

Clinical evidence of the use of pharmacological treatment compared to psychotherapy in  
the occurrence of suicidal ideation or suicide among adolescents and children

Submitted by

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We hereby recommend that the research project prepared under our supervision by Kristin Marlow entitled Clinical evidence of the use of pharmacological treatment compared to psychotherapy in the occurrence of suicidal ideation or suicide among adolescents and children will be accepted as partial fulfillment for the degree of Master of Physician Assistant.

Approved:



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## *Abstract*

Introduction: Depression among children and adolescents has become increasingly more recognized in the medical setting. Up until recently clinicians believed they were successfully and safely treating their patient's depression with a variety of antidepressant medication. Since the realization of the risk of treating with tricyclic antidepressant medication, selective serotonin reuptake inhibitors have been the first line of treatment. However, in 2004 the FDA labeled these medications with a black box warning stating there was a possible increase in the risk of suicide when using the medications among young patients. Since that time medical providers have been left to sift through the evidence in medical literature to ascertain the safest treatment options. Methodology: The purpose of this paper was to perform a systematic review of the literature and examine the cumulative data addressing the issue, in the end being able to present a clearer picture to providers. Articles used included children and adolescents, ranging from infancy to 18 years of age, who meet the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria of major depressive disorder from 1971-2004. Variables included psychotherapy, pharmacotherapy, and the combination of both, and suicide. Results: Twenty six articles matched the criteria and were reviewed using evidence-based methods. After close analysis of the presented data, it appeared there was no direct evidence linking antidepressant medications and an increase risk in suicide regardless of whether subjects were taking the medication alone or in combination with psychotherapy. The safest and best outcome was combination therapy. Conclusion: The most effective and safe treatment option for young patients with depression was a combination of cognitive based therapy and fluoxetine.

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## *Introduction*

Major Depressive Disorder (MDD) is a highly discussed topic among the medical and psychiatric communities. The disorder is commonly reported on, diagnosed, and studied. There is no denying that it affects all people, having no bias against gender, race, ethnicity, or age. Likewise, it was not that long ago that physicians refused to believe that depression was something that children or adolescents were developmentally capable of experiencing. It was thought that they lacked the psychological and cognitive abilities to experience any significant depressive problems.<sup>1</sup> Within the last few decades more research has focused specifically on childhood depression. The growing amount of evidence supportive of adolescent depression has convinced the medical community of the existence of the disorder and it is now a formally recognized problem. This recent acceptance of adolescent depression has left many concerned with its large prevalence in the United States. It is estimated that in the United States millions of people under the age of 18 have MDD, with an estimated 2% of children and 4% to 8% of adolescents diagnosed with the disorder.<sup>2</sup>

The increased awareness of depression among children and adolescents has led to many debates concerning the diagnosis and treatment of the disorder. According to the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV)<sup>2</sup>, diagnosis requirements are that the child has to experience five of the following nine criteria for at least two weeks: depressed or irritable nearly every day for most of the day; markedly diminished interest or pleasure in previously enjoyed activities; weight loss or weight gain; changes in sleep pattern; psychomotor agitation or retardation; fatigue or

loss of energy; feelings of worthlessness or excessive or inappropriate guilt; indecisiveness or diminished ability to concentrate; and recurrent thoughts of death.<sup>2</sup>

Even with these strict criteria there is still a continuous debate over what merits MDD, along with the constant struggle of trying to understand younger patients and how they present. This confusion has made this disorder the most widely missed and undiagnosed clinical condition in adolescents.<sup>3</sup> Many of the clinical manifestations of depression in children are similar to adult depression with regards to feelings of sadness, lack of pleasure in activities, or loss of energy. But in many cases children and adolescents present differently. For example, infants and preschoolers do not have the capability to express their sadness in words, instead they usually present with somatic symptoms such as headaches and abdominal pain. Even when children are capable of expressing their feelings, many times they will be quiet and withdrawn, refusing to talk and many times denying any depressed feelings. Adolescent depression is marked many times by poor academic performance, delusions, and acting out through behavioral disruptions. The average age of onset for MDD is late twenties, but it may start as early as infancy.<sup>4</sup> It is estimated that one in five young people will experience episodes of MDD before the age of eighteen, with females being twice as likely as males to have the disorder.<sup>5</sup> For girls their first episode is related to the onset of menarche, with a typical episode of depression lasting anywhere from seven to nine months, depending on the treatment received.<sup>6</sup>

A growing concern with MDD is the significant number of factors accompanying the disorder, including psychosocial problems, substance abuse, and the high risk for suicide. Studies show more than 5,000 young people in the United States commit suicide every year, making suicide the third leading cause of death among 15 to 24 year olds and

fourth leading cause of death among 10 to 14 year olds.<sup>2</sup> Suicide attempts and ideations are common among adolescents and should be taken seriously. Impulsivity of adolescents leads to a high risk of those with MDD committing suicide. Like adults, suicide attempts are more common among females, but males are five times more likely to be successful.<sup>2</sup> It is the responsibility of the health care professional to recognize these patients, as 40% of people that commit suicide have visited their health care provider within in one to six months of the suicide attempt.<sup>7</sup>

### *Literature Review*

Recognizing how common MDD was found to be in young patients, health care providers gladly embraced the idea of treating the disorder as they would an adult patient, with medication, therapy, or both. Up until recently, clinicians believed that they were helping young patients by treating them with a variety of antidepressant medications. It was thought that not only were these medications decreasing symptoms of depression, but also decreasing the high risk of suicide attempts and ideation among children and adolescents.

There is a wide variety of medicine available for depression; Tricyclics (TCAs), Selective Serotonin Reuptake Inhibitors (SSRIs), and newer generations like valafaxinine (Effexor), bupropion (Wellbutrin), and mirtiazapine (Remeron). After gaining some clinical experience with these medications it was discovered that while TCAs are effective in treating adult depression, they did not prove to be as useful with children. Their combination of side effects and high risk of fatal overdose have resulted in them not being recommended as a first line treatment for young people.<sup>8</sup> Since that time, more attention was placed on the SSRIs, which are now considered the first choice for

treatment of depression in young patients, and have been used extensively in the treatments process, as they are less dangerous when taken in overdose and have better medication adherence.<sup>9</sup>

Nevertheless, within the last year this security and confidence in certain antidepressant medication has dropped. In March of 2004 the Food and Drug Administration (FDA) released a statement concerning label warnings stating some antidepressants have potential danger of increasing risk of suicidal behavior, the very symptoms that they are commonly used to treat. The FDA claimed they did not have any causal links between increased suicide and the medications, but the risk were real and they were hoping to heighten prescriber awareness to the increased risks.<sup>10</sup> The drugs of concern were mostly SSRIs along with some other newer generation antidepressants: fluoxetine (Prozac), paroxetine (Paxil), sertraline (Zoloft), velafacine (Effexor), citalpram (Celexa), mirtazapine (Remeron), escitalopram (Lexapro), fluvoxamine (Luvox), nefazodone (Serzone), and bupropion (Wellbutrin).<sup>11</sup>

The release of this information left many confused and opened the doors to a new debate in the medical community. The American College of Neuropsychopharmacology (ACN) claims that the evidence linking the two factors is too weak to justify not prescribing the medications for depression. According to the ACN, suicides have actually decreased with the increased use of antidepressant medication. They argue that suicides are more likely to occur in depressed patients who do not take any medications or who take the wrong dose rather than taking the medication correctly.<sup>11</sup> European studies have also shown that the increased use of antidepressant medication has led to an inverse relationships with the occurrence of suicide rates falling.<sup>9</sup>

Another option besides prescribing antidepressant medications is the use of psychotherapy, an alternative that many are starting to consider now, since there is this new uncertainty in regards to prescribing antidepressants. The most commonly used are cognitive based therapy (CBT) and psychoeducational therapy. These include training in problem solving, social skills, social competence, self control therapy, and cognitive restructuring.<sup>12</sup> These forms of treatment have their own limitations as well. The therapy that is used is based off of techniques and interventions designed for adults and then adapted to adolescents. Psychiatrists complain that they do not take into consideration the developmental differences between the age groups.

#### *Purpose of Study*

Use of antidepressants versus psychotherapy has left health care providers to do their best in deciding which option is the safest for their young patients. As the research continues to accumulate a decision needs to be reached addressing pharmacological treatment and psychotherapy use in children and adolescents with depression in relation to the questionable risk of suicide.

The purpose of this study was to compile all the evidence regarding the treatment for depression in children and adolescents. By analyzing the data a clearer answer regarding the safest and most effective treatment plan was illustrated. The research question was stated as: What is the occurrence of suicidal ideation or suicide among children and adolescents with depression treated with pharmacology, psychotherapy, or both?

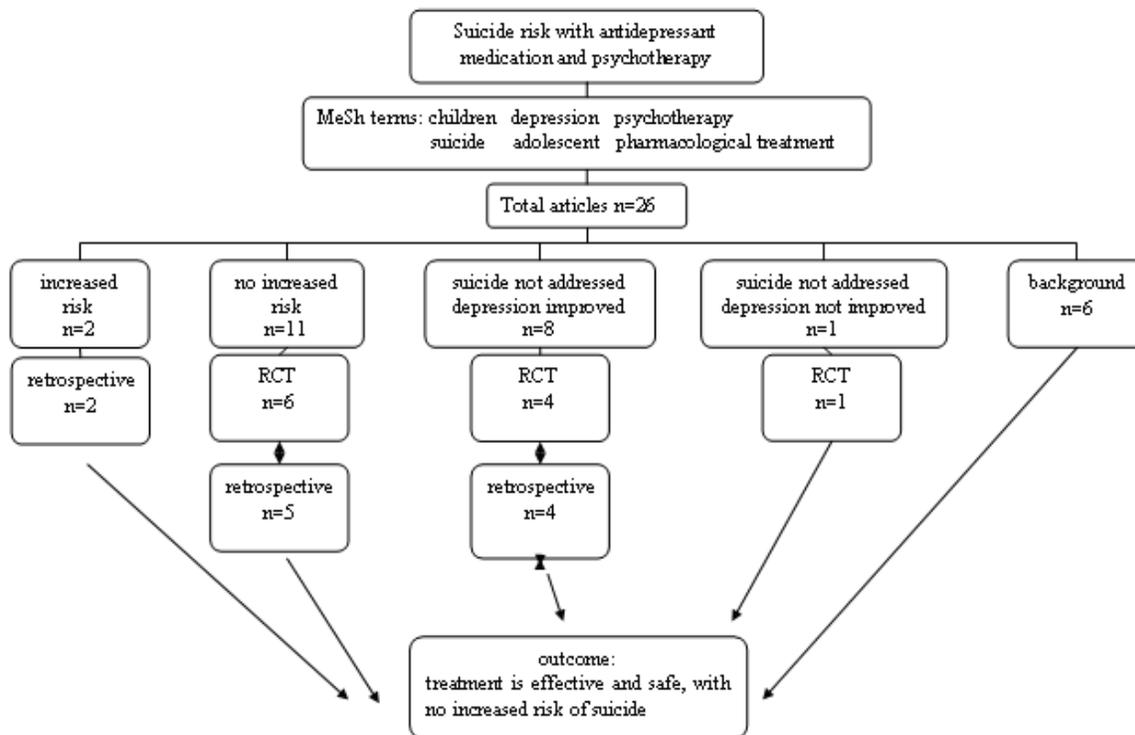
### *Methodology*

A systematic review of the literature using evidence-based techniques was completed pertaining to studies regarding treatment options for adolescent depression; assessing their efficacy and increased risk of suicidal ideation or suicide. These treatment options included pharmacologic, psychotherapy, or both. Subjects included children and adolescents ages ranging from infancy to 18 years who met the criteria for DSM-IV depression. Medline and PsychInfo were searched for articles meeting the defined inclusion criteria from 1971 to 2004. The peer reviewed articles used included background articles for epidemiology data and information on clinical presentation, along with foreground articles, including systematic reviews of data and randomized control studies. The following key terms were used: adolescent, children, depression, pharmacological treatment, psychotherapy, and suicide. From the selected articles data were examined, extracted, and compared with one another regarding the different treatments and their efficacy in treating depression, along with their relationship to suicide and suicidal ideation occurrences.

### *Results*

From 1971 through 2004, twenty-six articles met the inclusion criteria (Figure 1). It is important to note, some articles addressed more than one outcome, therefore, there was some overlap in the result section. Six of the articles contained background information regarding depression.<sup>1-4,6,7</sup> This included information concerning the diagnosis, symptoms involved, and epidemiology data regarding the prevalence of MDD and suicide in children and adolescents.

**Figure 1: Literature Review Flow Sheet**



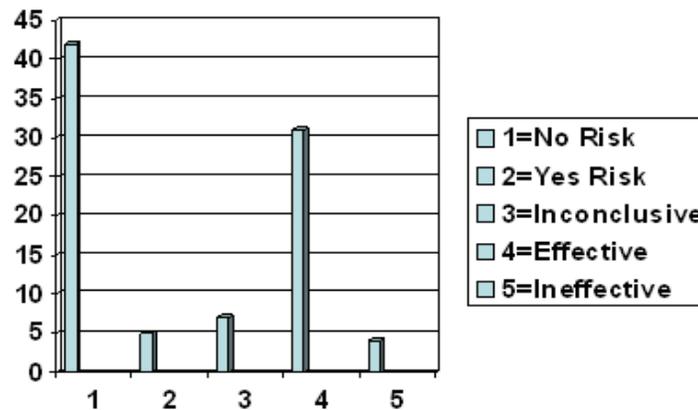
Nine articles did not address the topic of suicide but instead focused on the efficacy of treatment methods. Of these, one study found that depression did not improve with SSRI treatment, with the exception of fluoxetine.<sup>11</sup> Eight other articles, including the above mentioned, supported the efficacy of psychotherapy or pharmacotherapy in regards to improvement of depressive symptoms.<sup>5,10-16</sup>

Thirteen studies were found that directly addressed the risk of suicide when using antidepressant medication or psychotherapy to treat adolescents. Two of the thirteen studies showed an increased risk with the use of antidepressants based on the adverse side effects of agitation and suicidal ideation.<sup>5,13</sup> The other eleven studies that addressed the

issue found no statistically significant increase in suicide regarding the use of antidepressant medication and psychotherapy treatment.<sup>9,18-26</sup>

Overall 42% of the articles found no increased risk, 5% showed an increased risk. Thirty-one percent showed treatment to be effective in lowering depression symptoms, while 4% showed them to be ineffective for treatment purposes. These articles represented levels one and two in terms of “Levels of Evidence” which can be further graded as A or B recommendations (Figure 2, Appendix A).<sup>27</sup>

Figure 2. Results (Percent)



## *Discussion*

### *Evidence in Literature*

The issue of adolescent depression and suicide is a heavily debated and a confusing topic that has left not only health care providers, but some parents as well, uncertain on the best approach in regards to patient management. Numerous studies have been done claiming to have clear answers, but all the while contradicting each other, presenting unclear evidence, and in the end, leaving practitioners to make their own decision regarding the treatment of young patients. Until the FDA comes out with clearer

guidelines, medical personnel will be forced to shift through the evidence themselves. The purpose of this paper was to organize studies in an understandable and presentable fashion that shows the results to this greatly disputed topic.

After evaluating the data from articles used in the study, the vast majority have the same conclusion: the use of antidepressants in adolescents with depression does not show a statistically significant increase in suicide. Also, despite recent concern that antidepressant treatment is not effective for this age group, there is evidence that both pharmacotherapy and psychotherapy treatment does improve depressive symptoms.

Two pivotal studies appear to cause the most confusion regarding the use of antidepressants in young patients. In 2004, Garland published an article stating that not only was prescriptive treatment ineffective in comparison with a placebo, but the side effects of paroxetine included responses such as agitation and suicidal ideation.<sup>5</sup> A retrospective study done by Gunnell and Ashby reviewed data from SSRIs and time trends regarding suicides and the number of prescriptions written.<sup>17</sup> Their results showed that all the SSRIs have some suicide risk over placebo use. Gunnell and Ashby admitted later in their discussion that “direct evidence that prescription drugs caused suicide is hard to find and that the balance of risk and benefit may vary depending on an individual’s risk of suicide.”

Both of these articles stated that there is an increased risk of suicide with the use of antidepressant treatment, yet the evidence that they have to back up their conclusions is weak, indirect, and based on correlation data. Some argue that it is not the drug itself that causes the patient to commit suicide. Likewise, it is a possibility that the medication is not causing the suicidal thoughts and actions, but instead helping the patients to regain

their energy and motivation to plan and carry out their ideas that they may have been harboring.<sup>17</sup>

Beasley et al, completed a retrospective study in 1991 assessing the possible association of fluoxetine with suicide.<sup>13</sup> Subjects included 1,765 fluoxetine patients, 731 TCA patients, and 569 placebo patients. The results showed no difference in suicide acts between the three groups, but did show a decrease in suicidal ideation among patients receiving fluoxetine.

In 1998 a study completed by Barburi et al, reviewed antidepressant sales from 1988-1996 and suicide trends.<sup>22</sup> The results indicated no increased risk of suicide with the increased use of the medication.

Another study was published two years later by Rihmer et al. with the similar findings to Barburi after examining Hungary suicide rates between 1985 and 1997.<sup>23</sup> In this study, the reason for a decline in suicide rates was associated with an increase in medical and psychological training and an increase in antidepressant prescription drug use.

Grunebraum et al, completed a study in 2004 that examined suicide rates in the United States between 1985-1999 in correlation to antidepressant prescription writing.<sup>21</sup> After adjusting for unemployment and alcohol use, there was a four-fold increase in prescription writing with a 13.5% decrease in suicide. Their results showed an inverse relationship between SSRIs and other second generation antidepressants and suicide rates. It was concluded that the decline in the national suicide rates from 1985 to 1999 were a result of increased use of antidepressant medication. They also concluded that treatment of mood disorders might further reduce the suicide rates.

In 2003 Khan et al. analyzed reports from a random controlled study that included 48,277 depressed subjects who were being tested for a difference in reported rates of suicide after being randomly assigned to treatment with a FDA approved SSRIs.<sup>18</sup> The subjects were compared to similar subjects who were assigned to another standard antidepressant or to a placebo. Of those participating, 77 committed suicide. The results showed no statistical difference among patients assigned to SSRIs, a standard treatment, or a placebo.

In 2004 the Treatment for Adolescents with Depression Study (TADS) was published.<sup>19</sup> This was a randomly controlled trial with 439 patients ranging from 12 to 17 years of age with a primary DSM-IV diagnosis of major depressive disorder. Subjects were randomly assigned to four groups; one received fluoxetine alone, one received CBT alone, one received the combination of both, and one received a placebo pill. The results showed that the combination of fluoxetine with CBT was superior and statistically significant compared to either alone. Clinically significant suicidal thinking improved the most with the combination treatment.

#### *Weaknesses in the Literature*

An area that is not addressed in the literature is the problem with the drug approval process. For example, with all the recent attention to the adverse side effects of antidepressants, many are wondering why these effects are not being realized earlier in the testing process before being released in the market. There are a number of complaints and concerns regarding the testing of these antidepressants and other medications before they are approved for the general public.

Another problem with the drug approval process is the manner in which drugs are checked for safety and efficacy. Many times the population that participates in the pre-market trial is not representative of the population that will be using the medication once it is out on the market. Also, drug trials usually last an average of six to eight weeks before the drugs enter the market. An episode of depression typically lasts seven to nine months, with reoccurrence being very common, so there is not enough time to see a true effect of these medications in the short time that is allotted.<sup>6</sup>

There are also a number of difficulties in studying the relationship between antidepressant medications and suicide. Among these issues is the concern of random assignment to placebo control groups. Some youth who have serious psychological problems like suicidal ideation will not be accepted to receive treatment in studies. Many researchers disqualify those at a high risk of suicide, therefore eliminating the very factor that needs to be studied.<sup>10</sup>

### *Gaps in the Literature*

A complaint of many clinicians is that treatment options for depression, especially psychotherapy, are developed to treat adults and then extended downward to include children. Therefore, the therapy may not be as effective for children as it possibly could be. Future studies need to be done specifically for children, taking into account the different developmental stages with individual age groups.<sup>10</sup>

Another possible area to study is the causal link of suicide and antidepressant medication by monitoring patients who are not depressed but are taking the medication for other reasons, such as anxiety or obsessive compulsive disorder. By following these patients it may be helpful to determine whether they are or are not suffering from

potential suicidal behavior.<sup>6,9</sup> The FDA is considering the idea of this study, but there are no plans to conduct it at this time.

Another aspect that may be examined closer is the dose of the medicine in relation to side effects and the age of patients. It has been found that there is a relationship here, with there being an increase in adverse effects the higher the dose.<sup>15,26</sup> Therefore, one idea to explain the side effects seen in some children is that these patients are being overmedicated. By taking a closer look at this, following young patients at different ages and doses, and recording side effects, clinicians would be able to use this information to find an effective but safe dose of antidepressant medication.

#### *Validity of the review*

The article selection process was completed in a systematic fashion, collecting the original articles via Medline and PsychInfo with the above mentioned key words. Once obtained, the articles were examined closely, making sure all chosen met strict criteria mentioned in methodology section. The data was then separated and organized into Figure 1, where it was reevaluated and reviewed for accuracy by the research advisor. There were eight discarded articles that were found in the article search, but did not meet inclusion criteria. Refer to appendix B for a complete listing of unused articles.

#### *Weaknesses in the review*

As in any research or review process, there are always going to be some weakness that in hindsight would have made the results even more valid. In this project, the author names, institutions, and journals were not blinded from the author or advisor, therefore, not protecting against bias. Another limitation in the process of evaluating the research is that no mention was given to internal validity, such as the methodology of the included

articles. This gives the reader less opportunity to examine the strength of each article results, forcing them to rely only on this authors interpretation of what is valid research and data.

### *Conclusion*

As physician assistants, it is important to continuously assess the peer-reviewed literature and carefully examine the data in regards to the many heavily debated medical issues. As seen in most cases of medicine, there is no black and white answer to the question of how to treat young patients diagnosed with major depressive disorder. But there are some clear implications that can be drawn from the results of this paper, the most important being that physician assistants should not shy away from treating depression in young patients. The literature shows there is no significant statistical evidence of an increased risk in suicide in these patients and that antidepressants and CBT are helpful in most cases.

It is important to realize that each and every patient is different and needs to be managed on an individual basis. Medical providers, with the help of family members, need to monitor their patients closely, especially when first placed on the antidepressants, as their body adjusts to the treatment. Treatment plans need to be adjusted to fit the patient in regards to their suicide risk, with the best outcome resulting from combination therapy. This includes fluoxetine (the safest SSRI) and CBT (the most effective form of psychotherapy).<sup>4,10,13,14</sup>

Physician assistants have obligations to their patients, the first and foremost being, do no harm. By withholding treatment of young patients suffering from MDD, for fear of adverse effects, this may place patients at an even greater risk for committing

suicide. Until there are medications that are 100% safe, providers are forced to rely on the evidence available in the literature, along with medical knowledge and training to help treat adolescent patients with depression.

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Appendix A  
Raw Data

<b>Study year</b>	<b>Research Addresses</b> 1.pharmacotherapy 2.psychotherapy 3.both 4.background	<b>Level of Evidence</b> 1.random control 2.retrospective 3.background	<b>Demographics</b> main data	<b>Findings</b>	<b>Supportive of Research</b> 1.Yes increase risk w treatment 2.No increase risk w treatment 3.warning/no conclusion 4.suicide not addressed Depression improved w treatment 5.suicide not addressed depression not improved w treatment 6.background
<b>Khan et al</b> 2003	1	1	48, 277 depressed pt 77 committed suicide	*no stat difference among pts assigned to SSRI, other, placebo	2
<b>Whittington et al</b> 2004	1	1	5-18 yo	*SSRI vs placebo *Fluoxetine has favorable risk-benefit ratio *other-risk outweighs benefit no data on suicidal behavior	4 - Fluoxetine 5 - other SSRI
<b>Ranaud</b> 1998	2	1	100 depressed adolescents	*subj more likely to respond rapidly to therapy or not at all *milder forms of dep benefit from therapy *does not address suicide	4
<b>Son &amp; Kirchner</b> 2000	4	3	n/a	*background: intro, risk factors, signs and symptoms	4

<b>Malquist</b> 1971	4	3	n/a	*history	6
<b>Hautenstein</b> 2003	3	3	n/a	*symptoms, treatment	6
<b>Besseghini</b> 1997	4	3	na/	*background- statistics, intro, definitions	6
<b>Garland</b> 2004	3	2	n/a	*Rx minimal/no effect on childhood dep beyond placebo effect *evidence that CBT is effective *SE of paroxetine (agitation, suicidal ideation)	AD – 1 Therapy - 4
<b>Hamptom</b> 2004	1	3	n/a	*label warnings to heighten awareness, not to make causal link	2
<b>Herxheimer &amp; Mintzes</b> 2004	4	3	n/a	*background	6
<b>Beasely &amp; Beardslee</b> 1998	2	3	n.a	*types of therapy: CBT, individual, group, family *suicide not addressed	4
<b>Miller</b> 2002	3	2	n/a	*Therapy- supportive, educational, psychodyn, CBT, interpersonal, combo	4
<b>Emslie et al</b> 1997	1	1	96 7-17 yo fluox/placebo x 8 wks	*fluox superior to placebo *complete remission rare	4
<b>Kaslow &amp; Thompson</b> 2000	2	2	studying effectiveness of psychosocial interventions in depressed children	*all effective compared to no treatment *CBT shows best results	4

<b>Shugart &amp; Lopex</b> 2002	4	3	n/a	*symptoms, DSM-IV criteria, prevalence	6
<b>Wagner et al</b> 2003	1	1	376 outpt, 6-17 yo w/ DSM-IV MDD suicidal RF excluded	*sertraline stat sig greater improvement as compared to placebo *no diff bw groups regarding suicidal ideation *more adverse SE in children that adolesc, could be dose related	4
<b>TADS</b> 2004	3	1	439 12-17 yo	*combo fluox & CBT better than either alone greatest decrease in suicidal thinking *fluox alone, no better than placebo in lowering suicidal thinking *slight decrease with CBT alone	2
<b>Gunell &amp; Ashby</b> 2004	1	2	reviews data from SSRI & time trends regarding suicide & Rx writing	*"direct evidence that Rx prevent suicide is hard to find" *studies show increase in Rx writing contributes to decrease in suicide (weak evidence) *all SSRI have some suicide risk over placebo *balance of risk and benefits may vary depending on risk	1

<b>Jick et al</b> 1995	1	2	estimates rate and means of suicide among 172,598 pt taking 1 of 10 meds	*143 people committed suicide (8.5/10,000)  *increased risk in pt w higher dose *risk was equal among 10 meds	2
<b>Olfson et al</b> 2003	1	1	10-19 yo who filled a prescription for Rx 340,000 in '89 720,000 in '01	*area with largest increase in AD to 10-19 yo experienced the greatest decrease in suicide	3
<b>Healy &amp; Whitaker</b> 2003	1	1	review RCT, epidemiology studies	*many studies flawed in data analysis *increase risk not as significant as studies show if analyzed correctly *optimal suicide reduction plan-monitored tx for all pt restriction of tx for all pt at higher risk of suicide	2
<b>Grunebraum et al</b> 2004	1	1	suicide rate bw '85-'99 in correlation to Rx writing	*4x increase in Rx with 13.5% increase in suicide-adjusted for unemployment and alcohol use	2
<b>Barburi et al</b> 1998	1	2	review of AD sales bw 88-'96 & suicide trends	*SSRI do not help prevent suicide, but also do not cause an increase risk	2

<b>Rhimer et al</b> 2000	1	2	examined Hungary suicide 84-'97 and possible reasons for decrease	*decrease in suicide with only explanation being increase in med/psych training and increase in AD	2
<b>Khan et al</b> 2000	1	1	19,639 pt 7 new AD, 7 placebos	*no stat sig difference bw AD Rx and placebo regarding suicide	2
<b>Beasley Cm et al</b> 1991	1	2	assess possible association of fluox w suicide; 1,765 fluox pt, 731 TCA pt, 569 placebo pt	*no difference in suicidal act bw 3 groups  *suicidal ideation less often w fluox pt.	2
<p>CBT = Cognitive Based Therapy  SE = side effects  Rx = prescriptions  SSRI = Selective Serotonin Reuptake Inhibitor  AD = antidepressant medication  RCT = randomized controlled trial</p>					

Appendix B  
Discarded articles

1. Karlsson L et al. Current co morbidity among consecutive adolescent psychiatric outpatients with DSM-IV mood disorders. *Eur Child Adolesc Psychiatry*. 2006;2: 50-55.
2. O'kearney R, Gibson M, Christensen H, Griffiths KM. Effects of a cognitive-behavioral internet program on depression, vulnerability to depression and stigma in adolescent males: a school-based controlled trial. *Cogn Behav Ther*. 2006;35(1):43-54.
3. Wisdom JP, Clarke GN, Green CA. What Teens Want: Barriers to Seeking Care for Depression. *Adm Policy Ment Health*. 2006;23:54-61.
4. Lindsey MA, Korr WS, Broitman M, Bone L, Green A, Leaf PJ. Help-seeking behaviors and depression among African American adolescent boys. *Soc Work*. 2006; 51(1):49-58.
5. Jaycox LH, Asarnow JR, Sherbourne CD, Rea MM, Laborde AP, Wells KB. Adolescent Primary Care Patients' Preferences for Depression Treatment. *Adm Policy Ment Health*. 2006;72(1)32-40.
6. Udal AH, Groholt B. Bipolar disorders in children and adolescents. *Tidsskr Nor Laegeforen*. 2006 Jan 26;126(3):302-4.
7. Carter JC, Bewell C, Blackmore E, Woodside DB. The impact of childhood sexual abuse in anorexia nervosa. *Child Abuse Negl*. 2006;102-5.
8. Kessing LV. Gender differences in subtypes of late-onset depression and mania. *Int Psychogeriatr*. 2006;1-12.

## Vita

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