit to Weiss & Gorman, 2005 for their report on medication non adherence as a factor for increased suicidal ideation due to possible discontinuation effects. The explanations given in this article are that suicidality could be due to discontinuation effects possibly due to changes in serotonin blockade (maximum blockade of the serotonin transporter to no blockade). Fluctuations in this blockade could mean that medications with shorter ½ lives carry increased risk for suicidality. The results of the Revised FDA meta-analysis moved fluoxetine from the least risk ratio (#7) to an increased risk: #5. They also reported that the changes in the ranking of fluoxetine, due to the results of TADS could have been related to TADS including subjects who were already very depressed at baseline since high rates of depression at baseline often predict suicidal behavior. Limitations: difficult to find heterogeneity in the studies due to varied ages, diagnosis, severity of symptoms, dosing protocol and response to treatment.	The relationship between antidepressants and suicidality is not clear. There were no completed suicides in these trials, and the possibility of youths reporting suicidal ideation could be seen as an improvement because they are able to verbalize their symptoms. **Level o Evidence:** Recommended for practice **I** (1) – Meta-analysis of multiple well-designed, randomized, controlled clinical trials

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Tsapakis, EM., Soldani, F., Tondo, L., & Baldessarini, R.J. (2009). Efficacy of antidepressants in juvenile depression: meta-analysis	30 of 304 studies met inclusion criteria for this meta-analysis regarding the treatment of juvenile depression. All studies were randomized, double-blind and placebo controlled. One trial had a third arm: placebo v.SSRI v. tricyclic antidepressant. All trials used diagnostic criteria for major depressive disorder, such as the DSM–III or later, or ICD–9/10) to diagnose clinical depression, which included major depression, dysthymia or depression not otherwise specified. SRI – Serotonin reuptake Inhibitors	There were 3069 participants included. The mean participant age was 13.5 years; range 6–20). Most trials involved both children and adolescents. There we no reports for response rates for each age group separately. 14 studies involved tricyclic antidepressants, including amitriptyline, clomipramine, desipramine, imipramine and nortriptyline; Twelve studies included SRI-type agents: including citalopram, fluoxetine, paroxetine, sertraline and venlafaxine. There was only one trial for each of these agents: MAOI–moclobemide, and for mirtazapine, and nefazadone. One trial involved three arms, with paroxetine or imipramine v. placebo.	Different Scales were used in the chosen studies, but the severity of symptoms was similar, indicating moderate to severe scores in most trials. Researchers calculated a mean score from all the scales used in the studies. Baseline scores were similar for placebo and for antidepressant groups.	Serotonin reuptake inhibitors yielded a higher pooled response rate ratio (RR=1.23, 95% CI 1.14–1.33) than tricyclic antidepressants (RR=1.15, 95% CI 0.98–1.34), but the overlapping confidence intervals indicated statistical non-separation by drug type. SSRIs: fluoxetine showed a greater pooled efficacy RR=1.45, 95% CI 1.24–1.70. The largest effect size for fluoxetine was reported by March et al (RR=1.74, 95% CI 1.29–2.34). while other three trials involving SRI's yielded similar pooled effects between SRIs and other antidepressants.	80%of the studies (24/30) failed to demonstrated superiority of antidepressant over placebo. Of the six studies showing benefit over placebo, 5 of these trials involved an SSRI. Antidepressants of all types showed limited efficacy in Juvenile depression. Only fluoxetine might be more effective, especially in adolescents, (RR=1.45, 95% CI 1.24–1.70) The average exposure time was of 8.7 weeks. Adult studies have reported that an 8 week trial is needed to detect antidepressant effect. The exposure time varied in these medication trials. SRI had 1584-person weeks, 4 tricyclic antidepressants had 248, and other antidepressants: 1000. Major flaws detected included the difference in exposure time and the inability of the studies to account for subjects withdrawing from the studies. The largest effect size for fluoxetine was reported by March et al, 2004. (RR=1.74, 95% CI 1.29–2.34). This study also had the largest number of participants, n=221.	This systematic review and meta-analysis found that the therapeutic effect of all antidepressants is limited in short term randomized trials. This Meta-analysis found a small pooled drug to placebo response rate ratio: RR=1.22, 95% CI 1.15–1.31), with little separation between antidepressant types. The superiority of fluoxetine was detected based on only one large study showing a large separation from placebo. **Level of Evidence** Recommended for practice **I(**2) – Meta-analysis of randomized trials.

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Usala, T., Clavenna, A., Zuddas. A., & Bonati, M. (2008). Randomized controlled trials of selective serotonin reuptake inhibitors in treating depression in children and adolescents: a systematic review and meta-analysis	The search for the trials was done by 2 evaluators by searching the Cochrane Library's Central Register of Controlled Trials, the Embase, PsychINFO, and Medline until January 2007. Thirteen randomized, double-blind, controlled trials of SSRI for the treatment of depression in children and adolescents, published in 12 articles met the inclusion criteria. Studies were rated for quality in 4 different domains with a scale of 1-3 for a total of 12 points. The trials with the highest quality rating had the lowest treatment effect.	Studies included a total of 2530 between the ages of 6 and 20. Studies lasted from 6 to 14 weeks. It was reported that 1847 subjects completed the trials. Reasons for dropout were: 25.8% for adverse effects (52.9% were taking medication and 29.3 placebo), and 18.8 for lack of efficacy, 37.7 were treated with medication and 59.3% were from the placebo group. Trials involved the following SSRIs: Fluoxetine, paroxetine., Citalopram, Escitalopram and sertraline. Only 1 study by March, et al. 2004, evaluated combined treatment of fluoxetine and psychotherapy. Subjects in 9 studies were outpatient and the four other trials involved both inpatient and outpatient subjects.	A total of 23 instruments were used, among them: The Hamilton Rating Scale for Depression (HAM-D) Children's Depression Rating Scale-Revised (CDRS-R) Clinical Global Impressions; CGI-I Kiddie Schedule for Affective Disorders and Schizophrenia Present episode (K-SADS-P ≤2: depression and anhedonia) Montgomery Asberg Depression Rating Scale MADRS Reynolds' Adolescent Depression Scale (RADS)	When comparing medication vs. Placebo: 672 or 56.6% participants showed improvement in the SSRI group while 497 or 45.8% had decreased symptoms in the placebo group. A significant statistical difference was found only for Fluoxetine (OR=2.39; 95%CI 1.69–3.39). Citalopram and sertraline showed a moderate effectiveness. It was difficult for the authors to determine if baseline severity of symptoms was a predictor of efficacy because in these studies, only one trial included patients with moderate to severe depression.	These studies had different scales to determine efficacy. Some studies used the HAM-D, and this scale has been reported as flawed in some studies. The MADRS scale has only been validated for use in adults. Different scales may show different results. In one study of patients taking fluoxetine, when they were evaluated with CDRS-R they showed greater improvement than when assessed with the RADS. In previous studies with tricyclic medications, older children had a better response to medications, but in this meta-analysis, age did not influence results. Authors also found that studies included in this meta-analysis provided conflicting results. Psychiatric comorbidities in the studies included, the different parameters used to define levels of depression, and the diversity in the subjects varied from one study to another. Other possible limitations could be having no access to the raw data and the variation in methodological approaches.	Randomized clinical trials usually refer to treatment response as a 50% reduction of symptoms according to a rating scale. Remission is a period of at least 2 weeks (but less than 2 months) during which the subject experiences no more than one symptom of depression. Clinicians need to be aware that 20% to 40% of children and adolescents might develop bipolar disorder within 5 years following the onset of major depression. **Level of Evidence** Recommended for practice **I** (1) Systematic Review and Meta-analysis of multiple, well designed, randomized, controlled trials

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Von Knorring, A.L., Olson, G.I., Thomson, P.H. Lemming, O.M. , & Hulten, A. (2006). A randomized double-blind, placebo-controlled study of citalopram in adolescents with major depressive disorder.	This was a multicenter, 12 week, European trial in inpatients and outpatient subjects with a current episode of major depressive disorder lasting 4 weeks to one year. Recruitment started in Sweden in 1996, but due to inadequate recruitment, this phase lasted about 4 years. Enrollment also was extended to other countries to accomplish a higher sample.	Sample consisted of 244 adolescents ages 13 to 18. Participants were randomized to 124 to Citalopram and 120 to placebo.	Schedule for Affective Disorders and Schizophrenia for school-aged children– Present episode version (Kiddie-SADS-P) Montgomery Asberg Depression Rating Scale (MADRS) Secondary measures include the Beck Depression Inventory (BDI)	In this study, Citalopram did not show to be statistically significant when compared to placebo. 51% of the patients in Citalopram and 53% in the placebo group responded to treatment. About one-third of the participants in each treatment arm withdrew from the study. 79 subjects in the Citalopram group and 74 in the placebo completed the trial. Suicidal thoughts and tendencies were reported in 5 of the patients in the placebo group and in 14 of the Citalopram group. However, the item for suicidal ideation in the (Kiddie-SADS-P) showed an 8% increase in suicidal ideation in the Citalopram group and 18% in the placebo group.	Possible limitations include that about two thirds of the sample were taking psychotherapy. The duration of psychotherapy was not reported. Other limitations include, the multiple sites used, the longer time for recruitment (4 years instead of the planned 2).	Adverse events were reported by 91 (75%) of the Citalopram group and 79(71%) with placebo. Adverse events were considered as mild or moderate and it include headache, nausea, and insomnia. The only significant side effect was fatigue. **Level of Evidence** Recommended for practice **I**(2) well-controlled, randomized trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - PHARMACOLOGICAL						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Special Training Needs and Costs	Level of Evidence and Comments
Wagner, K.D., Jonas, J. Findling, R.L., Ventura, D., & Saikali, K. (2006). A double-blind, randomized, placebo-controlled trial of escitalopram in the treatment of pediatric depression	The purpose of this 8-week study was to examine the safety and efficacy of escitalopram, a selective serotonin reuptake inhibitor antidepressant, in the treatment of major depressive disorder (MDD) in adolescents.	Subjects, ages 6 to 17 years old, were recruited from 25 sites in the United States from December 2002 to February 2004. Participants had to be diagnosed with MDD according to DSM-IV criteria and the present episode had to have duration of at least 4 weeks. 264 participants met inclusion criteria and were randomized to double-blind treatment. 104 were 6-11 years old, and 160 were 12-17 years old. 102/131 patients in the escitalopram group and 115/133 subjects in the placebo treatment arm completed the study.	The outcome measure was the Children's Depression Rating Scale-Revised (CDRS-R) The secondary measures used were: The Clinical Global Impressions-Improvement (CGI-I) and the Children's Global Assessment Scale (CGAS)	No significant differences were detected among the two treatment groups, (p= 0.31) in the CDRS-R. Adverse events in both groups were similar. The only events that occur at a 10% greater rate in the escitalopram group, were headache and abdominal pain. Premature discontinuation rate was 1.5% for both groups.	There were no completed suicides in this study, but in the escitalopram a 16 y/o male reported self-inflicted superficial cuts to his wrist. Two subjects in the placebo group reported self-harm. An 11/y/o female reported a superficial scratch on her left leg. Two weeks after this incident, the same girl reported another self-inflicted scratch on the left wrist. A 17 y/o adolescents reported overdosing on study medication 5-days after receiving a bottle with 10 tablets. This participant discontinued treatment due to lack of therapeutic response. Researchers discussed the high placebo response also found in previous pediatric trials using antidepressants. This placebo effect could be due to structure and support provided in clinical trials to the participants. Authors stated that this study lacks generalizability due to the majority of subjects being white, mean age 12 years old, and also due to the exclusion of patients with comorbidities, subjects taking other psychotropic medications and also children receiving psychotherapy.	There is a high risk for suicide in adolescents diagnosed with depression. In one study, 7.7% of depressed adolescents committed suicide by early adulthood. **Level of Evidence**: Recommended for practice **I**(2) well-controlled, randomized trial with adequate sample size

TABLE 6

INTERVENTIONS FOR THE TREATMENT OF DEPRESSION IN ADOLESCENTS –

COMBINATION TREATMENT –

PSYCHOTHERAPY AND PHARMACOLOGICAL MANAGEMENT

Interventions for the Treatment of Depression in Adolescents – COMBINATION - TORDIA						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Asarnow, J.R., Emslie, G., Clarke, G., Wagner, K.D., Spirito, A., Vitiello, B.,…, ,Brent, D. (2009). Treatment of selective serotonin reuptake inhibitor-resistant depression in adolescents: predictors and moderators of treatment response	The purpose of this study was to find treatment strategies that matched adolescents who had been resistant to treatment with SSRIs. Researchers were looking for ways to help clinicians on selecting optimal treatment by increasing knowledge about predictors that may predict a positive outcome and moderators that may guide clinicians on how to choose subjects that will benefit from one treatment and not from another one.	Sample consisted of 334 adolescents who had a diagnosis of moderate to severe depression and were being treated actively with an SSRI. This study was a 12-week randomized, controlled clinical trial (TORDIA). In this study, patients were assigned to 4 groups: 1) Change to another SSRI 2) Change to Venlafaxine 3) Change to another SSRI plus Cognitive Behavioral Therapy (CBT) 4) Change to Venlafaxine plus CBT Participants received 12 to 15 sessions of psychotherapy in 12 weeks, and in 3-6 sessions parents were included.	Inclusion criteria included: A Total score of ≥ 40 in the Child Depression Rating Scale-Revised (CDRS-R). A score in the Clinical Global Impression-Severity (CGI-S) Subscale of ≥4 (indicating at least moderate severity of symptoms).	Even though no statistical significance was reached, combined treatment of medication plus CBT had greater levels of response Nonresponders had higher depression severity, chronicity, greater impairment, higher suicidal ideation, hopelessness, more family conflict and fewer months receiving SSRI medication. Moderators influencing response to CBT was absence of abuse history, low levels of hopelessness and more comorbid disorders. Beck Depression Inventory (BDI) scores were only a moderator in patients with low BDI scores, < 10. These subjects had a more beneficial effect when treated with venlafaxine instead of another SSRI. Response rate to venlafaxine and SSRIs was the same in the rest of the subjects.	Authors reported that they were able to replicate previous results linking poorer response to treatment with higher levels of depression and chronicity, and they emphasize the importance of early detection and treatment to avoid a disorder that may become chronic and nonresponsive to treatment. Researchers stated that the addition of CBT could be beneficial even when subjects are severely depressed. Future research is recommended with larger minority samples.	About 40% of adolescent with major depression do not achieve adequate improvement after they are managed with first-step treatments. Due to inaccessibility and high cost of psychotherapy, SSRIs are usually the first used alternative. Because of the cost of psychotherapy, researchers recommend personalizing treatment to the needs of the adolescent. In some cases adding CBT to antidepressants might be beneficial in patients not responding to treatment, but in other adolescents, medication monotherapy could be as effective as combination treatment. **Level of Evidence** Recommended for practice **I** (2) – well-controlled randomized clinical trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - COMBINATION - Primary Care						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Asarnow, J.R., Jaycox, L.H., Tang, L., Duan, N., LaBorde, A.P., Zeledon, L. R., . . . , Wells, K. B. (2009). Long-term benefits of short-term quality improvement Interventions for depressed youth in primary care	The Youth Partners in Care Programs was a randomized controlled trial from 1999 to 2003 in the United States. It involved 5 organizations. Its purpose was to test the effectiveness of a quality improvement intervention, cognitive behavioral therapy (CBT) to a placebo group receiving enhanced treatment as usual (TAU). This group had no access to CBT or to case management.	Sample consisted of 418 adolescents with current symptoms of depression, ages 13-21. Subjects were randomized to the quality improvement intervention (n=211) or to the control groups. (n=207). The mean number of CBT session was 3.85. Providers used "The Texas Medication Algorithm" to guide medication management when needed. This algorithm recommends the use of Selective Serotonin Reuptake Inhibitors first. 78% of the sample was female, 56% were Hispanic, 13% African American, 1% Asian, and 17% of mixed or other ethnicity. No differences were reported between the intervention and the control groups at baseline.	Subjects were assessed at baseline, 6 month follow-up, 12 month follow-up and 18 month follow-up. Outcome measures included: Center for Epidemiological Studies Depression Scale (CESD-S) Composite International Diagnostic Interview (CIDI).	There was a decline of >50% in suicide attempts in the intervention group, but there was also a decreased in the control group. At 6 months of the study, there was a significant difference favoring the intervention group because of reduced possibility of severe depression. This trend continued, but it was not statistically significant at 18 month follow-up (p=0.06).	No cost about training was provided. Primary care providers were trained for 1-2 hours on enhanced treatment as usual. This training emphasized education. CBT providers were psychotherapists prepared at the master's or PhD level. They received a 1-day training session on CBT and cultural competency. They also received a manual and consultation about the treatment fidelity. Researchers suggest future studies with larger sample sizes to detect intervention effects. They also state that due to high level of recovery with the low levels of treatment received, they recommend a proactive effort to identify, and to improve access to treatment for depressed youths.	Due to the decreased depression in this study, researchers encourage a proactive stance in the detection and the treatment of depression in youths in primary care. **Level of Evidence** Recommended for practice **I**(2) well-controlled, randomized trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - COMBINATION – Primary Care						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Asarnow, J.R., Jaycox, L.H., Duan, N., LaBorde, A. Rea, M. M., Murray, P., . . . , Wells, K. B. (2005). Effectiveness of a quality Improvement intervention for adolescent depression in primary Care clinics: a randomized controlled trial	The Youth Partners in Care Programs was a randomized controlled trial from 1999 to 2003 in the United States. It involved 5 organizations. The aim of this study was to examine the effectiveness of a quality improvement intervention when compared to usual care while increasing the use of evidence based treatments for the treatment of depression in adolescents. The treatment group included the use of cognitive behavioral therapy (CBT) plus antidepressants. The control group received treatment as usual. Subjects in this group had no access to CBT. Criteria for recruitment were determined by the scores in the CESD-S and the CIDI.	Sample consisted of 418 adolescents with symptoms of depression, ages 13-21. Subjects were randomized to the quality improvement intervention (n=211) or to the control groups. (n=207). 344 or 82% finished the study. The mean number of CBT session was 3.85. Researchers used The Texas Medication Algorithms to guide medication management. Selective Serotonin Reuptake Inhibitors was the first medication option used. 78% of the sample was female, 56% were Hispanic, 13% African American, 1% Asian, and 17% of mixed or other ethnicity. No differences were reported between the intervention and the control groups at baseline.	Subjects were assessed at baseline and at 6-mont follow-up. The outcome measure was the: Center for Epidemiological Studies Depression Scale (CESD-S) Secondary outcome measures were: Mental Health Summary Score (MCS-12) to assess mental health-related quality of life A 5-point scale to measure satisfaction with mental health care Composite International Diagnostic Interview (CIDI)	After patients participated in this 6-month quality improvement intervention, they had lower depressive symptoms (p=0.02), improved mental-health related quality of life (p=0.03), higher satisfaction with health care (p=0.04), and receiving more mental health care p=0.01. Study was not powered to detect suicidality, but the number of suicide attempts and self-harm declined in both groups, difference was not significant. Researchers reported no difference between groups regarding use of medication.	Clinicians received education about depression and care managers were trained in CBT. Treatment as usual was “enhanced” by providing educational materials (pocket cards and manuals) and training to clinicians about the evaluation and treatment of depression. This study included different professionals in addition to the primary care provider, such as an expert leader team in charge of implementing the intervention, care managers who supported primary care clinicians, No costs were reported for this intervention. Researchers recommend studies with larger sample to detect suicidality.	Due to the positive results in the intervention group, researchers recommend the use of evidence based treatments for adolescents in depression. They also advocated for resources to improve access to psychotherapy in this population. **Level of Evidence** Recommended for practice **I**(2) well-controlled, randomized trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents. PHARMACOLOGICAL/TORDIA - Other: Predictors						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Brent, D.A., Emslie, G.J., Clarke, G.N., Asarnow, J., Spirito, A., Ritz., L., . . . , Kellner, M. B. (2009). Predictors of spontaneous and systematically assessed suicidal adverse events in the treatment of SSRI-resistant depression in adolescents (TORDIA) study	The purpose of this study was to examine how treatment effects influenced predictors and moderators regarding suicidal and nonsuicidal self-injury. Subjects who had not responded to a Selective Serotonin Reuptake Inhibitor (SSRI) were randomly assigned to 4 groups: 1) Change to another SSRI 2) Change to Venlafaxine 3) Change to another SSRI plus Cognitive Behavioral Therapy (CBT) 4) Change to Venlafaxine plus CBT 5) Study did not include a placebo arm.	Sample consisted of 334 adolescents ages 12-18 who still had a diagnosis of moderate to severe depression, according to DSM-IV criteria, after receiving treatment with a Selective Serotonin Reuptake Inhibitor (SSRI) medication for 8 weeks (the last four doses had to be at least 40 mg of fluoxetine). .	Inclusion criteria included: A Total score of ≥ 40 in the Child Depression Rating Scale-Revised (CDRS-R). A score in the Clinical Global Impression-Severity (CGI-S) Subscale of ≥4 (indicating at least moderate severity of symptoms).	There were no statistical significant results across treatment effects for suicidal or nonsuicidal events. Adverse events were higher when assessed systematically than when they were self-reported. There were no suicides in this study. Suicidal self-injury presented in 14.3% of the subjects. The incidence of Nonsuicidal adverse events was 9.3%. The most important predictors of suicidal events were high suicidal ideation at baseline, family conflict and drug and alcohol use. History of Nonsuicidal events predicted nonsuicidal adverse events (median time: 2 weeks). No protective effect was found in CBT. The median time for a suicidal event was 3 weeks, possible due to not enough CBT yet or because of increased monitoring. Six of ten adolescents prescribed benzodiazepines experienced a non-suicidal event. Subjects with moderate to severe suicidal ideation at baseline had a significant increase in self-harm when they were treated with venlafaxine than with an SSRI (p= 0.002).	No costs for the interventions provided in this study were provided. Researchers advised to target behaviors associated with poor response and increased adverse events (high suicide ideation, family conflict, alcohol and drug use). The nonproductive effect of CBT was also explained by the possibility that nonsuicidal behaviors were not addressed in therapy. Authors state that the results seen in benzodiazepines could be due to the desinhibition associated with this type of medication, but researchers advise to take this result with caution due to the small sample who was exposed to these medications. Researchers recommend further studies to re-evaluate the risks and benefits of venlafaxine and of benzodiazepines in patients at high risk for suicide who have been resistant to treatment.	Treatment response in this study was a reduction of ≥ 50 in the CDRS-R scores or a score of ≤ 2 in the CGI score. Researchers first offered paroxetine as an option for SSRI medication, but they discontinued it after reports about adverse effects with paroxetine were taken into consideration. Since high levels of suicidal ideation and a recent suicide attempt are often reasons for initiating antidepressants, 60% of subjects in this study had suicidal ideation and one-third had a history of nonsuicidal self-injury. Authors included this type of subjects because they wanted the sample to represent patients seen in community settings. **Level of Evidence** Recommended for practice I (2) – well-controlled randomized clinical trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Brent, D., Emslie, G., Clarke, G., Wagner, K. D., Asarnow, J. R., Keller, M., . . . , Zelazny, J. (2008). Switching to another SSRI or to venlafaxine with or without cognitive behavioral therapy (CBT) for adolescents with SSRI resistant depression The TORDIA randomized controlled trial	The purpose of this trial was to study the relative efficacy of 4 treatment approaches in adolescents with a diagnosis of major depression disorder that had not had a positive response to treatment with an SSRI after 2 months. This study lasted twelve weeks and included 4 treatment arms. 1) switch to a different selective serotonin reuptake inhibitor (SSRI): 20-40 mgs of paroxetine, citalopram, or fluoxetine). 2) Switch to a different SSRI plus CBT. 3) switch to 150-225 mg of venlafaxine and 4) switch to venlafaxine plus CBT. Due to concerns published in 2003 in England, patients on Paxil were tapered off and switched to another SSRI.	This was a randomized controlled trial conducted from 2000-2006 in 6 academic and community clinics in the U.S. The sample consisted of 334 adolescents between 12 to 18 years who were receiving treatment for a diagnosis of major depressive disorder according to the Diagnostic and Manual of Mental Disorders, Fourth Edition (DSM-IV). To be included, participants had to had a score indicating "significant" depression as indicated by a score of no less than 40 in the Children's Depression Rating Scale-Revised (CDRS-R), and a score of at least 4 (at least moderate severity) in the Clinical Global Impressions-Severity subscale (CGI).	The Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version, a semistructured interview was used to verify the DSM-IV diagnosis.	From the 334 subjects, 231 (69.2%) completed the 12-week trial. Subjects who were switched to another SSRI or venlafaxine and who also received CBT had a higher response rate, 54.8%. Patients who were switched to another medication, but who did not receive CBT had a response rate of 40.5%. There were no differences in response between SSRIs and venlafaxine. Patients on venlafaxine had an increase in diastolic blood pressure and pulse. They also had more skin problems.	No costs were reported. Study protocol included 12 sessions of 60-90 minutes. Median number of CBT sessions was nine. This can be interpreted as subjects improving regardless of not attending the 12 sessions. However, subjects might have had a better response rate if they had attended all sessions. Patients taking sleep medications had a poorer response to treatment. Based on these findings, authors recommend that subjects who have never received CBT and suffer from treatment-resistant depression have a better chance of responding to treatment when CBT is added to the medication switch.	**Level of Evidence** Recommended for practice **I** (2) – well-controlled randomized clinical trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - COMBINATION		
Review of clinical practice Guidelines for treatment for adolescents with depression		
Weight-of-Evidence Category: Recommended for practice		I (1) Systematic Review
Guidelines Author Cheung, AH. Zuckerbrot, R.A., Jensen, P.S., Ghalib, K., Laraque, D. Stein, R.E., & the GLAD-PC Steering Group (2007). Guidelines for adolescent depression in primary care (GLAD-PC): II. treatment and ongoing management	Summary of Guidelines Researchers from the United States and Canada developed this guideline to aid primary care clinicians (PCCs) in the treatment of depression in youths ages 10 to 21. This guideline includes: the level of evidence for the continuous monitoring of youths with mild depression, the evidence-based treatment with medication and with psychotherapy of youths with moderate to severe depression, monitoring of possible medication side effects, consultation and coordination of care with mental health professionals, the determination of outcomes, and the steps to follow in the case of partial or no improvement. • The methods used to develop this guideline included: literature reviews of Medline, PsychINFO and the Cochrane database. RTC's used by the FDA to issue a safety report were also reviewed. • Expert consensus included a survey filled by experts on the topic of management of depression in adolescents. These experts met for a two-day workshop to develop "first line practices. • The recommendations based on expert consensus included 4 agreement categories: very strong had 90% agreement, strong: 70% fair > 50%, and weak < 50%. • In order for recommendations to be included in the guidelines, they needed a "strong agreement or 70% agreement.	Treatment In cases of mild depression, a period of 6 to 8 weeks should be considered prior to starting treatment. During this time, the youths are to receive monitoring and supportive weekly or biweekly meetings. If improvement is not seen within 6 to 8 weeks or ff symptoms do not subside, treatment with psychotherapy or antidepressant should be recommended. For youths presenting with moderate or severe depression with substance abuse or psychosis, the PCC should consider consultation with a mental health provider. • PCPs should recommend treatments that have been scientifically. Psychotherapies (CBT or IPT) and/or antidepressant medications, such as SSRIs. However, a recent trial has shown that combination therapy, CBT plus medication, is more effective than CBT alone. However, due to lack of trained staff and time constraints, psychotherapy may not be an option. Treatment should be acceptable to the patient and family, taking into consideration their preferences, the availability of the treatment, the severity of disease, risk of suicide and comorbid conditions. • Older antidepressants monoamine oxidase inhibitors, MAOIs, and tricyclic antidepressants were not included. Fluoxetine has the most positive studies, while paroxetine has the most negative results. • Results of a meta-analysis, reported 6 times more youths would benefit from antidepressant medications than would be harmed. • The FDA has recommended that youths taking antidepressants should be monitored for suicidality and for changes in behavior for the first 4 weeks; then biweekly for the next 4 weeks. Followed by another encounter at 12 weeks, and as needed after week 12. Treatment, goals and outcomes of treatment should be evaluated taking into consideration home, school and peer settings. • PCCs should continue to support youths referred to a mental health specialist: Also, regardless of the length of treatment, patients should be monitored on a monthly basis for 6 to 12 months. For recurrent episodes, adult literature advices that the patient be treated for 2 years after the symptoms have resolved. • PCCs are also advised to consult with a mental health specialist if the teenager becomes psychotic, suicidal, homicidal, or if new or worsening or comorbid conditions present.

Interventions for the Treatment of Depression in Adolescents - COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Clarke, G., Debar, L., Lynch, F., Powell, J. Gale, J,, O'Connor, E., . . . , Hertert, S. (2005). A randomized effectiveness trial of brief cognitive-behavioral therapy for depressed adolescents receiving antidepressant medication.	The purpose of this study was to integrate a collaborative care model that has been successful in treating depression in primary care clinics. This model consists of an on-site mental health specialist and the primary care provider. Authors conducted a randomized effectiveness trial of brief individual cognitive behavioral therapy (CBT) plus a selective serotonin reuptake inhibitor (SSRI) antidepressant and compared it to adolescents on an antidepressant plus treatment as usual (TAU).	152 youths were randomized who met DSM criteria for major depression. 120/152 participants were females. 77 subjects were assigned to the treatment group: CBT + SSRI, and 75 to the control group: TAU. The study was conducted by the Kaiser Permanente Northwest HMO in Portland, Oregon. Adolescents between ages 12-18, who met inclusion criteria, were invited to participate.	Blinded interviewers evaluated adolescents and an assigned parent at baseline and at weeks 6, 12, 26 and 52. Instruments used: The Schedule for Affective Disorders and Schizophrenia for Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL) The Child Behavior Checklist Depression, YSR-Depression Hamilton Depression Scale (CES-D)	There was only weak evidence for the effectiveness of CBT + SSRIs on the primary measure outcome, CES-D, but failed to find any advantage for major depression recovery. Researchers concluded that, in this trial, brief CBT, 5-9 sessions, did not improve results when added to an SSRI in primary care. Authors noted that TADS consisted of 15 acute sessions.	Patients in the TAU group were allowed to continue taking SSRI medications and to receive psychotherapy outside this study. Researchers reported that the inability of CBT to differentiate from the placebo group could be related to the high quality and frequency of TAU and also to the use of SSRI s according to established guidelines. Limitations include the high attrition rate in older adolescents due to youths leaving home or moving away. Obtaining results by phone may have also altered the results. Researchers also indicated that their results could have been due to the small sample size and for the reduction in dose of SSRIs in the treatment group.	**Level of Evidence**: Recommended for practice **I**(2) well-controlled, randomized trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Curry, J., Rohde, P., Simons, A., Silva, S., Vitiello, J., Kratochvil, C., . . . March, J. (2006). Predictors and moderators of acute outcome in the treatment for adolescents with depression study (TADS)	439 adolescents were randomly assigned to 4 treatment arms to fluoxetine (FLX), cognitive-behavioral therapy (CBT), combination of fluoxetine and CBT (COMB), or to placebo (PLO) which consisted of clinical management plus a placebo pill. Authors generated a list of moderators and predictors in depressed adolescents. To be included, moderators and predictors had to have a variable in TADS. The following six predictors were found: hopelessness, the adolescent's treatment expectancy, age, duration of symptoms prior to intervention, < 40 weeks, level of functioning, suicidal ideation, melancholic symptoms, anxiety, and the number of comorbid diagnosis. Moderators identified were: cognitive distortions, family income, and severity of symptoms.	The aim of this study was to identify moderators that could help clinicians choose the best treatment approach when working with depressed adolescents. Authors chose the outcome measure as the predicted scores at week 12, according to the Children's Depression Rating Scale-Revised (CDRS-R). Adolescents in TADS met criteria for recurrent, moderate to severe depression, and only 2% of the subjects were mildly depressed.	Researchers identified moderators and predictors by conducting a literature review and for each one authors devised a linear model to test the interaction between these variables on the predicted CDRS-R scores. Researchers first identified 21 candidate variables; nine were found to be predictors and three moderators.	More improvement was found in younger adolescents, <16 years old, and in patients who had decreased symptoms in the areas of depression, hopelessness, melancholia and suicidal ideation; as well as, decreased comorbid diagnoses, and a higher degree of functioning at baseline. When compared to FLX, COMB treatment was more effective in adolescents with mild to moderate depression and for subjects with higher cognitive distortions. Patients from higher income levels had a better response to CBT alone or to COMB. Authors expected, COMB to be more effective in severely depressed subjects, but adding CBT to FLX was not more effective than FLX alone. Both FLX and COMB were better than PLO. CBT and PLO were not different. COMB had a stronger response when moderators were present.	Researchers stated that this was an exploratory study because, even though, TADS included the largest sample to study adolescent depression up to date, it was not considered adequate to detect moderator effects. Another possible limitation was that expectations for COMB were high and the clinicians administering COMB were aware of treatment assignment. In the FLX and PLO, clinicians were blinded to the treatment assignment. TADS was an effectiveness study, and because of this, when needed, patients in the COMB received more treatment and patients in this group arm might have benefitted from the extra treatment. Researchers reported that this is more representative of clinical practice. A restrictive study would have limited the number of treatment sessions.	A predictor can have an effect on the outcome independently of the treatment received. A moderator may affect outcome by interacting with treatment. Moderators are more important to clinicians since moderators have the possibility of indicating the type of treatment adolescents might benefit from. **Level of Evidence** Recommended for practice **I**(2) well-controlled, randomized trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Domino, M.E., Foster, E. M.., Vitiello, B., Kratochvil, C.J. Burns, B.J., Silva, S. G., . . . , March J. S. (2009). Relative cost-effectiveness of treatments for adolescent depression: 36- week results from the TADS randomized trial	The purpose of this study was to examine the costs of three treatment arms when compared to the outcomes of the TADS study at 36 weeks. TADS took place in 13 U.S. academic and community clinics from 2000 to 2004. Patients participated first in a 3-month acute treatment phase followed by a six-month maintenance treatment plan. Costs of services received for the 36 weeks were estimated and examined in relation to the number of depression-free days and quality-adjusted life-years.	The sample for this study consisted of 327 patients diagnosed with major depression, ages 12 to 18. Randomized to three treatment modalities. 1) Fluoxetine alone (n=109) 2) Cognitive Behavioral Therapy (CBT) alone n=111 3) Combined: CBT plus Fluoxetine n= 107 To calculate the cost effectiveness ratio (ICER) researchers used the cost and outcome measures. To describe the uncertainty of the cost-effectiveness analysis, the cost-effectiveness acceptability curves (CEACs) were used. This analysis shows the payer if the intervention is a good value for the money invested.	The instruments used at 36 weeks as an outcome measure were: The Children's Depression Rating Scale, Revised (CDRSR). The Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire (PQ-LES-Q) The Health of the Nation Outcome Scales for Children and Adolescents (HoNOSCA), To aid in the analysis of cost effectiveness, authors utilized measurements of: Depression Free Days (DFDs) and Quality-adjusted Life Years (QALYs).	At 12 weeks, cost effectiveness was superior for Fluoxetine alone. There was also no increased use of emergency services at this time. At 36 weeks: Authors found no difference in costs and only few differences in outcomes in the three treatment modalities. Results showed no statistical significance at the 95% level for the CDRS-R. HoNOSCA or the PQ-LES-Q in any of the paired comparisons. However, results favored combination treatment for cost-effectiveness (90% certainty level over Fluoxetine), based on willingness to pay for a QALY starting at $100, 000. No difference was found between CBT and Fluoxetine. CBT showed improvement in CDRS-R scores, but in 25% of the estimates had inferior outcomes that Fluoxetine alone.	CBT was the most expensive intervention. The mean cost for CBT alone was $1,787. When CBT was used in combination with fluoxetine, the mean cost for CBT in the Combination treatment was $1,833. The cost for direct and indirect costs was higher for fluoxetine; mean $5,382, while for CBT the mean was $3,102. For patients in the combination group, the mean was $2,705. However, researchers did not take into consideration the services patients were receiving outside TADS, such as cost of medications or psychotherapy. Authors recognized there were missing data, and t the sample used was too small to conduct a cost-effectiveness analysis. Authors were aware costs reflected in this study do not include the entire costs of depression.	Combination treatment was the most effective since patients in the fluoxetine only arm had the highest cost for psychiatric ER visits and hospitalization, (authors were not able to report if these have been self-harm visits). Researchers stated that the conversion from CDRS-R to QALY units has not been validated for this population and its possible loss of utility with patients with comorbid disorders since half of the patients in TADs had other psychiatric disorders. Decisions about payments for services are determined by policy makers, private insurances and the financial possibilities of parents. **Level of Evidence** Recommended for practice **I (**2) Well-controlled, randomized trial

Interventions for the Treatment of Depression in Adolescents - COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Domino, M. E., Burns, B. J., Silva, S. G., Kratochvil, C. J., Vitiello, B., Reinecke, M. A. , . . . March, J. S. (2008). Cost-effectiveness of treatments for adolescent depression: results from TADS	TADS was a multisite randomized control trial comparing the effectiveness of 4 treatment arms: fluoxetine monotherapy: 1) Cognitive Behavioral Therapy (CBT) alone 2) Fluoxetine monotherapy 3) Combination therapy (COMB = fluoxetine + CBT) 4) Placebo With the purpose of guiding clinicians in the allocation of available funds, this study took into consideration the costs and treatment effects in a 12-week period. The cost for CBT and for medication management were calculated by using the unit cost as reported by the 2003 Medicare rate, CBT cost was 113.09 and for medication management 59.83. Costs related to research were not included, but payments for outside services, among them, psychiatric admissions were taken into consideration.	The sample used in TADS consisted of 369 adolescents with a diagnosis of major depressive disorder; ages 12-18 (mean age was 14.6). 57% of participants were female. Authors used QALY ratings to compare results to other treatment interventions.	Depression-free days were calculated using the scores on the Children's Depression Rating Scale—Revised (CDRS). Authors used depression free days to determine ratings for quality-adjusted life years (QALYS). This measurement is commonly used to calculate cost-effectiveness Clinical Global Impression severity	Results ranged from $24,000 per QALY for treatment with fluoxetine to $123,000 per QALY for COMB. Fluoxetine and COMB were found to be as cost-effective as other treatments provided in primary care when using a threshold of $125,000/QALY. Fluoxetine was the most cost-effective after 12 weeks of treatment. Fluoxetine and COMB were more cost-effective than placebo because they both fell under a threshold of $100,000/QALY. If assigning $200,000 per QALY, both fluoxetine and COMB were found to be cost-effective with a high degree of certainty (≥ 95%). The only difference found by researchers was CBT was the least effective treatment in participants with higher baseline severity of symptoms, and the cost-effectiveness for CBT was not reported due to lack of positive clinical effects.	Total median costs were: For COMB therapy, $2,832; for CBT, $2,287; for fluoxetine $942; and for placebo, $841. No difference in cost was found for CBT either in monotherapy or as part of combination therapy. The cost for individual appointments for fluoxetine was $90 for monotherapy and $74 in COMB. COMB therapy had the highest median cost, $762, followed by CBT, $580 and fluoxetine, $315. There were no differences in costs for any treatment arm for out-of-protocol time, travel costs and hospital services (breakdown for costs were: 13% for fluoxetine, 9% for CBT, 18% for COMB and 11% in the placebo group). One of the limitations was the comparison condition for the three active arms was placebo, and it is known that placebo can be more costly than active interventions. Another limitation is this study did not add suicide behavior and other adverse events in the cost-effectiveness analysis. Researchers attempted to include out-of-protocol costs, but this can be very difficult. Cost, such as the impact of depression on parents and siblings, other than time, was not included.	**Level of Evidence** Recommended for practice **I** (2) – well-controlled randomized clinical trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Dudley, A.L., Melvin, G.A., Williams, N.J., Tonge, B.J.., & King, N.J. (2005). Investigation of consumer satisfaction with cognitive-behavior therapy and sertraline in the treatment of adolescent depression	The purpose of this study was to test the psychometric properties of a new instrument, the Adolescent Depression Treatment Satisfaction Questionnaire (ADTSQ) in Australia. The consumer satisfaction questionnaire was filled by participants and one of their parents.	This study included 38 patients who participated in a randomized trial consisting of three treatment arms: cognitive behavioral therapy (CBT), sertraline monotherapy (SRT), Combined treatment of (SRT + CBT). Patients and one of their parents were asked to rank their most preferred treatment modalities: medication, individual counseling, group therapy and family therapy. Also, 37 parents filled out the questionnaire. Participants were 12-18 years old, with a mean age of 15.3 years, 67% were female and 68% of the parents were also female.	ADTSQ	No differences were found between the children's and the parents' total satisfaction scores in most areas, except for a significant difference (p=0.01) between groups in skills gained. However, addolescents reported a higher satisfaction with the skills learned than parents. Subjects treated with CBT had higher levels of skill acquisition than the patients treated with SRT monotherapy. Adolescents rated treatment preference as: 66% individual counseling, 29% medication, 5% group therapy and 0% family therapy. For parents, 74% preferred individual counseling, 17% medication, 6% group therapy and 3% family therapy.	Researchers reported that the higher levels of consumer satisfaction could be related to subjects accepting to participate in this type of structured trials to be more pleasing than the people who refuse to participate. Clinicians were aware that patients were going to be asked about their satisfaction, and the higher scores received could be related to clinicians ensuring that they were providing high quality treatment.	**Level of Evidence** Recommended for practice **I** (2) - Randomized trial with small sample size

Interventions for the Treatment of Depression in Adolescents - COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Emslie, G., Kratochvil, C., Vitiello, B., Silva, S. Mayes, T., McNulty, S., . . . , March, J. (2006). Treatment for adolescents with depression study (TADS): safety results	TADS was a multisite trial conducted in the United States recruited between spring 2000 and summer 2003. The purpose of this study was to examine the rates of physical, psychiatric and suicide related events in TADS at the end of 12 weeks of treatment.	TADS consisted of 439 subjects with a primary diagnosis of major depressive disorder (MDD) randomly assigned to 4 treatment arms: Fluoxetine (FLX), Cognitive Behavioral Therapy (CBT), FLX and CBT (Combined Treatment, COMB) and to placebo pills. At the end of the acute phase of treatment, 12 weeks, 359 (81%) of the participants were still in their assigned treatment group.	Adverse events were "spontaneously" reported by participants and clinicians Suicidal incidents were reviewed by the Columbia Group by using the Columbia Classification Algorithm Clinical Global Improvement (CGI) was used to rate psychiatric symptoms (depression, mania, irritability, depression, agitation, anxiety and other).	As depression rates decreased, participants had less physical complaints, the least improved treatment modality was the CBT group. Adverse effects were present in 11% of FLX patients, 5.6% in COMB, and 4.5% in CBT. 2% of patients reported sedation, insomnia, vomiting and upper abdominal pain. The rate of these complaints was twice in the FLX and COMB groups. Psychiatric Adverse Events were present in 11% of the patients in the FLX group, 5.6% in the COMB, 4.5% in placebo and 0.9% in CBT. Suicidal ideation decreased in all treatment groups. There were 5 suicide attempts and no completions (2 FLX, 2 COMB, 1 CBT, and 0 in PLO).	Researchers reported that different ways of reporting adverse events may affect the results. Self-report to therapists may have played a role in CBT. CBT had higher adverse events at weeks 6 and 12 than the other treatment arms. This may mean underreporting by CBT therapists at other assessment times. Clinicians should also be knowledgeable about distinguishing between suicide attempts and self-injurious behavior. Another limitation from TADS was that clinicians and patients were not blind to treatment assignment. Only FLX and PBO were double blind. Due to warnings about possible adverse effects with antidepressants, clinicians are advised to assess for hostility, agitation and mania in adolescents taking these types of medications.	Researchers recommend that future trials should include a structured systematic measurement to compare adverse effects in different treatment modalities. Authors concluded that as depression decreases, physical complaints and suicidal ideation also diminish. The FDA recommends that patients, when first prescribed antidepressants, should be evaluated for worsening of symptoms, suicidality and behavioral changes. Evaluation has to take place face-to-face by a clinician: 1). Weekly for 4 weeks 2). Every other week for one month, and at 3). 12 weeks **Level of Evidence** Recommended for practice **I**(2) well-controlled, randomized trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Goodyer, I.M., Dubicka, B., Wilkinson, P., Kelvin, R., Roberts, C., & Byford, S., (2008). A randomized controlled trial of cognitive behavior therapy in adolescents with major depression treated by selective serotonin reuptake inhibitors. The ADAPT Trial.	510 patients were evaluated between 2000 and 2004 from two centers in England, six Child and Mental Health Services (CAMHS) participated, two in Cambridge and four in Manchester. Unless subjects were very impaired, they were offered support, and if the subjects responded to this intervention they were excluded from the trial. 208 patients were randomized to receiving an SSRI (n=102), or to an SSRI plus CBT (n=106). The evaluation of outcomes was done by staff blinded to the intervention. Patients on both groups received typical treatment, such as support for patients and their families, psychoeducation, reflection and monitoring of mental state.	Subjects were referred by PCPs to CAMHS. Participants were mainly White European, with a female ratio of 3:1, and ½ of them lived with only one parent. **SSRI Treatment** Plan: Max. Fluoxetine dose: 60 mg/day. If not effective, subjects were switched to another SSRI. For participants already taking another SSRI at the beginning of treatment, they were continued on that same medication, and if not effective, they were changed to Fluoxetine. **SSRI plus CBT** In addition to receiving an SSRI, patients in this group also received CBT for 12 weeks, followed by sessions every two weeks for the next 12 weeks, and a final session at 28 weeks, for a total of 19 sessions. To ensure reliability and validity, audiotapes of CBT were made following the Quality of Therapy Scale.	**Primary Outcome**: Health of the Nation Outcome Scales for Children and Adolescents (HoNOSCA). Children's Global Assessment Scale (CGAS) <40. **Secondary Outcome** Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS-PL). Mood and Feelings Questionnaire (MFQ). Revised Children's Rating Scale (CDRS-R), modeled after the Hamilton Rating Scale. Health Related Quality of Life questionnaire.	AFTER 28 weeks, this study found no difference between the SSRI only and the SSRI plus CBT groups, and both groups showed the same level of improvement over time. No action was required in 90% of the reported side effects. In 18 or 10% of the patients, medication was stopped due to side effects. The most common side effects were: nausea, headaches and tiredness. Also, 2% of patients had problems with irritability, and 0.5% reported disinhibition.	Resource use was higher in the SSRI plus CBT group because this group had more hospital days. At the end of 12 weeks, the SSRI plus CBT group was significantly more expensive, this difference continued at 28 weeks, but it was no longer significant. HoNOSCA scores were 0.81 points worse over 28 weeks in the SSRI plus CBT group.	Since patients in both groups received support treatment, it is unknown if this had a role in the results, especially in the fluoxetine group since researchers found that spending more resources on SSRI + CBT was associated with poorer outcomes. **Level of Evidence** Recommended for practice **I**(2) - Well controlled, randomized clinical trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Goodyer, I., Dubicka, B., Wilkinson, P., Kelvin, R., Roberts, C., Byford, S., . . . , Harrington, S.. (2007). Selective serotonin reuptake inhibitors (SSRIs) and routine specialist care with and without cognitive behavior therapy in adolescents with major depression: randomized controlled trial	510 subjects ages 11 to 17, were recruited from 200 to 2004 at six outpatient clinics in Cambridge and Manchester. From 510 adolescents, 249 were considered and 164 were eligible to participate in a Brief Initial Intervention (BBI). N=126 did no respond to BBI 208 Youths were randomized: n=103 adolescents received an SSRI and routine care; n=105 received an SSRI, routine care, and CBT. CBT was offered weekly for first 12 weeks and every two weeks until week 28. Usual care consisted of explanations about depression. It also took it consideration recent peer or family conflicts. Interventions with schools and other agencies were included if needed.	Authors purpose was to test if, in the presence of routine specialist clinical care, cognitive behavioral care (CBT) plus an SSRI would be more beneficial than receiving only medication, an SSRI. at 12 or 28 weeks. The trial lasted 12 weeks followed by 16 weeks of maintenance. This study was labeled d as a pragmatic randomized superiority trial. Authors reported that, since this was a pragmatic study, they used manuals to guide treatment that could be generalized to general practice. Authors had data for 204(98%) of the subjects at least one of the assessment points over the 28 week period.	Measurements were given at baseline, 6, 12 and 28 weeks. For inclusion, subjects needed a ≥7 points in the Health of the Nation scale (mod. to severe symptoms). The Kiddie Schedule of affective disorders and schizophrenia present and lifetime version was later utilized (KSADS-PL).	One in five subjects showed improvement with the initial Brief Psychosocial Intervention. By 28 weeks, 57 of 94 subjects, or 61%, in the SSRI group and 52 of 98 adolescents, 53%, in the CBT plus SSRI group were found "much or very much improved. 16/94 (17%) of youths in the SSRI only group and 24/98 (25%) of subjects in the CBT plus SSRI group had worsening of symptoms or no response. No protective benefits from CBT were detected for suicidality.	The strengths of this study was that they included subjects who were very depressed including youths who showed severe impairment, including suicidality and self harm. To make sure only subjects with clinical depression were included, researchers did not include subjects who responded to a Brief Initial Intervention. This study was limited by the lack of a placebo group. Researchers also recommend further studies to detect long term effect. For depressed patients in community settings, with moderate to severe depression, researchers concluded that, adding CBT to "specialist active clinical care", in patients taking an SSRI. does not add benefit. Also, authors reported that the decreased response to CBT could be related to absenteeism to therapy sessions. Reduction in suicidal ideation and self-harm were identified in both treatment arms, but contrary to a US study (TADS), the present study did not find that SSRI + CBT offered protection against suicidal events. However, authors explain that they included subjects that were excluded from TADS, such as, adolescents with "active suicidal intent, self harm, thought disorder, severe conduct disorder and active substance misuse." Authors also asserted subjects in this study were probably the most symptomatic when compared to previous randomized trials.	**Level of Evidence:** Recommended for practice **I** (2) well-controlled randomized clinical trial

Interventions for the Treatment of Depression in Adolescents - COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Herman, K.C., Ostrander, R., Walkup, J.T., Silva, S.G., & March, J. S. (2007). Empirically Derived Subtypes of Adolescent Depression: Latent Profile Analysis of Co-Occurring Symptoms in the Treatment for Adolescents with Depression study (TADS)	The purpose of this study was to determine the incident of comorbidities in 423 adolescents participating in TADS, a multisite trial conducted in the United States recruited between spring 2000 and summer 2003. Subjects had a primary diagnosis of major depressive disorder MDD.	Cross-sectional study. Participants had a mean age of 14.6 years. 45.6% of the subjects were male and 73.8% were white.	Researchers used the Conner's Parent Rating Scale – Revised (CPRS-R) subscales scores as indicators. Researchers focused on common symptoms for which adolescents are referred for treatment: depression, anxiety, oppositional/ conduct problems, and inattention/ hyperactivity. Adolescents were assigned to 5 classes according to elevations in 1 or more subscales of the Children's Depression Rating Scale- Revised. Structured Clinical Interviews	Class 1. Depressed only, accounted for 20% of the participants. None of the mean indicators reached clinical significance. Only the psychosomatic indicator reached moderate level of impairment. Class 2. Anxious, 19% of the sample, with significant indicators for anxiety, social problems and psychosomatic subscales. They also had moderate scores on inattention and oppositional behavior. Class 3. Oppositional, was the highest indicator, 32%. Class 4. Non-anxious, severely disruptive, 19% of the subjects. Class 5. Anxious, severely disruptive, 10%.	No cost were reported for this study. Researchers reported that 80% of the subjects showed elevations on one of more subscales of the CPRS-R. This finding is consistent with prior results in the literature. Authors also used other measurements to validate the CPRS-R findings as well as child-rated symptoms and functional impairment as rated by a clinician. Limitations include that researchers used the CPRS-R, home version, as class indicator. Participants' symptoms did not include information from teachers or self.	This study presented a first set in finding common co-occurring disorders that can be present in adolescent depression. This knowledge is important to study treatment response and possible new approaches. Researchers recommend more studies in different samples. They also advise gathering information from different informants. In this case, parents were the exclusive source of information. **Level of Evidence** Recommended for practice **I**(2) well-controlled, randomized trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Kennard, B. D., Clarke, G.N., Weersing, V. R., Asarnow, J. .R. Shamseddeen, W., Porta, W., . . . , Brent, D. A. (2009). Effective Components of TORDIA Cognitive-Behavioral Therapy for Adolescent Depression: Preliminary Findings	Researchers conducted a secondary analysis to examine the effect of cognitive behavioral therapy (CBT), and its dosing, on patients participating in the Treatment of SSRI-Resistant Depression in Adolescents (TORDIA). 22 different CBT modules were included. Sessions were tailored to the needs of the patient. The protocol included 12 weekly sessions of 90 minutes durations. From the 12 sessions, 3 to 6 could be family sessions. .	Sample consisted of 334 subjects ages 12 to 18 years with a diagnosis of major depressive disorder who had to benefitted from a trial of a selective serotonin reuptake inhibitor (SSRI). Participants were randomized to four treatment arms: 1) Switch to a different SSRI plus CBT 2) Switch to a different SSRI without CBT 3) Switch To Venlafaxine plus CBT. 4) Switch To Venlafaxine without CBT. N=166 subjects were randomized to receive CBT. Their mean age was 16 years; 116 of the youths were female. The average age of onset of depression was 12.9 years old and the current episode had been present for almost 2 years.	Inclusion criteria included a diagnosis of clinical depression according to the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime Version, a score of ≥40 on the e Children's Depression Rating Scale-Revised (CDRS-R), and a score of ≥4 on the Clinical Global Impression—Severity scale (CGI-S).	Researchers found that the number of CBT sessions were important to obtain benefit from treatment. They also discovered a positive effect for the subjects who received problem-solving and social skills during their CBT sessions. Adolescents who received more than 9 therapy sessions were 2.5 times more likely to be responsive to treatment. Youths who had problem-solving and social skills during their CBT sessions were 2.3 to 2.6 times respectively more likely to respond to treatment.	Therapists received two (2) days of training, the first one at the beginning of this trial and the second one at midpoint. The quality of the sessions was conducted by rating the sessions according to the Cognitive Therapy Rating Scale. Limitations listed by the authors included lack of randomization to the different CBT modules since treatment was delivered according to the needs of the adolescents. Authors also did not rate the quality of the modules. In addition, they were not able to separate the dose of CBT and the modules used. Authors reported that these results might not be generalized to depressed adolescents in general because the adolescents in this study were receiving either an SSRI or venlafaxine. Also, Subjects had been resistant to SSRI medications and were chronically depressed.	Authors stress the benefit of using the treatment modules of problem solving and social skills training when delivering CBT to depressed adolescents. **Level of Evidence** Recommended for practice **I(**2) – Well-controlled, randomized clinical trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Kennard, B., D., Emslie, G.J., Mayes, T.L. Nightingale, J., Nakonezny, P A. Hughes, J. L., . . . Jarrett, R. B. (2008). Cognitive-behavioral therapy to prevent relapse in pediatric responders to pharmacotherapy for major depressive disorder.	This study was designed to prevent relapse in subjects who had responded to acute treatment. Acute treatment was defined as 12 weeks of pharmacotherapy with fluoxetine. This study was funded in part by the National Institute of Mental Health (NIMH), and it lasted 9 months.	Sample consisted of 46 subjects 11 to 18 years of age old with a diagnosis of major depressive disorder for at least 4 weeks. Responders were randomized to continue medication management (MM): n=24 or to relapse prevention (RP). This last group received MM plus cognitive behavioral therapy (MM + CBT), n= 22. Youths received 8 to 11 sessions over a period of 6 months with a minimum of three family sessions. Assessments were completed at weeks 12, 24, and 36. .	Response to treatment was described as 50% decreased in the a Children's Depression Rating Scale/Revised (CDRS-R) and a score of 1 or 2 in the Clinical Global Improvement (CGI) Relapse was defined as a score of ≥40 in the CDRS-R with two weeks of increased symptoms of depression as reported by patient and parent. Relapse could also be detected by clinicians even when the CDRS-R was <40. The Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL) was also used to determine the course and severity of symptoms.	The MM group had a higher risk of relapse than the MM + CBT subjects (hazard ratio 8.80, p = 0.049). Patients in the medication only group had an 8-fold possibility of relapse at 36 weeks. Possibility y of relapse at 36 weeks was 37% for the medication group and 15% for the MM + CBT group.	No reports regarding the cost of the intervention were given, but authors explained that therapists started training 6 months prior to the start of this study. Limitations include small sample size and the absence of a placebo intervention in place of CBT.	Relapse rates in pediatric major depression can be as high as 35% to 75%. This population also faces the possibility of residual symptoms with low remission rates. This study presents efforts to develop adequate response rates for adolescent depression, and it shows that continuation CBT following acute treatment could be an option to prevent relapse and to enhance the properties of antidepressants. **Level of Evidence** Recommended for practice **I** (3) – well-controlled randomized clinical trial with small sample size

Interventions for the Treatment of Depression in Adolescents – COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Kennard, B., Silva, S., Vitiello, B., Curry, J., Kratochvil, C., Simons, A., . . . , March, J. (2006) Remission and residual symptoms after short-term treatment in the treatment of adolescents with depression study (TADS)	Researchers conducted a secondary analysis of the TADS database to find out the number of patients who no longer met criteria for major depression disorder (MDD) after 12 weeks of treatment and to assess residual symptoms in responders. Before this study, there were no studies in children or adolescents comparing psychotherapy, medication and placebo on rates of remission.	The study sample include 439 adolescents who met DSM-IV criteria for MDD. Participants also had a score of ≥45 in the (CDRS-R). TADS was a multisite trial conducted from 2003 to 2005. It included 439 adolescents, ages 12 to 17 years old, who were randomized to four treatment arms: fluoxetine (FLX, cognitive-behavioral therapy (CBT), combination of fluoxetine and CBT (COMB), or to placebo (PBO) which consisted of clinical management plus a placebo pill	A score of ≤ 28 in the Children's Depression Rating Scale-Revised (CDRS-R) was used to determine remission Clinical Global Impressions-Improvement, (CGI) score of 1(very much improved) and 2(much improved).	102 of the 439 (23%) subjects remitted at the end of 12 weeks. COMB was superior with a 37% remission rate (FLX 23%, CBT 16%, PBO, 17%). FLX, CBT, and PBO rates were not statistically different from one another (p = .05). Response rates were higher for COMB,(71%), FLX (60.6%), CBT, 43.2%, PBO, (34.8%. 271 of 379 participants no longer met criteria for MDD after 12 weeks of treatment. The treatment allocation for these patients was: 85% for COMB, 78.6% for FLX, CBT, 61.1%, and PBO, 60.4%.	No costs were reported in this study. Limitations include the definition used for remission which was based in previous pharmacotherapy studies. Researchers recommend that the of definitions of remission should be related to levels of functioning and impairment.	Among the 271 subjects who no longer met criteria for MDD at the end of this trial, 174(64.2%) were nonremitters and 97 (35.8%) were remitters. The major difference in these two groups, was that nonremitters had the highest baseline severity of symptoms. 50% of the patients who no longer met criteria for MDD, and 75% of responders who did not reach remission, continued to have one or more residual symptoms (mainly sleep, mood disturbances, fatigue and poor concentration). **Level of Evidence** Recommended for practice **I**(2) well-controlled, randomized trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents – COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Kratochvil, C., Emslie, G. Silva, S., McNulty, S., Walkup, J., Curry, J., . . . , March, J. (2006) Acute time to response in the treatment for adolescents with depression study (TADS)	The purpose of this study was to examine the time to response in patients exposed to pharmacotherapy (PT) psychotherapy (CBT), combined treatment (COMB), consisting of PT plus CBT) and placebo in the Treatment for Adolescents with Depression Study (TADS). Since some patients did not maintain the initial response to treatment, authors also looked at the time to attaining a stable response.	TADS was a multisite conducted from 2003 to 2005. This trial included 439 adolescents, ages 12 to 17 years old, who were randomized to four treatment arms: fluoxetine (FLX, cognitive-behavioral therapy (CBT), combination of fluoxetine and CBT (COMB), or to placebo (PLO) which consisted of clinical management plus a placebo pill	Response was defined as "very much improved" or "much improved" according to the Clinical Global Impression-Improvement Scale (CGI-I) Children's Depression Rating Scale-Revised (CDRS-R)	Pharmacotherapists' scores showed: COMB and FLX treatment arms had a faster onset of benefit than PLO on time to respond and time to stable response ($p<0.001$). COMB was faster than FLX on time to stable response ($p = .034$). Psychotherapists' scores: COMB was faster in achieving first and stable response than CBT ($p<0.001$). The probability of sustained early response was approximately: three-fold higher for COMB than PLO Two-fold for FLX when compared to PBO, and 1.5 more for COMB than FLX	Researchers recommended training across raters for future studies. One limitation was that COMB, and CBT clinicians were aware of treatment assignment. In the FLX and PLO, clinicians were blind to the treatment assignment. Another limitation was the difficulty to evaluate all treatment arms at a scheduled time because CBT and PT protocols were different. Visits were less frequent in the pharmacotherapy groups than for CBT. Authors recommend that when considering treatment options, the efficacy, side effects, the ease of use, the cost, the availability and the time to achieve response should be taken into consideration.	Prior to TADS, there had been about 16 randomized, double-blind, placebo-controlled studies in pediatric depression, but in only one-third of these trials, the active drug separated from placebo. In the present study, according to therapists' ratings, stable response at week 12 had been achieved by 87.1 % of patients in the COMB group and 50.8% in the CBT. The pharmacotherapists' ratings also showed an increased benefit throughout treatment. In COMB, there was a steady response of 34.3% at week 6, and 70% by week 12. **Level of Evidence** Recommended for practice **I**(2) well-controlled, randomized trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents – COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Lewis, C. C., Simons, A. D. Silva, S. G., Rohde, P., Small, D. M., Murakami, J. L., . . . , March, J. (2009). The role of readiness to change in response to treatment of adolescent depression	Researchers conducted this study to determine if a treatment is more beneficial when it fits the individual's readiness' to change. Subjects were a subsample of the TADS (Treatment for Adolescents with Depression Study), a multisite randomized trial studying the effectiveness of fluoxetine, cognitive behavioral therapy (CBT), the combination of fluoxetine and CBT, and placebo.	The sample consisted of 332 adolescents with a diagnosis of major depressive disorder. To meet the inclusion criteria, subjects had to finish the first 12-weeks of TADS in their original assigned group, Participants were 12 to 17 years old (M= 14.60.). 46% were male and 74% were Caucasian. 10.2 African American, 9.3% Hispanic and 0.3% Pacific Islander. Subjects participated in a baseline assessment of the Stages of Change measurement. Depression assessments were correlated to the Stages of Change questionnaire. Subjects were assessed at baseline, Week 6, and Week 12. Assessments were conducted by an independent evaluator blinded to treatment assignment. CBT was manual-based which included effective features of past trials.	Children's Depression Rating Scale—Revised (CDRS–R) Stages of Change Questionnaire, abbreviate version, was used to evaluate 4 readiness to change scores: pre-contemplation, contemplation, action, and maintenance. Subjects were assessed at baseline, amid at weeks 6 and 12.	The hypothesis guiding this study stated that adolescents with high Action Scores would have a better response to CBT, and that the Action scores would not impact response to medication. This hypothesis was not statistical significant (p=.11). Researchers stated that the TADS might not have been adequately powered to detect this type of change. Even though subjects with the highest Action scores had the best response to treatment regardless of group assignment, authors found that the subjects with the highest Action scores were the patients receiving psychotherapy. High Action scores translated into decreased depression.	No cost was specified for this intervention. Authors were not sure if the positive results obtained in the CBT groups were related to therapists providing readiness to change content during their sessions. Since adolescent depression has a response rate of approximately 60%, it would be crucial to take into consideration features that could make a difference in the outcome of treatment. In the case of psychotherapy, this treatment modality requires that the patient participates actively in treatment since it involves homework assignments. It also involves learning and practicing new coping skills. The limitations of this study were: the use of a short version of the Stages of Change questionnaire to decrease time and costs, and authors recognized difficulty with the use of the Contemplations subscale. They also were not sure if this scale was the best one to assess readiness for change. Authors also reported a the lack of power in this study to detect a significant result, and authors suggest recruiting more subjects when conducting this type of study. Researchers indicated the need to assess for readiness for change by using different measurement tools.	The addition of motivational intervention to treat depressed adolescents improved treatment outcomes. Researchers recommend future trials to examine if the level of readiness is associated with homework compliance in CBT. **Level of Evidence** Recommended for practice **I (**2) Well-controlled, randomized trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
March, J., Silva S., Curry, J., Wells, K., Fairbank, J., Burns, B., . . . , Bartoi, M. (2009). The treatment for adolescents with depression study (TADS): outcomes over 1 year of naturalistic follow-up	The purpose of stage IV in the TADS was to test the hypothesis that longer-term treatment would show improvement and would promote remission after the end of TADS. TADS consisted of three stages, Stage I lasted 12 weeks (known as acute treatment, the second phase was a -6 week consolidation phase, and the third stage or continuation of treatment lasted 18 weeks. At the completion of Stage III, subjects were referred to continue treatment in outpatient settings and youths were assessed at 3, 6 9, and 12 months.	327 subjects entered Stage IV. They were between the ages of 12 and 17 and had a diagnosis of major depressive disorder, as indicated by the DSM-IV. During this stage, 215 or 65.7% of participants reported receiving a type of mental health service. 2.8% had received inpatient treatment, 34.0% with a non-physician mental health provider, and 17.2 % from a physician mental health provider. Even though this study had 4 planned assessments, it was reported that only 66% of participants were involved in at least one assessment.	1) Children's Depression Rating Scale—Revised 2) responder meant much improved or very much improved on the CGI improvement scale 3) Remission Status was rated using a cut off score of 28 or less on the Children's Depression Rating Scale 4) Reynolds Adolescent Depression Scale 5) Adolescent self-report in was used to assess for suicidal ideation, as well as a "flag" score of 31 or greater on the Suicidal Ideation Questionnaire—Junior High School Version was utilized.	The authors found that the Stage IV results replicated previous finds that combined treatment provided benefit starting at week 18, while for fluoxetine was 30 and for CBT 36 weeks. Also, that regardless of treatment, 9 months is superior to only providing 12 weeks of treatment. Previous studies have shown clinical decline after 12 weeks of treatment, Stage IV found that most subjects continued to improve even after treatment was discontinued. TADS, Authors also reiterated that combined therapy was superior numerically to monotherapy.	In contrast to previous reports on epidemiological showing high rates of clinical deterioration after short-term treatment, longer-term treatment results in sustained improvement even when active treatment is discontinued. Loss of benefit, defined as very mild deterioration, was experienced by 6% to 33% of the TADS patients during Stage IV, following the cessation of TADS (results might have depended on the measure chosen). While this is smaller than the 69% relapse rate identified in a recently completed study using placebo during withdrawal of fluoxetine, it remains substantial and indicates a need for long-term treatment in the treatment of major depressive disorder in youth. Although not statistically significant, combined treatment generally maintained numerical superiority relative to CBT and fluoxetine on many but not at all stage IV endpoints.	Three major limitations: 1) Lack of a placebo group. 2) "Substantial" missing data. 3) Lack of detail about services being utilized by participant. Researchers concluded that for therapeutic effect to be continued, 6 to 9 months of treatment are required, and that longer treatment may decrease the possibility of relapse once treatment is discontinued. It also reiterates that adding CBT to fluoxetine decreases suicidal ideation and events seen with medication therapy. Also, the benefits reported at the completion of TADS, at week 36, continued during the 1- year follow up on all measures of depression and suicidality. **Level of Evidence** Recommended for practice **I (**2) Well-controlled, randomized trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - COMBINED						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
March, J. S., Silva, S., Petrycki, S., Curry, J., Wells, K., Fairbank, J., Burns, B., . . . , Severe, J. (2007). The treatment for adolescents with depression Study (TADS): long-term effectiveness and safety outcomes	TADS was a randomized, controlled trial conducted in 13 academic and community facilities in the United States. This study examined the impact of treatment throughout 36 weeks of TADS in participants who had a main DSM-IV diagnosis of major depressive disorder. Effectiveness outcomes were reported for combination therapy (COMB), fluoxetine, and cognitive behavioral therapy (CBT).	327 adolescents entered the continuation intervention and 243 (74.3%) finished the 36 weeks of treatment. Mean age was 14.6 years. 149 participants left the study in the 36 weeks it lasted.	Children's Depression Rating Scale Revised And Clinical Global Impressions Improvement Score. Patients were assessed by an evaluator who was blind to the treatment at weeks 6, 12, 18, 24, 30, and 36. Suicidal ideation was assessed by a score of 31 or greater on the Suicidal Ideation Questionnaire–Junior High School Version (SIQ-Jr).	Response Rates: AT WEEK 12: 71% for combination therapy, 61% for fluoxetine therapy, 43% for CBT AT WEEK 18: 85% for combination therapy, 69% for fluoxetine therapy, and 65% for CBT. AT WEEK 36: 86% for combination therapy, 81% for fluoxetine therapy, and 81% for CB. At 36 weeks, suicidal events were: 14.7% for FLX, 8.4% for COMB, and 6.3% for CBT	10% of the patients attempted suicide during this trial (there were no completed suicides), and suicidal ideation decreased in all 4 groups even though it was present in 97/320 patients, 30.3%, of the sample at baseline. The greatest improvement was in the group receiving combination of fluoxetine and CBT During 36 weeks of treatment, suicide attempts were more common in patients receiving: Fluoxetine alone: (14.7%) Combination therapy (8.4%) CBT (6.3%). Findings: Treatment with fluoxetine alone or in combination with CBT showed faster improvement relative to CBT. CBT alone stated was closer to the effects of fluoxetine alone at the middle of the trial and to combination therapy at the end of the treatment. Patients treated with fluoxetine alone had double suicide events and this was interpreted as CBT having protective effects on suicidal events related to treatment. Patients in combination therapy proved superior at the end of 12 weeks in probability of remission and quality of life	Possible Limitations: Lack of Placebo Group at the end of 12 weeks: Researchers reported they were unable to determine if the positive effects were due to the passage of time and the attention given to participants. The passage of time is based on information that adolescent with MDD recover during the first year of illness. Patients in the COMB group had greater contact time that the patients in the fluoxetine or CBT groups. **Level of Evidence**: Recommended for practice I **(2)** - Well-controlled; randomized clinical trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
March, J., Silva, S., Vitiello, B., & The TADS team. (2006). The Treatment for Adolescents with Depression Study (TADS): methods and message at 12 weeks.	The primary effectiveness and safety analyses were conducted using an intention-to-treat principle The significant level was set a priori at 0.05. Participants were randomized to four treatment arms: fluoxetine (FLX, cognitive-behavioral therapy (CBT), combination of fluoxetine and CBT (COMB), or to placebo (PBO) which consisted of clinical management plus a placebo pill. TADS provided information on clinical questions regarding the short and longer-term benefits of these four treatment arms.	The study sample was composed of 439 adolescents, mean age 14.6, who met DSM-IV criteria for MDD. Participants also had a score of ≥45 in the (CDRS-R). TADS was a multisite conducted from 2003 to 2005. 45.6% of the subjects were male, 73.8% were white, 12.5% African American and 8.9% Hispanic. 41% of the participants lived with a single parent and 27% had been suspended from school.	First, participants filled the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime to clarify the diagnosis of major depressive disorder (MDD) at recruitment. Subjects were also evaluated at baseline and at weeks 6, 12, 18, 24 1n336 by an independent evaluator blind to treatment assignment, with two outcome measures: The CDRS-R and the Clinical Global Impressions-Improvement Scale (CGI-I). Researchers also used two secondary outcome measures: the Reynolds Adolescent Depression Scale and a the Suicidal Ideation Questionnaire-Junior High School version.	After 12 weeks, there was a statistically significance for COM arm (p=.001), but not for FLX (p=.096) or for CBT (p=.401). COMB was superior to FLX (p=.020) and CBT (p=0.001). FLX was found to be superior to CBT (p=0.013). 30% of the TADS participants were clinically suicidal at the beginning of the study, and 2% were severely suicidal. Suicidal ideation decreased in all 4 treatment arms, but there were more clinician-identified suicidal events in the FLX monotherapy group (11.9%), COMB, 8.4%, CBT 4.5% or PLO, 2.7%.	Out of the 439 patients (13.7%) had also a diagnosis of ADHD and 21 of them (4.8%) took an approved psychostimulant during the acute phase. Limitations, the lack of a CBT + placebo group, not masking the two CBT conditions were CBT was offered (the COMB and the CBT groups), lack of percentages of improvements in the FLX versus the PBO group, not reporting worsening of suicidality, and concern about how truly positively was the risk-benefit. Authors reported that, because of the lack of a CBT plus placebo group, it is difficult to know if the "modest" superiority of COMB over FLX was because of the expectation and because participants in the COMB group received more time and attention.	TADS results are open to clinical interpretation even when evidence was found favoring the use of COMB for MDD. Because of the risk of suicidal events attributed to FLX, providers may choose to start with CBT monotherapy and move to antidepressants only if CBT is not working. Also, when suicidality is present, providers may opt for COMB therapy to offer protection with CBT from the possible increased risk for suicidal ideation with FLX alone. Calculating the number needed for a suicidal event, the risk attributable to FLX would be in boys, one in 20,000 and for girls, one in 180,000. **Level of Evidence** Recommended for practice **I**(2) - well-controlled, randomized trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - COMBINED						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
March, J., Silva, S., Petrycki, S., Curry, J., Wells, K., Fairbank, J., . . . , Severe, J. (2004). Fluoxetine-cognitive-behavioral therapy, and their combination for adolescents with depression: treatment for adolescents with depression Study (TADS): randomized controlled trial.	Subjects participated in a randomized controlled trial for 12 weeks in which they were assigned to: 1) Fluoxetine alone (10-40 mgs/day) 2) Cognitive behavioral therapy (CBT) alone 3) Fluoxetine with CBT combined\ 4) Pill Placebo: Equiv to 10-40mgs/day.	439 adolescent subjects ages 12-17 diagnosed with major depressive disorder were randomized to 4 groups for 12 weeks. This trial took place at 13 US academic and community clinics during spring 2000 and summer 2003. Dispensing of placebo and fluoxetine was double-blind through the first 12 weeks only. Patients in the placebo group were treated as needed at the end of 12 weeks, but were no longer part of this study. At the end of 12 weeks, 327 patients continued treatment in their assigned treatment modality: combination therapy (n=107), fluoxetine therapy (n=109), and CBT (n=111).	Children's Depression Rating Scale Revised and Clinical Global Impressions Improvement Score	Compared with Placebo: The combination of fluoxetine and CBT was statistically significant (p=0.001). Rates for response were 71%. When compared to fluoxetine or CBT alone, the combination of CBT and fluoxetine was superior Fluoxetine alone was superior to treatment with CBT alone (p=.01). Fluoxetine had a response rate of 60.6 and CBT 43.2%. Response for placebo was 34.8%.	Suicidal ideation decreased in all 4 groups even though it was present in 29% of the sample at baseline, The greatest improvement was in the group receiving combination of fluoxetine and CBT. However seven or 1.6% of the patients attempted suicide during this trials (there were no completed suicides). It was not reported the group these patients belonged to.	**Level of Evidence** Recommended for practice I (**2**) - well-controlled. randomized clinical trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Melvin, G. A., Tonge, B.J., King, N.J., Heyne, D., Gordon, M.S, & Klinkeit (2006). A comparison of cognitive-behavioral therapy, sertraline and their combination for adolescent depression	Adolescents were randomly assigned to three treatment arms: Cognitive Behavioral Therapy (CBT). Antidepressant medication alone (MED). The medication used was Sertraline. Combined CBT + MED (COMB). Acute treatment included 12 sessions of CBT, 12 weeks of medication management, or 12 weeks of the COMB of CBT + MED. After participants finished the Acute Phase, they received 3 monthly booster sessions for each treatment.	Researchers recruited 73 subjects, ages 12 to 18 years. All subjects met DSM-IV criteria for a diagnosis of major depressive disorder (MDD), Dysthymic disorder (DD), or depressive disorder not otherwise specified (DDNOS). This study took place in two clinics in Melbourne and in one in Victoria, Australia. Seven participants withdrew from this study, 4 for improvement in symptoms, and 3 for minor adverse events.	Subjects were evaluated at pretreatment, right after acute treatment, and 6 months after termination of the study with the following outcome measurements: Reynolds Adolescent Depression Scale, Revised Children`s Manifest Anxiety Scale, Suicidal Ideation Questionnaire	The three treatment arms demonstrated a reduction in depression symptoms after the acute phase ended, and this improvement was present after 6 months of treatment. COMB was not superior to MED or to CBT. CBT was found to be more effective than MED for the treatment of mild to moderate depression. Remission at post-treatment was present in 71% of the CBT subjects, 33.3% in MED and 46.7% in COMB.	Sertraline was titrated to up to 100 mgs/day. Treatment integrity was achieved by using a manual for CBT. Clinicians were involved in weekly supervision and peer supervision weekly. Limitations include the lack of a placebo-control condition, the limited number of patients with severe depression (COMB treatment may be more effective in severe depression), the lower dose of sertraline used in this study might not have allowed for medication to show more effectiveness than CBT, and the independent raters were not blind to treatment assignment. Authors also reported that the small sample size might not have detected a difference even if present. 45 (88%) of 51 adolescents in the MED group reported adverse events. The most common adverse events were fatigue, decreased concentration and insomnia. One patient in the COMB was admitted to a psychiatric hospital due to suicidal ideation.	Researchers discussed that the results from the present study differ from the ones in TADS. In TADS, COMB was superior to MED and to CBT. **Level of Evidence** Recommended for practice **I**(3) - well-controlled, randomized trial with < 100 sample size

Interventions for the Treatment of Depression in Adolescents – COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Rohde, P., Silva, S.G., Toney, S.T., Kennard, B.D., Vitiello, B., Kratochvil, C. J., . . . , March, J. S., (2008). Achievement and maintenance of sustained response during the treatment for adolescents with depression study (TADS): continuation and maintenance therapy	The TADS study has been explained in previous studies. During the present study, authors addressed 2 concerns: To what degree do patients who had not responded to treatment during acute therapy will have a positive outcome during continuation and maintenance periods? Will patients who responded to treatment during the acute phase continue these results during continuation and maintenance therapy?	TADS sample consisted of 439 adolescents, ages 12 to 17, recruited in 13 sites in the United States from 2000 to 2003. All participants had a diagnosis of major depressive disorder according to DSM-IV criteria. From the original 439 subjects, 327 subjects entered the 12 weeks of acute treatment, and 242 adolescents completed this phase. At Week 12, 147 (60.7%) were considered as having a sustained response. These subjects had received: COMB 70.9%, FLX 67.5, and CBT 42.1%. Ninety-five (39.3%) of the 242 youths were considered as having a non-sustained response: COMB., 29.1%, FLX, 32.5% and CBT, 57.9%. Differences in treatment were significant for COMB and FLX (p=0.001).	Participants were assessed at baseline and at weeks 6, 12, 18, 24 and 36 with: Children's Depression Rating (CDRS-R) and the Clinical Global Impression-Improvement (CGI-I).	Subjects. who had not achieved definite or possible sustained response by week 12, achieved these responses by week 36. (COMB, 80%, FLX, 61.5%; CBT, 77.3%). Differences in sustained response were not significant at weeks 18 and 36 across the different treatments. Sustained Response rate was continued in 82.3% of the subjects who achieved a sustained response in Phase 1. Fifteen percent of the participants failed to maintain response in Phases 2, and 3. Youths who relapsed were from the following treatment groups: COMB, 11.5%, FLX, 25.9%, CBT, 31.3%. Possibly 19% of 55% of subjects who had not reached sustained response at the end of acute phase, responded with additional treatment.	No costs were reported in this study. Assessments were carried out by an independent evaluator blind to treatment condition. Authors noted that treatment response tended to happen slowly with CBT since there was no significant difference across treatments at the end of weeks 18 and 36 for this treatment modality. Limitations included not assessing for relapse or recurrence on a weekly basis, not having a placebo group following the acute phase, or Phase I, and the lack of data regarding compliance or adherence to treatment.	Since patients classified as "clear non-responders", n=28, were referred to treatment outside, TADS, the results in this study may be generalized only to patients who have had a partial response to CBT or to antidepressants after 12 weeks of treatment. **Level of Evidence** Recommended for practice **I** (2) - well-controlled randomized clinical trial with adequate sample size

Interventions for the Treatment of Depression in Adolescents - COMBINATION						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Vitiello, B., Rohde, P., Susan, S., Wells, K., Casat, C., Waslick, B., . . . , March, J. (2006). Functioning and quality of life in the Treatment for Adolescents with Depression Study (TADS)	TADS was a multisite conducted from 2003 to 2005. This trial included 439 adolescents who were randomized to four treatment arms: fluoxetine (FLX0, cognitive-behavioral therapy (CBT), combination of fluoxetine and CBT (COMB), or to placebo (PLO) which consisted of clinical management plus a placebo pill.	Researchers were interested on examining the effect of treatment after 12 weeks on functional impairment, overall health and quality of life of adolescents with depression.	Health of the Nation Outcome Scales for Children and Adolescents (HoNOSCA) Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire (PQ-LES-Q) Children's Global Assessment Scale (CGAS)	Compared with PLO, COMB was effective on the CGAS ($p<0.0001$), HoNOSCA ($p< .05$) and PQ-LES-Q ($p< .001$). Fluoxetine was superior to CBT and to PLO only on the CGAS ($p< .01$. CBT monotherapy was not statistically significant in any of the measures assessed. COMB treatment improved functioning, global health, and quality of life. FLXT improved functioning only when compared to PLO and to CBT.	Researchers reiterate that the combination of fluoxetine and CBT (COMB) was more effective than the other treatment arms. Authors emphasized the importance of longer treatment than 12 weeks since patients continued to improve regardless treatment assignment. One limitation includes the difficult to generalize results to practice settings since this was a trial that was closely monitored. Another possible limitation was that COMB, and CBT clinicians were aware of treatment assignment. In the FLX and PLO, clinicians were blind to the treatment assignment.	At 12 weeks, monotherapy with FLX and COM were not statistically significant, but were superior to PLO and to CBT monotherapy in reducing symptoms of depression. **Level of Evidence** Recommended for practice **I**(2**)** - well-controlled, randomized trial with adequate sample size

TABLE 7

INTERVENTIONS FOR THE TREATMENT OF DEPRESSION IN ADOLESCENTS – OTHER APPROACHES – PHYSICAL ACTIVITY

Interventions for the Treatment of Depression in Adolescents - OTHER/Dance						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Jeong, Y., Hong, S.C., Lee, M.S. & Park, M.C., Kim, Y. K., & Suh, C. M. (2005). Dance movement therapy (DMT) improves emotional responses and modulates neurohormones in adolescents with mild depression	The aim of this study was to examine the effectiveness of DMT in the reduction of symptoms of mild depression in adolescents and identify the possible physiological mechanisms underlying their benefit. The treatment group participated in a 45-DMT session three times a week for 12 weeks. DMT combines music, light exercise and sensory stimulation.	40 girls, mean age 16, in Korea, diagnosed with depression were randomly assigned to a dance movement group or to a control group.	Beck Depression Inventory Symptom Checklist List--90 Revised (SCL-90-R) Measurements for Neurohormones: Plasma serotonin Plasma dopamine Plasma cortisol concentrations	Results were consistent with previous studies that showed that DMT "reduces emotional disturbance, relieves tension, and improves self-esteem". Since there were increased levels of serotonin, decreased dopamine the benefits of DMT is attributed to the modulation of these Neurohormones. There were no significant changes in cortisol levels.	It is not explained how the providers of the DMT were trained. This type of intervention will require special training. Researchers compared positive results to previous studies that have shown that DMT improves emotional stability and self-esteem. It also decreases anxiety. These changes have been attributed to reduction of muscle tension and also to the decrease of stress hormones (cortisol concentrations).	Authors recognized the need for nonpharmacological approaches since psychotherapy or pharmacological options are not always effective or well tolerated. **Level of Evidence** Likely to be effective **I** (2) - randomized trials with small sample size.

Interventions for the Treatment of Depression in Adolescents - OTHER/ Exercise						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Nabkasorn, C., Miyai, N., Sootmongkol, A., Junprasert, S. Yamamoto, H., Arita, M., & Miyashita, K. (2006). Effects of physical exercise on depression, neuroendocrine stress hormones and physiological fitness in adolescent females with depressive symptoms	Authors examined the effects of physical exercise in adolescent females with mild to moderate depressive symptoms by designing a randomized control trial. Subjects were assigned to a physical exercise program or to usual daily activities' for 8 weeks. Subjects were crossed-over to the alternate group for another 8 weeks.	Data from 49 participants were considered for the analysis. Subjects were randomly assigned to: Physical exercise, 21, and to activities as usual, 28. Subjects were nursing students at a university in Chonburi, Thailand. Their average age was 18.7 years. Physical exercise consisted of group jogging for 50-minute sessions, 5 days a week.	The main outcome measure was: Centre for Epidemiologic Studies Depression (CES-D), cut off score was 16/60 to be included in the study. Tests for twenty-four hour urinary secretions of cortisol and epinephrine were done at baseline and at the end of the exercise program. These two measurements were done to evaluate psychophysical stress conditions.	For the group who received exercise first, decreased CES-D scores were found (p= 0.003). This score increased during the activity as usual group (p=0.037). For the group who received exercise after the cross-over, the CESD also was lower 8 weeks was p=0.008. Decreases in cortisol and epinephrine levels were seen after groups finished the intervention: Physical exercise.	No costs were reported for this activity. Authors found that a mild level of jogging lowered levels of depression and it also decreased the levels of cortisol and epinephrine levels.	**Level of Evidence** Likely to be effective **I** (3) well-designed, cross-sectional trial

Interventions for the Treatment of Depression in Adolescents - OTHER/ Exercise						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Johnson, C.C., Murray, D.M., Elder, J.P., Jobe, J.B., Dunn, A. L. , Kubik, M., & Schachter, K. (2008). Depressive symptoms and physical activity in adolescent girls	This study was designed to study the relationship of depressive symptoms and physical activity, by using self report measurements and accelerometry. 1397 girls participated in (three) cross-sectional measurements. Their mean age was 12 years old.	1721 adolescents were part of the Trial of Activity for Adolescent Girls (TAGG), a randomized, multicenter trial to evaluate the benefits of physical activity on heart disease. TAGG involved 36 schools. 46.7% of the sample was white, average age of 12 years old, 72.2% lived with both parents. From the 1721 TAGG participants, 1397 chose to complete the CES-D (a score of >16 indicated the "presumption of depression," and >24 "clinically meaningful" symptoms of depression in adolescents). Mean score in TAGG participants was 14.7, and about 18% adolescents had a score of >24 in the CES-D.	Center for Epidemiological Studies-Depression Scale (CES-D) MTI ActiGraph accelerometer. This monitor detects different levels of intensities of physical activity. 3DPAR – Physical Activity Recall. Participants completed this questionnaire to self-report physical activity. Sample also had measurements for body-mass-index, BMI, and filled out the Mediators and Moderators Student Questionnaire (MSQ).	No significant association between depression and physical activity was observed in this study. These girls had 24 min. of moderate-intensity and less than 6 min/day of vigorous physical activity a day. These levels of physical activity were below current public health recommendations of 60 min of MVPA (moderate to vigorous physical activity a day).	No costs were reported for this study. Authors reported that the results of this study could be due to the young age of the participants. First there is the possibility that these girls did not have symptoms of depression yet or that they were not yet able to identify symptoms of depression because of their age. The low levels of physical activity in these girls may also have impacted results.	Authors discussed how the majority of studies found an inverse relationship between depression and physical activity in adolescents. However, there are studies that have shown mixed results. For example, some trials have found that only physical activity of high-intensity has shown positive psychological effects. Depression is known to be higher in females, and boys are known to be almost twice as physically active than girls. 18% of the adolescents had a score greater than 24. This is concerning due to the relationship between subsyndromal symptoms of depression and psychosocial impairment, as well as the possibility of the development of depression in adulthood. **Level of Evidence** Likely to be effective **I** (3) - well-designed, cross-sectional trial without randomization.

TABLE 8

INTERVENTIONS FOR THE TREATMENT OF DEPRESSION IN ADOLESCENTS –

OTHER APPROACHES –

COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM)

Interventions for the Treatment of Depression in Adolescents - OTHER/CAM Approaches						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Jorm, A.F., Allen, N.B., O'Donnell, C.P, Parslow, R.A. Purcell, R,. & Morgan, A.J. (2006) Effectiveness of complementary and self-help treatments for depression in children and adolescents	Authors did a systematic literature search of PubMed, PsycINFO and the Cochrane Library. They also explored 20 CAM websites retrieved by Google. Searches included interventions up to February 2006 for all Complementary and Alternative Medicine (CAM) treatments, except for Omega-3 fatty acids which included information until August, 2006. Authors found 13 intervention studies in children and adolescents of ≤ 19 years of age.	Studies selected were evaluated by two reviewers following the Oxford centre for Evidence-based Medicine, and consensus had to be reached. Researchers only reviewed studies with 3 or higher level on the Oxford Scale. Treatments that did not have relevant evidence were: Homeopathic remedies Physical treatments (for example, acupuncture), physiological and lifestyle treatments and dietary interventions.	Measurements were only cited in two of the studies. Children's Depression Rating Scale was used in a Study for Omega-3 with children ages 6-12. A massage intervention used electroencephalogram to detect asymmetry (a possible marker for depression).	Omega 3 fatty acids decreased more than 50% symptoms in 7 out of 10 children after one month. Light Therapy: 2 randomized trials. First study had, unknown number of subjects, and (2) with 28 subjects. Results showed that parents reported improvement in their children, but the patients did not. Also, researchers found that light therapy had "reasonable supporting evidence" for use in winter depression. Massage Therapy: A trial of 32 adolescents randomized to either massage or relaxation therapy. After 5 weeks, there was report of immediate, but not of sustained benefit for the massage intervention. Authors also reviewed "psychological or lifestyle treatments:" Art therapy (not effective), bibliotherapy (not enough evidence), distraction techniques (insufficient evidence), and Relaxation Therapy (only possible immediate effects).	Authors recognized that all the studies they reviewed were of small sample size. They reported that they had found "relevant evidence" for glutamine, S-adenosylmethionine and for St. John's Wort, but these treatment modalities were not represent in this report. Authors recognized the need for treatment either by CAM or by conventional approaches due to need to decrease symptoms in a present depressive episode and to prevent relapse and the possibility of chronic disability. They also recommend the need for children and adolescents to have access to different treatments for depression since antidepressants are not first line of treatment for mild and moderate depression and the treatment with psychotherapy has yielded "modest" results.	**Level of Evidence** Effectiveness not well established **II**(7) - systematic review of conflicting evidence

Interventions for the Treatment of Depression in Adolescents - OTHER/CAM Approaches						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Simeon, J., Nixon, M.K., Millin, R., Jovanovic, R., & Walker, S. (2005). Open-label pilot study of St. John's wort in adolescent depression	This was an 8-week open label study to evaluate the efficacy and safety of St. John's Wort (SJW).	11 of 26 adolescents completed this study (patients withdrew due to increased depression and noncompliance). Participants were ages 12 to 17. They were recruited from the outpatient and inpatient programs in Ottawa and in Ontario, Canada. Subjects who finished this trial 7 were male and 4 female. Patients were screened by psychiatrists to determine if patients met a diagnosis of major depressive disorder (MDD).	Clinician Rating Scales: Montgomery Asberg Depression Rating Scale (MADRS) Clinical Global Improvement (CGI) Hamilton-Anxiety Children's Depression Rating Scale – Revised (CDRS-R) Self-Rating Scales Beck Depression Inventory (BDI) Visual Analog Scale (VAS)	9 of the patients had a significant change in the Clinical Global Improvement (CGI) scale (much improved or very much improved.	Limitations included lack of a placebo group, small sample, and dosing. Subjects were on a fixed dose of 300 mg tid.	Researchers monitored laboratory tests, EKG, weight and blood pressure, and they concluded that SJW was safe for this population and that may be effective in the treatment of "some adolescents" suffering from mild depression. **Level of Evidence** Effectiveness not well established **I**(3) well designed trial, without randomization of small sample size

TABLE 9

INTERVENTIONS FOR THE TREATMENT OF DEPRESSION IN ADOLESCENTS –

OTHER APPROACHES –

REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (RTMS)

Interventions for the Treatment of Depression in Adolescents – Other/ rTMs						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Bloch, Y., Grisaru, N., Harel, E.V., Beitler, G., Faivel, N., Ratzoni, G., . . . Levkovitz, Y. (2008). Repetitive transcranial magnetic stimulation in the treatment of depression in adolescents: an open-label study	Treatments were given for 20 min/d over 14 working days, at 10 Hz for 2seconds per train, with an intertrain interval of 58 seconds. These parameters were set by the review board as a safety measure, and they are considered to be of low intensity, It was reported that participants had also other psychiatric comorbidities.	This study included 9 subjects ages 16 to 18 (2 male and 7 female) years, diagnosed with resistant depression. Resistant depression was defined as depression persisting after failing 1 course of psychotherapy and two medication trials, one of the medications had to be fluoxetine initiated at 20 mg and titrated to 40 mg/d. for 8 weeks.	1)Child Depression Rating Scale (CDRS) 2)Screen for Child Anxiety-Related Disorders 3)Suicide Ideation Questionnaire 4) Clinical Global Impression Scale (CGIS). 5)Neuropsychological Test Automated Battery. rTMS was delivered by a Caldwell high-speed machine magnetic stimulator with a 9-cm-diameter circular coil.	There was a significant decrease in depression levels at days 7 - 10 and one months after finishing treatment according to Beck, CDRS, and anxiety levels. However, suicide ideation did not change with rTMS therapy. Adverse effects in memory, attention, set shifting, attention were not affected according to the Cambridge Neuropsychological Automated Battery test.	This was the first study using rTMS for the treatment of resistant depression in adolescents. The study does not mention the training needed to administer rTMS. It reports the side effects as mild, but they were not listed.	Small sample size This study did not mention the cost associated with this type of treatment. It also did not mention the possible risks. **Level of Evidence** Effectiveness not established **II (6)** – uncontrolled study

Interventions for the Treatment of Depression in Adolescents - OTHER/rTMs						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Loo, C., McFarquhar, T., & Walter, G. (2006). Case reports: transcranial magnetic stimulation in adolescent depression	The purpose of this 4-week study was to test the safety and efficacy of repetitive transcranial magnetic stimulation (rTMs) for the treatment for adolescents with depression. This trial was conducted in Sidney, Australia and published under "Case Reports."	This study was described as a double-blind, sham-controlled trial using random allocation. It included only two participants. However, both subjects were randomly assigned to rTMs. Subject 1: female, age 16 with a 2 year history of depression with worsening symptoms. She also had concerns about her sexual orientation with a history of "voices inside her head" that would criticize her. Subject 2: female, age 16. She had a history of mood deterioration for 18 months, and for the last months she had been cutting and picking at her wrists. Her medications were continued during the trial: venlafaxine 225 mg/day, and methylphenidate 20mg/day.	Assessments were conducted at baseline and weekly until treatment ended. Patients were also evaluated 1 month after the treatment had ended. Scales used were: the Montgomery-Asberg Depression Rating Scale, (MADRS) Clinical Global Impression Severity Scale, (CGI-S) Beck Depression Inventory (BID) Centre for Epidemiological Studies-Depression-Child Scale (CES-DC)	Subject 1. Received 29 rTMs over a 6-week period. Subject 2: Missed about one session per week, and had 13 days without treatment for 13 days due to transportation problems. When she went back to receive rTMs, she received 20 more sessions over 5 weeks. Depression scores improved for both subjects and their symptoms of depression decreased. No side effects were reported and their cognitive test results did not show any change. The benefit of rTMs had persisted for 4 months after ending treatment for Subject 1. Subject 2 was last evaluated three months after she had rTMs and improvement was still present.	Subject 2 showed a slower rate of improvement possible due to missed treatments (studies reporting efficacy on the use of rTMs have been delivered on consecutive weekdays). Subjects received different amount of rTMs over a different number of weeks.	The authors offered more of a qualitative description when reporting improvement of symptoms. Graphs provided a decrease in the outcome measures. Study provided information on rTMs as a possible treatment for depression in adolescents. **Level of Evidence** Effectiveness not established **II (**5)- case-control study

TABLE 10

INTERVENTIONS FOR THE TREATMENT OF DEPRESSION IN ADOLESCENTS –

OTHER APPROACHES –

ELECTROCONVULSIVE THERAPY (ECT)

Interventions for the Treatment of Depression in Adolescents/Other ECT						
Author and Year	Characteristics of the Intervention	Sample and Setting Study Design	Measures	Results and Conclusions	Limitations, Flaws, Cautions, Training Needs and Costs	Level of Evidence and Comments
Ghaziuddin, N., Kutcher, S.P., Knapp, P., and the Work Group on Quality Issues. (2004). AACAP Official Action: Practice parameter for use of electroconvulsive therapy (ECT) with adolescents	The purpose of this parameter was to aid clinicians make decisions when treating adolescents with severe, recurrent major depression. To develop this parameter, authors evaluated the literature and requested clinical consensus from experts. To be considered for ECT, symptoms need to be severe and disabling, such as cases of life-threatening symptoms, such increased suicidality and the refusal to eat or drink,, extreme mania and psychotic symptoms. Patients also have to have failed at least two adequate trials of pharmacological agents in conjunction with other treatment modalities, such as psychotherapy	Authors searched Medline; they also contacted professionals to obtain their expert opinion. Studies included subjects ages 13 to 18. Clinicians need to be aware of state and institutional guidelines for adolescents to be age eligible for ECT. In Texas and Colorado, patients have to be 16 or older to receive this type of treatment, in Tennessee not younger than 14, and in California the cut off age is 12 years old.	Outcome measures included: The Children's Depression Rating Scale (CDRS) The Clinical Global Improvement (CGI) The Hamilton Rating Scale for Depression (HAM-D)	Results from different studies were as follows: 1. Included 11 adolescents who had not responded to three or more antidepressants and 64% of them achieved response with ECT. 2. Adolescents ages 16 to 18 years old, n=13, 76% response rate. 3. The review of 60 studies, involving 396 subjects, found a 63% remission rate for patients with depression. 4. A Study of ECT with 42 patients, ages 14 to 18, had a 51% response across diagnosis. 5. In a trial of ECT with 21 adolescents, ages 14 to 19, had a 100% response for patients with depression. 6. Adolescents, ages 13 to 17, were treated with ECT from 1978 to 1996, authors reported complete remission in 60% of the subjects and partial remission in 40% of the subjects. The results were maintained at one-month follow-up.	Adverse events regarding ECT include difficulty learning new material, seizures and the risks associated with general anesthesia. Because of the side effects involved, clinicians still consider ECT to be an unethical and controversial treatment. As of 2004, only two studies had studied cognitive impairment associated with ECT in adolescents. In one study, 10 adolescents were compared to controls 3.5 years after completion of ECT and no significant group differences were found. The second study compared cognitive functioning before and after ECT and found that patients at 7 ± 10.3 days after their last ECT treatment showed significant impairment in concentration, attention, verbal and visual delayed recall and verbal fluency, but at 8.5 ± 4.9 months after the last treatment, participants had completed recovered and had returned to their pre-ECT baseline.	Authors reported that the available studies demonstrated that only a few providers had the necessary experience to evaluate for ECT. Many psychiatrists also lack the training to administer it. ECT is an effective treatment during periods of high acuity, but it will not prevent relapse. At the time this article was written, there were also no specific guidelines about the use of maintenance ECT in adolescents, and researchers advised for adolescents to be placed in a therapeutic schedule to maintain treatment response. **Level of Evidence** Benefit is balanced with harms **II** (4) Well-conducted systematic review of non-experimental design studies

REFERENCES

AACAP Official Action (2007). Practice parameters for the psychiatric assessment of children and adolescents. *Journal of the American Academy of Child & Adolescent Psychiatry*, *36* (10), 4S-10S (Supplement).

Abela, J.R.Z., Parkinson, C., Stolow, D., Starrs, C. (2009). A test of the integration of the hopelessness and response styles theories of depression in middle adolescence. *Journal of Clinical Child & Adolescent Psychology*, *38*(3), 354-364.

American Academy of Child & Adolescent Psychiatry (2005). Practice parameter for the assessment and treatment of children and adolescents with reactive attachment disorder. *Journal of the American Academy of Child & Adolescent Psychiatry, 44*, 1206-1219.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (DSM-IV-TR) (4th ed.). Washington, DC: American Psychiatric Press.

Arias, E. MacDorman, M.F., Strobino, D.M., & Guyer, B. (2002). Annual summary of vital Statistics, *Pediatrics, 112*(6), 1215-1230.

Asarnow, R.J., Emslie, G., Clarke, G., & Wagner, K.D., Spirito, A., Vitiello, B., . . . & Brent, D. (2009). Treatment of selective serotonin reuptake inhibitor-resistant depression in adolescents: predictors and moderators of treatment response. *J. Am. Acad. Child &* Adolesc. *Psychiatry*, *48*(3), 330-339.

Asarnow, J. R., Jaycox, L. H., Tang, L., Duan, N., LaBorde, A. P., Zeledon, L. R., . . . & Wells, K. B. (2009). Long-term benefits of short-term quality improvement interventions for depressed adolescents in primary care. *American Journal of Psychiatry, 166*(9), 1002-10.

Asarnow, J.R., Jaycox, L.H., Duan, N., LaBorde, A.P., Rea, M.M., Murray, P., . . . & Wells, K. B. (2005). Effectiveness of a quality improvement intervention for adolescent depression in primary care clinics: a randomized controlled trial. *JAMA, 293*(3), 311-9.

Badger, T. (2010). Depression in Families. In J. J. Fitpatrick & P. A. Wilke (Eds.), *Psychiatric mental health nursing research digest* (pp. 188-191). New York, NY: Springer Publishing Company.

Barnet, B., Liu, J., & Devoe, M. (2008). Double jeopardy: depressive symptoms and rapid subsequent pregnancy in adolescent mothers. *Archives of Pediatrics & Adolescent Medicine, 162*(3), 246-252.

Beck, A.T. & Alford, B.A. (2009). *Depression. Causes and treatment* (2nd ed.). Philadelphia, PA: University of Pennsylvania Press.

Bennett, D.S. (1994). Depression among children with chronic medical problems: a meta-analysis. *Journal of Pediatric Psychology, 19*(2), 149-169.

Berard, R., Fong, R., Carpenter, D.J., Thomson, C., & Wilkinson, C. (2006). An international, multi-center, placebo-controlled trial of paroxetine in adolescents with major depressive disorder. *Journal of Child & Adolescent Psychopharmacology, 16*(1-2), 59-75.

Birmaher, B., Brent, D. AACAP Work Group on Quality Issues. Bernet, W., Bukstein, O., Benson, W.H., Chrisman, R.S., . . . & Medicus, J. (2007). Practice parameter for the assessment and treatment of children and adolescents with depressive disorders. *Journal of the American Academy of Child & Adolescent Psychiatry, 46*(11), 1503-1526.

Bloch, Y., Grisaru, N., Harel, E.V., Beitler, G., Faivel, N., Ratzoni, G., . . . & Levkovitz. Y. (2008). Repetitive transcranial magnetic stimulation in the treatment of depression in adolescents: An open-label study. *J. ECT, 24*(2), 156-159.

Boyce, W.T. & Ellis, B.J. (2005). Biological sensitivity to context: An evolutionary-developmental theory of the origins and functions of stress reactivity. *Developmental Psychopathology, 17*, 271-302.

Brent, D.A., Emslie, G.J., Clarke, G.N., Asarnow, J., Spirito, A., Ritz, L., . . . & Keller, M.B. (2009). Predictors of spontaneous and systematically assessed suicidal adverse events in the treatment of SSRI- Resistant Depression in Adolescents (TORDIA) study. *Am. J. Psychiatry, 166*(4), 418-426.

Brent, D., Emslie, G., Clarke, G., Wagner, K.D. Asarnow, J.R., Keller, M., . . . & Zelazny, J., (2008). Switching to another SSRI or to venlafaxine with or without cognitive behavioral therapy for adolescents with SSRI-resistant depression: The TORDIA randomized trial. J*AMA, 299*(8), 901-913.

Bridge J.A., Iyengar S., Salary, C.B., Barbe, R.P., Birmaher, B., Pincus, H.A., . . . & Brent, D. (2007). Clinical response and risk for reported suicidal ideation and suicide attempts in pediatric antidepressant treatment: a meta-analysis of randomized controlled trials. *JAMA, 297*(15), 1683-1696.

Bridge, J.A. Barbe, R.P., Birmaher, B., Kolko, D., & Brent, D.A. (2005). Emergent suicidality in a clinical psychotherapy trail for adolescent depression. *American Journal of Psychiatry, 162*(11), 2173-5.

Brunstein-Klomek, A., Zalsman, G., & Mufson, L. (2007). Interpersonal psychotherapy for depressed adolescents (IPT-A). *Israel Journal of Psychiatry & Related Sciences, 44*(1), 40-6.

Byford, S., Barrett, C., Roberts, P., Wilkinson, B., Dubicka, R.G., Kelvin, R.G., . . . & Goodyer, I. (2007). Cost-effectiveness of selective serotonin reuptake inhibitors and routine specialist care with and without cognitive behavioural therapy in adolescents with major depression. *British Journal of Psychiatry, 191*, 521-527.

Callan, J.A, & Howland, R.H. (2009). Adolescent repression: Assessment and treatment. *Journal of Psychosocial Nursing. 47*(7), 11-12.

Campo, J.V. & Bridge, J.A. (2009). Editorial: Treatment of Youth Depression. *Am. J. Psychiatric, 166*(9), 958-960.

Canals, J., Domenech-Laberia, Fernandez-Ballart, J., & Marti-Henneberg, C. (2002). Predictors of depression at eighteen. A 7 year follow-up study in Spanish nonclinical population. *European Child & Adolescent Psychiatry, 11*, 226-233.

Centers for Disease Control (CDC). (Summer, 2008). Suicide. Retrieved from: http://www.cdc.gov/ViolencePrevention/pdf/Suicide-DataSheet-a.pdf

Chaiton, M., Sabiston, C., O'Loughlin, C., McGrath, J., Maximova, K., & Lambert, M.A. (2009). Structural equation model relating adiposity, psychosocial indicators of body image and depressive symptoms among adolescents. *International Journal of Obesity, 33*(5), 588-596.

Cheung, A., Kusumakar, V., Kutcher, S., Dubo, E., Garland, J., Weiss, M., . . . & Levitt, A. (2008). Maintenance study for adolescent depression (Brief report). *Journal of Child and Adolescent Psychopharmacology, 18*(4), 389-394.

Cheung, A., Zuckerbrot, R.A., Jensen, P.S., Ghalib, K., Laraque, D., Stein, R.E., & the GLAD-PC Steering Group (2007). Guidelines for adolescent depression in primary care (GLAD-PC): II treatment and ongoing management. *Pediatrics. 120*(5):e1313-1326.

Cheung, A.H., Emslie, G.J., & Mayes, T.L. (2005). Review of the efficacy and safety of antidepressants in youth depression. *Journal of Child Psychology and Psychiatry, 46*(7), 735-754.

Chism, L.A. (2009). Toward clarification of the doctor of nursing practice degree. *Advanced Emergency Nursing Journal, 31*(4), 287-297.

Clarke, G., Debar, L., Lynch, F., Powell, J., Gale, J., O'Connor, E., . . . & Hertert, S. (2005). A randomized effectiveness trial of brief cognitive-behavioral therapy for depressed adolescents receiving antidepressant medication. *Journal of the American Academy of Child & Adolescent Psychiatry, 44(*9), 888-898.

Cohen, D., Deniau, E., Maturana, A., Tanguy, M.L., Bodeau, N., Labelle, R., . . . & Guile, J.M. (2008). Are child and adolescent responses to placebo higher in major depression than in anxiety disorders? A systematic review of placebo-controlled trials. *PLoS, 3*(7), e2632.

Committee on Psychosocial Aspects of Child and Family Health and Task Force on Mental Health (2009). The future of pediatrics: mental health competencies for pediatric primary care. *Pediatrics, 124*(1), 410-421.

Cooper, H. (1998). *Synthesizing research. A guide for literature reviews. Applied social research methods series*: Volume 2 (3rd ed.). Thousand, Oaks, CA: Sage Publications.

Cuijpers, P., van Straten, A., Smits, N., & Smit, F. (2006). Screening and early psychological intervention for depression in schools: Systematic review and meta-analysis. *European Child & Adolescent Psychiatry, 15*(5), 300-307.

Craighead, W.E. & Wilcoxon Craighead, L. (2001). The role of psychotherapy in treating psychiatric disorders. *Medical Clinics of North America, 85*(3), 1-10.

Crossing the Quality Chasm; A New Health Care System for the 21st Century. (2001). Institute of Medicine. Retrieved on October 22, 2010: from: http://www.iom.edu/~/media/Files/Report%20Files/2001/Crossing-the-Quality-Chasm/Quality%20Chasm%202001%20%20report%20brief.pdf

Cummings, E.M., Schermerhorn, A.C., & Davies, P.T. (2006). Interparental discord and child adjustment: Prospective investigations of emotional security as an explanatory mechanism. *Child Development, 77*(1), 132-152.

Curry, J., Rohde, P., Simons, A., Silva, S., Vitiello, J., Kratochvil, C., . . . & March, J; TADS Team. (2006). Predictors and moderators of acute outcome in the treatment for adolescents with depression study (TADS). *J. Am. Acad. Child Adolesc. Psychiatry, 45*(12), 1427-1439.

Danielson, C.K., Kilpatrick, M.A., Saunders, D.G., & Riesnick, B.E. (2005). Child maltreatment in depressed adolescents: Differences in symptomatology based on history of abuse. *Child Maltreatment, 10*(1), 37-48.

Davidson, K.W., Rieckmann, N., & Lesperance, F. (2004). Psychosocial theories of depression: Potential application for the prevention of acute coronary syndrome recurrence. *Psychosomatic Medicine, 66*, 165-173.

Depression Center. (2006). *Suicide in the United States*. Retrieved from: http://www.everydayhealth.com/depression/understanding/suicide.aspx

Depression Help for You. (2009). *Old terms for Types of Depression*. Retrieved from: http://www.depression-help-for-you.com/types-of-depression.html

Diamond, A. (2009). The interplay of biology and the environment broadly defined. *Developmental Psychology, 45*(1), 1-8.

Dicenso, A., Guyatt, G., & Ciliska, D. (2005). *Evidence-based nursing: A guide to Clinical practice.* St. Louis, MO: Elsevier Mosby.

Domino, M.E., Foster, M., Vitiello, B., Kratochvil, C.J., Burns, B., Silva, S.G., . . . & March, J.S. (2009). Relative cost-effectiveness of treatments for adolescent depression: 36-week results from the TADS randomized trial. *J. Am. Acad. Child/Adolesc. Psychiatry,48*(7), 711-720.

Domino, M.E., Burns, B.J., Silva, S. G., Kratochvil, C.J., Vitiello, B., Reinecke, M.A., . . . & March, J.S. (2008). Cost-effectiveness of treatment for adolescent depression: results from TADS. *American Journal of Psychiatry, 165*(5), 588-596.

Donaldson, D., Spirito, A., & Esposito-Smythers, C. (2005). Treatment for adolescents following a suicide attempt: Results of a pilot trial. *Journal of the American Academy of Child & Adolescent Psychiatry, 44*(2), 113-1120.

Donnelly, C.L., Wagner, K.D., Rynn, M., Ambrosini, P., Landau, P., Yang, R., & Wohlberg, C.J. (2006). Sertraline in children and adolescents with major depressive disorder. *J. Am. Acad. Child Adolesc. Psychiatry, 45*(10), 1162-1170.

Driever, M. (2002. Issues in Clinical Nursing Research: Are evidence-based practice and best practice the same? *Western Journal of Nursing Research 4*(5), 591-597.

Dubicka, B., Hadley, S., & Roberts, C. (2006). Suicidal behaviour in adolescents with depression treated with new-generation antidepressants: Meta-analysis. *British Journal of Psychiatry, 189,* 393-398.

Dudley, A.L., Melvin, G.A., Williams, N.J., Tonge, B.J. & King, N.J. (2005). Investigation of consumer satisfaction with cognitive-behavior therapy and sertraline in the treatment of adolescent depression. *Australian & New Zealand Journal of Psychiatry, 39*(6), 500-506.

Eaton, L.H. & Tipton, J.M. (2009). *Putting evidence into practice: Improving oncology patient outcomes*. Pittsburgh, PA: Oncology Nursing Society Publishing Division.

Emslie, G.J., Findling, R.L., Yeung, P.P., Kunz, N.R., & Li, Y. (2007). Venlafaxine ER for the treatment of pediatric subjects with depression: Results of two placebo-controlled trials. *J. Am. Acad. Child Adolesc. Psychiatry, 46*(5), 573-581.

Emlie, G.J., Heilingstein, J.H., Hoog, S.L., Wagner, K.D., Findling, R.L. McCraken, J.T., . . . & Jacobson, J.G. (2004). Fluoxetine treatment for prevention of relapse of depression in children and adolescents: A double-blind, placebo controlled study. *Journal of the American Academy of Child & Adolescent Psychiatry, 43*(11), 1397-1405.

Emslie, G.J., Kennard, B.D., Mayes, T.L., Nightingale, J., Carmody, T., Hughes, C.W., . . . & Rintelmann, J.W. (2008). Fluoxetine versus placebo in preventing relapse of major depression in children and adolescents. *Am. J. Psychiatry, 165*(4), 459-467.

Emslie, G., Kratochwil, C., Vitiello, B., Silva, S., Mayes, T, McNulty, S., . . . & March, J.; Columbia suicidality classification group; TADS Team. (2006). Treatment for adolescents with depression study (TADS): Safety results. *J. Am. Acad. Child Adolesc. Psychiatry, 45*(12), 1440-1455.

Emslie, G.J., Ventura, D., Korotzer, A., & Tourkodimitris, S. (2009). Escitalopram in the treatment of adolescent depression: A randomized placebo-controlled multisite trial. *J. Am. Acad. Child Adolesc. Psychiatry, 48*(7), 721-729.

Emslie, G.J., Wagner, K.D., Kutcher, S., Krulewicz, S. Fong, R., Carpenter, D.J., . . . & Wilkinson, C. (2006). Paroxetine treatment in children and adolescents with major Depressive disorder: A randomized multicenter, double-blind, placebo-controlled trial. *Journal of the American Academy of Child & Adolescent Psychiatry, 45*(6), 709-719.

Emslie, G.J., Yeung, P.P., & Kunz, N.R. (2007). Long-term, open-label venlafaxine extended-Release treatment in children and adolescents with major depressive disorder. *CNS Spectrums, 12*(3), 223-233.

Fear, J.M., Champion, J.E., Reeslund, K.L., Forehand, R. Colletti, C., Roberts, L., & Compas, B. (2009). Parental depression and interparental conflict: children and adolescents' self-blame and coping responses. *Journal of Family Psychology, 23*(5), 762-6.

Feder, A., Nestler, E. ., & Charney, D.S. (2009). Psychobiology and molecular genetics of resilience. *Nature Reviews Neuroscience, 10*, 446-457.

Findling, R.L., Bose, A., Aquino, D., Korotzer, A., & Tourkodimitris, S. (2008). Six-month double-blind escitalopram treatment of depressed adolescents. *AACAP. 56th Annual Meeting.* New Research Poster 3.2. Chicago, Ill.

Fitzgerald, P. (2008). Brain stimulation techniques for the treatment of depression and other psychiatric disorders. *Australian Psychiatry, 16*(3), 183-190.

Fleming, L.C. & Jacobsen, K.H. (2009). Bullying and symptoms of depression in chilean middle school students. *Journal of School Health, 79*(3), 130-137.

Garber, J., Clarke, G.N., Weersing, V.R., Beardslee, W.R., Brent, Gladstone, T.R., . . . & Iyengar, S. (2009). Prevention of depression in at-risk adolescents: a randomized controlled trial. *JAMA, 301*(21), 2215-2224.

Garcia-Toro, M., Ibarra, O., Gili, M., Salva, J., Monzon, S., Vives, M., . . . & Roca, M. (2010). Effectiveness of hygienic-dietary recommendations as enhancers of antidepressant Treatment in patients with depression: Study protocol of a randomized controlled trial. *BMC Public Health, 10*, 404-410.

Garofalo, R., Wolf, R.C., Kessel, S., Palfrey, J., & Durant, R.H. (1998). The association between health risk behaviors and sexual orientation among a school-based sample of adolescents. *Pediatrics, 101,* 895-902.

Ghaziuddin, N., Kutcher, S.P., Knapp, P., Bernet, W., Arnold, V., Beitchman, J., . . . & Ptakowski, K. (2004). Practice parameter for use of electroconvulsive therapy with adolescents. *J. Am. Acad. Child Adolesc. Psychiatry, 43*(12), 1521-1539.

Gibb, B.E. & Alloy, L.B. (2006). A prospective test of the hopelessness theory of depression in children. *Journal of the Clinical Child and Adolescent Psychology, 35*(2), 264-274.

Gilbert, P. (2006), Evolution and depression: issues and implication. *Psychological Medicine, 36*, 287-297.

Gillispie, N.A., Whitfield, J.B., Williams, B., Heath, A.C., & Martin, N.G. (2005). The relationship between stressful life events, the serotonin transporter (5-HTTLPR) genotype and major depression. *Psychol. Medicine, 35*, 101-111.

Ginicola, M.M. (2007). Children's unique experience of depression: using a developmental approach to predict variation in symptomatology. *Child and Adolescent Psychiatry and Mental Health, 1*(1), 1-9.

Glasgow, R.E. & Emmons, K.M. (2007). How can we increase translation of research into practice? Types of evidence needed. *Annual Review of Public Health, 28*, 413-433.

Glied, S., Garret, A.B., Hoven, C., Rubio-Stipec, M., Regier, D., Moore, R.E., . . . & Bird, H. (1998). Child outpatient mental health service use: Why doesn't insurance matter? *The Journal of Mental Health Policy and Economics, 1*(4), 173-187. Retrieved from: http://www.icmpe.org/test1/journal/journal.htm

Glied S., Hoven, C.W., Moore, R.E. Garrett, A.B., & Regier, D.A. (1997). Children's access to mental health care: does insurance matter? *Health Affairs, 16*(1), 167-1774.

Goodyer, M., Bacon, A., Ban, M., Croudace, T., & Herbert, J. (2009). Serotonin transporter genotype, morning cortisol and subsequent depression in adolescents. *The British Journal of Psychiatry, 195*, 39-45.

Goodyer, I.M., Dubicka, B., Wilkinson, P., Kelvin, R., Roberts, C., . . . & Byford, S. (2008). A randomised controlled trial of cognitive behaviour therapy in adolescents with major depression treated by selective serotonin reuptake inhibitors. The ADAPT trial. *Health Technology Assessment (Winchester, England), 12* (14), iii-iv, ix-60.

Goodyer, I., Dubicka, B., Wilkinson, P., Kelvin, R., Roberts, C., Byford, S., . . . & Harrington, S. (2007). Selective serotonin reuptake inhibitors (SSRIs) and routine specialist care with and without cognitive behavior therapy in adolescents with major depression: Randomized controlled trial. *BMJ, 335,* 142-150.

Gould, M. (2009). Is teen suicide contagious*?* Posted on 11/03/09, and retrieved from the web on 11/07/09 from: http://www.sphere.com/2009/11/03/is-teen-suicide-contagious/

Gould, M., King, R., Greenwald, S., Fisher, P., Schwab-Stone, M., Kramer, R., Flisher, A.J., . . . & Shaffer, D. (1998). Psychopathology associated with suicidal ideation among children and adolescents. *J. Am. Acad. Child & Adolesc. Psychiatry*, *37*, 915-923.

Gould, M., Velting, D., Kleinman, M., Lucas, C., Graham Thomas, B.S., & Chung, M. (2004). Teenagers' attitudes about coping strategies and help-seeking behavior for suicidality. *Journal of the American Academy of Child & Adolescent Psychiatry, 43*(9), 1124-1133.

Grewal, P.K. & Porter, J.E. (2007). Hope theory: A framework for understanding suicidal action. *Death Studies 31,* 131-154.

Greening, L., Stoppelbein, L., Dhossche, D., & Martin, W. (2005). Evaluation of a measure of Beck's negative cognitive triad for youth: Applications of African-American and Caucasian adolescents. *Depression and Anxiety, 21*, 161-169.

Hammard, T.A., Laughren, T., & Racoosin, J. (2006). Suicidality in pediatric patients treated with antidepressant drugs. *Archives of General Psychiatry, 63*(3), 332-339.

Hadorn, D.C., Baker, D., Hodges, J.S., & Hicks, N. (1996). Rating the quality of evidence for clinical practice guidelines. *Journal of Clinical Epidemiology, 49*(7), 749-754.

Halligan, S.L., Herbert, J., Goodyer, I.M. & Murray L. (2007). Disturbances in morning cortisol secretion in association with maternal postnatal depression predict subsequent depressive symptomatology in adolescents. *Biol. Psychiatry, 62*, 40-46.

Hazell, P., O'Connell, D., Heathcote, D., & Henry, D. (2009). Tricyclic drugs for depression in children and adolescents. *Cochrane Database of Systematic Reviews, 1.* Retrieved from*:* http://www2.cochrane.org/reviews/en/ab002317.html

Heiligenstein, J.H., Hoog, S.L., Wagner, K.D., Findling, R.L., Galil, N., Kaplan, S., . . . & Jacobson, J.G. (2006). Fluoxetine 40-60 mg versus fluoxetine 20 mg in the treatment of children and adolescents with a less-than-complete response to nine-week treatment with fluoxetine 10-20 mg: A pilot study. *Journal of Child & Adolescent Psychopharmacology, 16*(1-2), 207-217.

Herman, K.C., Ostrander, R., Walkup, J.T, Silva, S.G., & March, J.S. (2007). Empirically derived subtypes of adolescent depression: Latent profile analysis of co-occurring symptoms in the Treatment for Adolescents with Depression Study (TADS). *Journal of Consulting & Clinical Psychology, 75*(5), 716-728.

Hetrick, S., Merry, S., McKenzie, J., Sindahl, P., & Proctor, M. (2007). Selective serotonin reuptake inhibitors (SSRIs) for depressive disorders in children and adolescents. Review. *Cochrane Database of Systematic Reviews*, (3), CD004851.

Hitt, E. (March 2009). Escitalopram approved for the treatment of major depressive disorder in adolescents. *Medscape Medical News*. Retrieved on March 23, 2010 from: http://www.medscape.com/viewarticle/590006

Holmes, J. (1995). Supportive psychotherapy: The search for positive meanings. *British Journal of Psychiatry, 167,* 439-445.

Hollander, G. (2000). Questioning adolescents: challenges to working with adolescents forming identities. *School Psychology Review, 29*(2), 173-179.

Hornor, G. (2008). Reactive attachment disorder. *Journal of Pediatric Health Care, 22*(4), 234-239.

Horowitz, J.L., Garber, J., Ciesla, J.A., Young, J.F., & Mufson, L. (2007). Prevention of depressive symptoms in adolescents: A randomized trial of cognitive-behavioral and interpersonal prevention programs. *Journal of Consulting & Clinical Psychology, 75*(5), 693-706.

Horowitz, J.L. & Garber, J. (2006). The prevention of depressive symptoms in children and Adolescents: A meta-analytic review. *Journal of Consulting & Clinical Psychology, 74*(3), 401-415.

Hughes, C.W., Emslie, C.J., Crismon, M.L., Posner, K., Birmaher, B., Jensen, P., . . . Trivedi, M. H. (2007). Texas children's medication algorithm project: Update from Texas consensus conference panel on medication treatment of childhood major depressive disorder. *Journal of the American Academy of Child & Adolescent Psychiatry, 46*(6), 667-686.

Jacka, F.N., Kremer, P.J., Leslie, E.R., Berk, M., Patton, J.W., Toumborou, J.W., & Williams, J.W. (2010). Associations between diet quality and depressed mood in adolescents: Results from the Australian healthy neighbourhoods study. *Australian & New Zealand Journal of Psychiatry, 44*, 435-442.

Jeong, Y.J., Hong, S.C., Lee, M.S., Park, M.C., Kim, Y.K., & Suh, C.M. (2005). Dance movement therapy improves emotional responses and modulates neurohormones in adolescents with mild depression. *International Journal of Neuroscience, 115*(2), 1711-1720.

Johnson, C.C., Murray, D.M., Elder, J.P., Jobe, J.B., Dunn, A.L., Kubik, M., . . . & Schachter, K. (2008). Depressive symptoms and physical activity in adolescent girls. *Medicine & Science in Sports & Exercise, 40*(5), 818-826.

Jorm, A.F., Allen, N.B., O'Donnell, C.P., Parslow, R.A., Purcell, R., & Morgan, A.J. (2006). Effectiveness of complementary and self-help treatments for depression in children and adolescents. *Medical Journal of Australia, 185*(7), 368-372.

Kazak, A.E., Hoagwood, K., Weisz, J.R., Korey, H., Kratochwill, T.R., Vargas, L.A., & Banez, G.A. (2010, February-March). A meta-systems approach to evidence-based practice for children and adolescents. *American Psychologist,* 85-97.

Kendler, K.S., Gatz, M., Gardner, C.O., & Pedersen, N.L. (2006). A Swedish national twin study of lifetime major depression. *American Journal of Psychiatry, 163*(1), 109-114.

Kennard, B.D., Stewart, S.M., Hughes, J.L., Patel, P.G., & Emslie, G.J. (2006). Cognitions and depressive symptoms among ethnic minority adolescents. *Cultural Diversity and Ethnic Minority Psychology, 12*(3), 578-592.

Kennard, B.D., Clarke, G.N., Weersing, V.R., Asarnow, J.R., Shamseddeen, W., Porta, W., . . . & Brent, D.A. (2009). Effective components of TORDIA cognitive-behavioral therapy for adolescent depression: Preliminary findings. *Journal of Consulting & Clinical Psychology, 77*(6):1033-1041.

Kennard, B.D., Emslie, G.J., Mayes, T.L., Nightingale, J., Nakonezny, P.A., Hughes, J.L., . . . & Jarrett, R.B. (2008). Cognitive-behavioral therapy to prevent relapse in pediatric responders to pharmacotherapy for major depressive disorder. *J. Am. Acad. Child Adolesc. Psychiatry, 47*(12), 1395-1404.

Kennard, B.D., Silva, S.G., Mayes, T.L., Rohde, P., Hughes, J.L., Vitiello, B., . . . & March, J.S. (2009). Assessment of safety and long-term outcomes of initial treatment with placebo in TADS. *Am. J. Psychiatry, 166*(3), 337-344.

Kennard, B., Silva, S., Vitiello, B., Curry, J., Kratochvil, C., Simons, A., . . . & March, J. (2006). Remission and residual symptoms after short-term treatment in the Treatment of Adolescents with Depression Study (TADS). *Journal of the American Academy of Child & Adolescent Psychiatry, 45*(12), 1404-1411.

Kessler, R.C., Avenevoli, S., & Merikangas, K.R. (2001). Mood disorders in children and adolescents: An epidemiologic perspective. *Biological Psychiatry, 49*(12), 1002-1014.

Klein, D.N., Shankman, S., Lewinsohn, P., & Seeley, J.R. (2009). Subthreshold depressive disorder in adolescents: Predictors of escalation to full-syndrome depressive disorders. *Journal of the American Academy of Child & Adolescent Psychiatry, 48*(7), 703-710.

Klein, J.B., Rachel, H., Jacobs, B.A., & Reinecke, M.A. (2007). Cognitive-behavioral therapy for adolescent depression: A meta-analytic investigation of changes in effect-size estimates. *Journal of the American Academy of Child and Adolescent Psychiatry, 44*(11), 1403-1413.

Knowles, D. (2009). *Is Teen Suicide Contagious*? Posted on 11/03/09 and retrieved on 11/07/09 from: http://www.sphere.com/2009/11/03/is-teen-suicide-contagious/

Kratochwil, C., Emslie, G., Silva, S., McNulty, S., Walkup, J., Curry, J., . . . & March, J. (2006). Acute time to response in the treatment for adolescent with depression study (TADS). *Journal of the American Academy of Child & Adolescent Psychiatry, 45*(12), 1412-1418.

Kratochwil, C.J., Vitiello, B., Walkup, J., Emslie, G., Waslick, B.D., Weller, E.B., Burke, W.J., & March, J.S. (2006). Selective serotonin reuptake inhibitors in pediatric depression: Is the balance between benefits and risks favorable? *Journal of Child and Adolescent Psychopharmacology, 16*(1-2), 11-24.

Kuyken, W., Watkins, E., Holden, E., & Cook, W. (2006). Rumination in adolescents at risk for Depression. *Journal of Affective Disorders, 96*, 39-47.

Lakdawalla, Z., Hankin, B.L., & Mermelstein, R. (2007). Cognitive theories of depression in children and adolescents: A conceptual and quantitative review. *Clinical Child and Family Psychology Review, 10*(1), 1-24.

Larun, L., Nordheim, L.V., Ekeland, E., Hagen, K.B. & Heian, F. (2006). Exercise in prevention and treatment of anxiety and depression among children and young people. *Cochrane Database Systematic Reviews. Issue 3. Art. No.: CD004691*.doi 10.1002/14651858.CD004691.pub2.

Lewis, C.C., Simons, A.D., Silva, S.G., Rohde, P., Small, D.M., Murakami, J.L., . . . & March, J.S. (2009). The role of readiness to change in response to treatment of adolescent Depression. *Journal of Consulting & Clinical Psychology, 77*(3), 422-428.

Lewis, M. (2002). *Child and adolescent psychiatry: A comprehensive textbook*. (3rd ed.). Philadelphia PA: Lippincott Williams & Wilkins.

Logsdon, M.C., Hertweck, P., Ziegler, C., & Pinto-Foltz, M. (2008). Testing a bioecological model to examine social support in postpartum adolescents. *Journal of Nursing Scholarship, 40*(2), 116-123.

Logsdon, M.C., Birkimer, J.C., Simpson, T., & Looney, S. (2005). Postpartum depression and social support in adolescents. *J. Obstet. Gynecol. Neonatal Nurs., 34*(1), 46-54.

Loo, C., Martin, D., Pigot, M., Arul-Anandam, P., Mitchell P., & Sachdev P. (2009). Transcranial direct current stimulation priming of therapeutic repetitive transcranial magnetic stimulation: A pilot study. *Journal of ECT, 25*(4), 256-260.

Luppa, M., Heinrich, S., Angermeyer, M.C., Konig, H.H., & Riedel-Heller, S.G. (2007). Cost-of-illness studies of depression: A systematic review. *Journal of Affective Disorders, 98*, 29-43.

Lynch, F.L., Hornbrook, M., Clarke, G.N., Perrin, N., Polen, M.R., O'Connor, E., & Dickerson, J. (2005). Cost-effectiveness of an intervention to prevent depression in at-risk teens. *Arch. Gen. Psychiatry, 62*(11), 1241-1248.

Machi, L.A. & McEvoy, B.T. (2009). *The literature review*. Thousand Oaks, CA: Corwin Press.

Mannie, Z.N., Harmer, C.J., & Cowen, P.J. (2007). Increased waking salivary cortisol levels in young people at familiar risk of depression. *Am. J. Psychiatry, 164*, 617-621.

March, J., Silva, S., Curry, J., Wells, K., Fairbank, J., Burns, B., . . . & Bartoi, M. (2009). The Treatment for Adolescents with Depression Study (TADS): Outcomes over 1 year of naturalistic follow-up. *American Journal of Psychiatry, 166*(10), 1141-1149.

March, J.S., Silva, S., Petrycki, S., Curry, J., Wells, K., Fairbank, J., Burns, B., . . . & Severe, J. (2007). The Treatment for Adolescents with Depression Study (TADS): Long-term effectiveness and safety outcomes. *Archives of General Psychiatry, 64*(10), 1132-1143.

March, J., Silva, S., Vitiello, B., & the TADS Team. (2006). The Treatment for Adolescents with Depression Study (TADS): Methods and message at 12 Weeks. *J. Am. Acad. Child Adolesc. Psychiatry, 45*(12), 1393-1403.

March, J., Silva, S., Petrycki, S., Curry, J., Wells, K., Fairbank, J., . . . & Severe, J. (2004). Fluoxetine, cognitive-behavioral therapy and their combination for adolescents with depression: Treatment for Adolescents with Depression Study (TADS): Randomized controlled trial. *JAMA, 292*(7), 807-820.

Mathew, R.J., Largen, J., & Claghorn, J.L. (1979). Biological symptoms of depression. *Psychosomatic Medicine, 41*(6), 439-443.

McGrath, E.P. & Repetti, R.L. (2002). A longitudinal study of children's depressive symptoms, self-perceptions, and cognitive distortions about the self. *Journal of Abnormal Psychology, 111*(1), 77-87.

McLaughlin, E., Levaivre, M.J., & Cummings, E. (2010). Experimentally-induced learned helplessness in adolescents with type I diabetes. *Journal of Pediatric Psychology, 35(4),* 405-415.

McPheeters, M. & Lohr, K. (1999). Evidence-based practice and nursing: Commentary. *Outcomes Management for Nursing Practice, 3*(3), 99-101.

Melvin, G.A., Tonge, B.J., King, N.J., Heyne, D. Gordon, M.S., & Klimkeit, E. (2006). A comparison of cognitive-behavioral therapy, sertraline and their combination for adolescent depression. *Journal of the American Academy of Child & Adolescent Psychiatry, 45* (10), 1151-1161.

Meredith, L.S., Stein, B.D., Paddock, S.M., Jaycox, L.H. Quinn, V.P. Chandra, A., & Burnam, A. (2009). Perceived barriers to treatment for adolescent depression. *Medical Care, 47*(6), 677-685.

Miller, L., Gur, M., Shanok, A., & Weissman, M. (2008). Interpersonal psychotherapy with pregnant adolescents: Two pilot studies. *J. Child Psychol. Psychiatry, 49*(7), 733-742.

Morbidity. (2009). In *Mosby's dictionary of medicine, nursing & health professions* (8th ed.). St. Louis, MO: Mosby Elsevier.

Moreno, C., Arango, C., Parellada, M., Shaffer, D., & Bird, H. (2007). Antidepressants in child and adolescent depression: Where are the bugs? *Acta Psychiatr. Scand., 115*, 184–195.

Morris, M.C. & Ciesla, J.A., & Garber, J. (2008). A prospective study of the cognitive-stress model of depressive symptoms in adolescents. *Journal of Abnormal Psychology, 117* (4), 719-734.

Mufson, L. Dorta, K.P., Wickramaratne, P., Nomura, Y. Olfson, M., & Weissman, M.M. (2004). A randomized effectiveness trial of interpersonal psychotherapy for depressed adolescents. *Archives of General Psychiatry, 61*(6), 577-584.

Munro, B.H. (2005). *Statistical Methods for Health Care Research.* (5th ed). Philadelphia, PA: Lippincott Williams & Wilkins.

Nabkasorn, C., Miyai, N., Sootmongkol, A., Junprasert, S., Yamamoto, H., Arita, M., & Miyashita, K. (2006), Effects of physical exercise on depression, neuroendocrine stress hormones and physiological fitness in adolescent females with depressive symptoms. *European Journal of Public Health, 16*(2), 179-184.

National Institute of Mental Health (2009). *Depression.* Retrieved on 6/11/2009 from: http://www.nimh.nih.gov/health/publications/depression/how-do-children-and-adolescents-experience-depression.shtml

O'Kearney, R., Kang, K., Christensen, H., & Griffiths, K. (2009). A controlled trial of a school-based Internet program for reducing depressive symptoms in adolescent girls. *Depression & Anxiety, 26*(1), 65-72.

Oncology Nursing Society (ONS). *Rating the quality of evidence for clinical practice guidelines table*. Retrieved on 09/27/09 from: http://onsopcontent.ons.org/toolkits/evidence/Process/levels.shtml#table

Papanikolau, C., Richardson, A., Pehlivanidis, A., & Papadopoulou, Z. (2006). Efficacy of antidepressants in child and adolescent depression. *Journal of Neural Transmission, 113*, 399-415.

Posner, K., Oquendo, M.A., Gould, M., Stanley, B., & Davies, M. (2007). Columbia classification algorithm of suicide assessment (C-CASA): Classification of suicidal events in the FDA's pediatric suicidal risk analysis of antidepressants. *Am. J. Psychiatry, 165*(7), 1035-1043.

Phillips, L. & Ziggler, E. (1996). Social competence: The action-thought parameters and vicariousness in normal and pathological behavior. *Journal of Abnormal Psychology, 63*, 137-146.

Pumariega, A.J., Rogers, K., & Rothe, E. (2005). Culturally competent systems of care for children's mental health: Advances and challenges. *Community Mental Health Journal, 41*(5), 539-555.

Pumariega, A.J., Rothe, E., & Rogers, K. (2009). Cultural competence in child psychiatric practice. *J. Am. Acad. Child & Adolescence Psychiatry, 48*(4), 362-366.

Raphael, S. (2009). Eye on Washington: New recommendations on screening and treatment for major depressive disorder in children and adolescents. *JCAPN, 22*(3), 170-171.

Regan, J., DeWire, M., Whithy, B., Bess, T., & Wright, A. (2005). The "black box" controversy. *Journal of the Tennessee Medical Association, 98*(1), 41-42.

Remafedi, G., Farrow, J.A., & Deisher, R.W. (1991). Risk factor for attempted suicide in gay and bisexual youth. *Pediatrics, 87*, 869-875.

Rey, J.M. & Birmaher, B. (2009). Treating child and adolescent depression. Republic of China: Lippincott Williams & Wilkins, a Wolkers Kluwer business.

Robinson, R.G., Chemerinski, E., & Jorge, R. (2009). Pathophysiology of secondary depressions in the elderly. *Journal of Geriatric Psychiatry and Neurology, 12*, 128-132.

Rohde, P., Silva, S.G., Toney, S.T., Kennard, B.D., Vitiello, B., Kratochvil, C.J., . . . & March, J.S. (2008). Achievement and maintenance of sustained response during the treatment for adolescents with depression study continuation and maintenance therapy. *Arch. Gen. Psychiatry, 65*(4), 447-455.

Rose, H.A., Boyce-Rodgers, K., & Small, S.A. (2006). Sexual identity confusion and problem behaviors in adolescents: A risk and resilience approach. *Marriage & Family Review, 40*(2/3), 131-150.

Rosselló, J., Bernal, G. & Rivera-Medina, C. (2008). Individual and group CBT and IPT for Puerto Rican adolescents with depressive symptoms. *Cultural Diversity & Ethnic Minority Psychology, 14*(3), 234-245.

Rutter, P.A. & Behrendt, A.E. (2004), Adolescent suicide risk: Four psychosocial factors. *Adolescence, 39(154),* 295-302.

Rynn, M., Wagner, K. D., Donnelly, C., Ambrosini, P., Wohlberg, C. J., Landau, P., & Yang, R. (2006). Long-term sertraline treatment of children and adolescents with major depressive disorder. *Journal of Child & Adolescent Psychopharmacology, 16*(1-2), 103-116.

Sadock, B.J. & Sadock, V.A. (2003). *Synopsis of psychiatry* (9th ed.). Philadelphia, PA: Lippincott, Williams & Wilkins.

Sanford, M., Boyle, M., McCleary, L., Miller, J., Steele, M., Duku, E., & Offord, D. (2006). A pilot study of adjunctive family psychoeducation in adolescent major depression feasibility and treatment effect. *Journal of the American Academy of Child & Adolescent Psychiatry, 45*(4), 386-495.

Shaffer, D., Gould, M.S., Fisher, P. Trautman, P., Moreau, M.D., & Kleinman, M. (1996). Psychiatric diagnosis in child and adolescent suicide. *Archives of General Psychiatry, 53*(4), 339-348.

Shaw, S.K. & Dallos, R. (2005). Attachment and adolescent depression: the impact of early attachment experiences. *Attachment & Human Development, 7(*4), 409-424.

Sharp, S.C. & Hellings, J.A. (2006). Efficacy and safety of selective serotonin reuptake inhibitors in the treatment of depression in children and adolescents. Practitioner review. *Clinical Drug Investigation, 26*(5), 247-255.

Sheffield, J.K., Spence, S.H., Rapee, R.M., Kowalenko, N., Wignall, A., Davis, A., & McLoone, J. (2006). Evaluation of universal, indicated, and combined cognitive-behavioral approaches to the prevention of depression among adolescents. *Journal of Consulting & Clinical Psychology, 74*(1), 66-79.

Sheldon, T.A. & Haines, A. (1998). Getting research findings into practice. *BMJ, 317*, 139-142.

Shirazi, E. & Alaghband-Rad, J. (2005). An open trial of citalopram in children and adolescents with depression. *Journal of Child & Adolescent Psychopharmacology, 15*(2), 233-239.

Simeon, J., Nixon, M.K., Milin, R., Jovanovic, R., & Walker, S. (2005). Open-label pilot study of St. John's wort in adolescent depression. *Journal of Child & Adolescent Psychopharmacology, 15*(2), 293-301.

Slattery, D.A., Hudson, A.L., & Nutt, D.J. (2004). Invited review: The evolution of Antidepressant mechanisms. *Fundamental & Clinical Pharmacology, 18*(1), 1-21.

Smith, E.G. (2009). Association between antidepressant half-life and the risk of suicidal ideation or behavior among children and adolescents: Confirmatory analysis and research implications. *Journal of Affective Disorders, 114*, 143-148.

Spence, S.H., Sheffield, J.K., & Donovan, C.L. Long-term outcome of a school-based, universal approach to prevention of depression in adolescents. *Journal of Consulting & Clinical Psychology, 73*(1), 160-167.

Stice, E., Shaw, H., Bohon, C., Marti, C.N., & Rohde, P. (2009). A meta-analytic review of depression prevention programs for children and adolescents: Factors that predict magnitude of intervention effects. *Journal of Consulting & Clinical Psychology, 77*(3), 486-503.

Stice, E., Rohde, P., Seeley, J.R., & Gau, J.M. (2008). Brief cognitive-behavioral depression program for high-risk adolescents outperforms two alternative interventions: A randomized efficacy trial. *Journal of Consulting and Clinical Psychology, 76*(4), 595-606.

Strober, M., Rao, U., DeAntonio, M., Liston, E., State, M., Amaya-Jackson, L., & Latz, S. (1998). Effects of electroconvulsive therapy in adolescents with severe endogenous depression to pharmacotherapy. *Biological Psychiatry, 43*(5), 335-338.

Substance Abuse and Mental Health Services Administration, Office of Applied Studies (May, 2009). *The NSDJH Report: Major depressive episode and treatment among adolescents*. Retrieved from: http://ncadistore.samhsa.gov/catalog/productDetails.aspx?ProductID=18120

Tandon, D.S. & Solomon, B.S. (2009). Risk and protective factors for depressive symptoms in urban African American adolescents. *Youth & Society, 41*(1), 80-99.

Tang, T.C., Jou, S.H., Ko, C.H., Huang, S.Y., & Yen, C.F. (2009). Randomized study of school-based intensive interpersonal psychotherapy for depressed adolescents with suicidal risk and parasuicide behaviors. *Psychiatry and Clinical Neurosciences, 63*, 463-470.

Temple, R. (2004). Anti-depressant drug use in pediatric populations. Statement before the senate subcommittee on oversight and investigation. *Committee on Energy and Commerce*. Retrieved on 11/17/09 from: http://www.fda.gov/NewsEvents/Testimony/ucm113265.htm

Thapar, A., Collishaw, S., Potter, R., & Thapar, A.K. (2010). Clinical Review: Managing and preventing depression in adolescents. *BMJ, 340*(30), 254-258.

Thapar, A. & McGuffin, P. (1996). Genetic influences on life events in childhood. P*sychological Medicine, 26,* 813-820.

The TADS Team (2007). The Treatment for Adolescents with Depression Study (TADS). Long-term effectiveness and safety outcomes. *Archives of General Psychiatry, 64*(10), 1132-1143.

Titler, M.G. & Everett, L.Q. (2001). Translating research into practice. *Critical Care Nursing Clinics of North America 13*(4), 587-604.

Transtheoretical Model. (n.d). *Cancer Prevention Research Model*. Retrieved on April 28, 2010 from: http://www.uri.edu/research/cprc/TTM/StagesOfChange.htm

Tsapakis, E.M., Soldani, F., Tondo, L., & Baldessarini, R.J. (2008). Efficacy of antidepressants in juvenile depression: meta-analysis. *The British Journal of Psychiatry, 193*, 10-17.

Trowell, J., Joffe, I., Campbell, J., Almqvist, F., Soininen, M., Koskenranta-Aalto, U., . . . & Tsiantis, J. (2007). Childhood depression: A place for psychotherapy. *Eur. Child Adolesc. Psychiatry, 16*(3), 157-67.

Tusaie, K., Puskar, K., & Sereika, S.M. (2007). A predictive and moderating model of psychosocial resilience in adolescents. *Journal of Nursing Scholarship, 39*(1), 54-60.

U.S. Food and Drug Administration (FDA). (2004). *FDA News Release*. Retrieved on 07/02/10: from: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2004/ucm108363.htm

U.S. Preventive Services Task Force. (2009). Screening and treatment for major depressive disorder in children and adolescents: U.S. preventive services task force recommendation statement. *Pediatrics, 123*(4), 1223-1228.

Usala, T., Clavenna, A., Zuddas, A., & Bonati, M. (2008). Randomized controlled trials of selective serotonin reuptake inhibitors in treating depression in children and adolescents: A systematic review and meta-analysis. *European Neuropsychopharmacology, 18*(1), 62-73.

Van Voorhees, B.W., Fogel, J., Reinecke, M.A. Gladstone, T., Stuart, S., . . . & Bell, C. (2009). Randomized clinical trial of an Internet-based depression prevention program for adolescents (Project CATCH-IT) in primary care: 12-week outcomes. *Journal of Developmental & Behavioral Pediatrics, 30*(1), 23-37.

Vitiello, B., Rhode, P., Susan, S., Wells, K., Casat, C., Waslick, B., . . . & March, J. (2006). Functioning and quality of life in the treatment for adolescents with depression study (TADS). *J. Am. Acad. Child Adolesc. Psychiatry, 45*(12), 1419-1426.

Von Knorring, A.L., Olson, G.I., Thomsen, P.H., Lemming, O.M., & Hulten, A. (2006). A randomized, double-blind, placebo-controlled study of citalopram in adolescents with major depressive disorder. *Journal of Clinical Psychopharmacology, 26*(3), 311-315.

Waddell, C., Hua, J.M., Garland, O.M., Peters, R.D., & McEwan, K. (2007). Preventing mental disorders in children: A systematic review to inform policy-making. *Canadian Journal of Public Health. Revue Canadienne de Sante Publique*, 98(3), 166-173.

Wagner, K.D., Jonas, J., Findling, R.L., Ventura D, & Saikali, K. (2006). A double-blind, randomized, placebo-controlled trial of escitalopram in the treatment of pediatric depression. *Journal of the American Academy of Child & Adolescent Psychiatry, 45*(3), 280-288.

Watanabe, N., Hunot, V., Omori, I.M., Churchill, R., & Furukawa, T.A. (2007). Psychotherapy for depression among children and adolescents: a systematic review. *Acta Psychiatrica Scandinavica, 116,* 84-95.

Weissman, M.M. & Markowitz, J.C. (1994). Interpersonal Psychotherapy. *Arch. Gen. Psychiatry, 51*, 599-606.

Weisz, J.R., Southam-Gerow, M.A., Gordis, E.B., Connor-Smith, J.K., Chu, B.C., Langer, D.A., . . . & Weiss, B. (2009). Cognitive-behavioral therapy versus usual clinical care for youth depression: An initial test of transportability to community clinics and clinicians. *Journal of Consulting & Clinical Psychology, 77*(3), 383-396.

Weisz, J.R., McCarty, C.A., & Valeri, S.M. (2006). Effects of psychotherapy for depression in children and adolescents: A meta-analysis. *Psychological Bulletin, 132*(1), 132-49.

Weller, E.B., Kloos, A., Kang, J., & Weller, R.A. (2006). Depression in children and Adolescents: Does gender make a difference*? Current Psychiatry Reports, 8*(2), 108-14.

Westfall, J.M., Mold, J., & Fagnan, L. (2007). Practice-based research – "blue highways" on the NIH roadmap. *The Journal of the American Medical Association, 297*(4), 403-406.

Whittemore, R. & Knafl, K. (2005). Methodological issues in nursing research. The integrative review: updated methodology. *Journal of Advanced Nursing, 52*(5), 546-553.

Wilkinson, P., Dubicka, B., Kelvin, R., Roberts, C., & Goodyer, I. (2009). Treated depression in adolescents: Predictors of outcome at 28 weeks. *The British Journal of Psychiatry, 194*(4), 334-441.

Williams, S.B., O'Connor, E.A., Eder, M., & Whitlock, E.P. (2009). Screening for child and adolescent depression in primary care settings: A systematic evidence review for the U.S. preventive task force. *Pediatrics, 123*(4), 716-735.

Woolf, S.H. (2008). The meaning of translational research and why it matters. *JAMA, 299*(2), 211-213.

Yiliu, C. & Kuo, F.Y. (2007). A study of Internet addiction through the lens of the interpersonal theory. *CyberPsychology & Behavior, 10*(6), 799-803.

Young, J.F., Mufson, L., & Davies, M. (2006). Efficacy of interpersonal psychotherapy-adolescent skills training: An indicated preventive intervention for depression. *Journal of Child Psychology and Psychiatry, 47*(12), 1254-1262.

Young, J.F., Mufson, L., & Davies, M. (2006). Impact of comorbid anxiety in an effectiveness study of interpersonal psychotherapy for depressed adolescents. *Journal of the American Child & Adolescent Psychiatry, 45*(8), 904-912.

Zhou, Z., Siu, C.R., & Xin, T. (2000). Promoting cultural competence in counseling Asian American children and adolescents. *Psychology in the Schools, 46* (3), 290-298.