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## The Safety and Efficacy of Antidepressant Use in The Adolescent Population

Jason Marcello

University of North Dakota, [jason.marcello@und.edu](mailto:jason.marcello@und.edu)

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The Safety and Efficacy of Antidepressant Use in The Adolescent Population

by

Jason Marcello, MRS, RRA, PA-S

Masters of Radiologic Science, University of North Carolina Chapel Hill, 2011

Contributing Author: Jay Metzger, MSPAS, PA-C

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### Abstract

This literature review was conducted to determine the safety and efficacy of antidepressants in the adolescent population based on the currently available research. Specifically, are antidepressants safe and efficacious in treating depression in adolescents and is their use associated with increased risk of suicide. Data was collected by searching medical databases including: Clinical Key, CINAHL Complete, PsycINFO, PubMed, DynaMed Plus, and Cochrane Review. The review of the literature included systematic reviews, meta-analysis, cross-sectional, longitudinal, randomized control trials, and survey methods. All literature works selected were published within the past 14 years. A focused search was performed to gather information on antidepressant safety and efficacy in adolescents. Upon analysis, the literature showed a significant increase in the rate of depression and suicide amongst adolescents. However, other studies demonstrated mixed results regarding the risk of suicide in adolescents who were prescribed antidepressants. Based on the literature reviewed, there is not a clear correlation between increased suicide and antidepressant use in adolescents. In fact, some studies show a significant decrease in suicide amongst subjects who were taking an antidepressant. The research indicates that antidepressants and cognitive behavioral therapy (CBT) are both efficacious and relatively safe when used by themselves. When used alone, antidepressants are slightly more efficacious than CBT alone. The literature also indicates that the combinations of CBT and antidepressants are the most efficacious in treating depression in the adolescent population.

Keywords: *adolescent depression, antidepressants, adolescent antidepressants, antidepressant safety, antidepressant efficacy, adolescent suicide, and suicide rates*

## **Introduction**

Depression is one of the most common mental health disorders in the country. The prevalence of depression among the adolescent population continues to rise. When considering treating depression in adolescents there has been much debate regarding the safety and efficacy of antidepressant medications. Recently it was estimated that nearly 3.2 million children ranging from the ages of 12-17, have been affected by depression (National Institute of Mental Health [NIMH], 2017). Along with this rise comes the increased use of antidepressants for the treatment of depression. According to the Centers for Disease Control (CDC, 2017), nearly 80% of children ages 6-17 that have been diagnosed with depression have also undergone treatment. The healthcare industry has been surrounded by controversy regarding antidepressant use in young adults. This began in 2004 when the Food and Drug Administration (FDA) added a black-box warning for many antidepressant medications linking their use to suicidal thoughts and behavior. Even more concerning is the rising rate of suicide in adolescents. In fact, the CDC (2017) estimated a 30% increase in suicide rate from the year 2007 to 2015 in males and a 50% rate increase for females ages 15-19. The above statistics indicate there is a legitimate concern regarding the safety of antidepressant use in the adolescent population.

## **Statement of the Problem**

Despite having improved resources for the treatment of depression, the rate of suicide in the adolescent population is on the rise. More providers are specializing in depression, and more adolescents are being treated for depression than ever before. If this is the case, then why is the rate of adolescent suicide continuing to rise? Healthcare providers take an oath to do no harm when providing care to patients. However, there may be a chance that prescribing

antidepressants is causing more harm than good in the adolescent population. If this is the case, should adolescents even be treated with antidepressants for depression?

### **Research Question**

In the adolescent population, is the use of antidepressants for treating depression, safe and efficacious, and is the use of antidepressants associated with increased risk of suicide?

### **Methodology**

An extensive literature review was conducted to investigate the use of antidepressant medication in the adolescent population. Academic libraries were accessed to perform an in-depth analysis of the available scholarly literature. The medical databases utilized include: Clinical Key, CINAHL Complete, PsycINFO, PubMed, DynaMed Plus, and Cochrane Review. The use of MeSH terms included adolescent depression, antidepressants, adolescent antidepressants, antidepressant safety, antidepressant efficacy, adolescent suicide, and suicide rates. Research material reviewed consisted of available systematic reviews, meta-analysis, cross-sectional, longitudinal, randomized control trials, and survey methods. Upon a thorough review of sources, any material that had biased, opinionated, or did not directly pertain to my project was eliminated.

### **Review of the Literature**

#### **Prevalence of Depression in Adolescents.**

It is well known that the rate of depression in the adolescent population has been on the rise. The cause of increased depression among adolescents has been under substantial discussion. Several factors may or may not be behind the flux of depression in children. According to the CDC (2017) from 2003 to 2012, there was a three percent increase in the rate of adolescents diagnosed with having either depression or anxiety. Additionally, there was a 52%

increase from 2005-2017 in the rate of the adolescents aged 12-17 who reported having a major depression episode based on results of the National Survey on Drug use and Health (Twenge, Cooper, Joiner, Duffy, & Dinan, 2019).

Avenevoli, Swendsen, He, Burstein, and Merikangas, (2015) conducted a survey study by utilizing the specialized interview staff of the Institute for Social Research at the University of Michigan. The objective of this survey analysis was to investigate the prevalence of major depressive disorder (MDD), comorbidity, service use, and colorations with sociodemographic data. The data utilized for the analysis consisted of 10,123 in-person surveys of adolescents living in the US, ranging in the age of 13-18. A response rate of 82.9% was calculated for the face-to-face surveys. The World Health Organization (WHO) Composite International Diagnostic Interview Version 3.0 was utilized as a diagnostic tool to collect data for DSM-IV. This tool enables the lifetime assessment and 12-month assessment for the presence of MDD and other associated mental health disorders. In addition, a self-administered questionnaire (SAQ) was mailed to the caregiver of each participating adolescent. A total of 6,491 complete questionnaires were collected in addition to 1,994 partially completed questionnaires. The response rate for the SAQ was calculated to be 83.3%. Many sociodemographic variables were evaluated including: demographics, parent educations, marital status, and household income. Finally, the Sheehan Disability Scale (SDS) was used to determine the amount of role impairment and comorbidity by assessing the extent to which MDD impaired routine daily tasks.

Avenevoli et al. (2015) revealed that based on their survey analysis, the prevalence of MDD in the US adolescent population was 11% lifetime prevalence and 7.5% for a 12-month prevalence. According to the study, 87.6% of adolescents who report having lifetime MDD and 90.6% who report MDD within the past 12 months also report suffering from dysthymia



(Aveneloi et al., 2015). Female adolescents had approximately a two to three times higher risk of having MDD compared to males. Furthermore, the prevalence of MDD is directly related to age, demonstrated via a calculated 4-fold risk of MDD in older adolescents (Aveneloli et al., 2015). It was estimated that 63.7% of subjects who reported having MDD within the past 12 months also had other mental health disorders such as anxiety or another behavioral disorder. Impairment of routine daily tasks was documented in 63% of adolescents with MDD within the past year (Avenevoli et al., 2015). The outcome of the survey describes that 30% of adolescents with MDD have had recent suicidality, and 10.8% have attempted suicide (Avenevoli et al., 2015). Findings also suggested that 60.4% of adolescents who reported having depression have received some form of treatment for their disorder (Avenevoli et al., 2015).

This study was not without its limitations. Limitations of the study were mostly due to it being a cross-sectional survey. A cross-sectional survey may limit the ability to distinguish differences in the progression of depression over time or to make predictions accurately. Limitations were also present in the ability to assess lifetime depression due to reliance on retrospective recall. Lastly, the researchers did not include findings of mild depression, which likely affects a large number of adolescents potentially impacting the results. The strength of this study was that it was partly conducted by a professional research team that is highly specialized in conducting survey interviews.

A second study performed by Ghandour et al. (2019) determined the prevalence of depression, anxiety, behavioral conditions, and their treatment among children in the US. survey analysis was performed using the 2016 National Survey of Children's Health (NSCH), orchestrated by the US Census Bureau. A total of 50,212 surveys were completed out of a total 365,000 that were delivered. Among the completed surveys, 43, 283 report children age 3-17

years-old living in the household. It was this population of patients that were utilized in the study. Differences in social and demographics were considered, and bivariate analysis was performed to demonstrate findings.

The results of the study demonstrated that in 2016, there was a 3.2% prevalence rate of depression in children aged 3-17 (Ghandour et al., 2019). It is estimated that approximately 1.9 million children in the US are affected by depression (Ghandour et al., 2019). There was a direct relationship between the prevalence of depression and age. In fact, older children were more likely to have depression (Ghandour et al., 2019). Children were also more likely to have depression if they or their caregivers had poor health conditions or had low household incomes (Ghandour et al., 2019). The study also revealed that nearly eight out of 10 children with depression were being treated for their condition, and those with depression were far more likely to be treated when compared to those with anxiety or other behavior conditions (Ghandour et al., 2019).

Information provided for the study was self-reported, allowing for possible limitations such as recall bias. Also, there may be some limitations on reporting treatment in this study mainly because questions in this section of the survey were vague. The strength of this study is that it was completed recently and involved an extensive amount of data gathered within the past three years.

Lu (2019) investigated the trends related to the prevalence, treatment, and risk factors for depression in the adolescent population of the United States. The purpose also included researching discrepancies with the use of mental health care providers in the population stated above. This study focused on 95,856 adolescents aged 12-17. An annual cross-sectional survey, the National Survey on Drug Use and Health (NSDUH) conducted by the Substance Abuse and

Mental Health Services Administration (SAMHSA), was utilized to collect data from the years 2011 through 2016. Additionally, the study evaluated differences in several different types of sociodemographic attributes. Statistical analysis was performed using Pearson's chi-squared test to reveal discrepancies in the data sets.

Results of the study demonstrated a (4.6%) increase in the prevalence of depression among the adolescent population from the year 2011 to 2016 (Lu, 2019). Also, this study revealed that although there was a flux in prevalence, there was not a reported increase in the use of mental health providers observed. Furthermore, results concluded higher rates in the prevalence of depression in older adolescents, females, and those raised at home by a single mother (Lu, 2019). There was a significantly higher incidence of adolescent depression among those who had parents that were not authoritative, and those who reported a negative experience associated with school (Lu, 2019). The study also revealed a lower usage of medication among adolescents of minority and those without insurance (Lu, 2019). The study concluded that there had been a steady increase in untreated adolescent depression. It also concluded that efforts for improvement are needed (Lu, 2019).

A limitation to this study suggested by the author, is the NSDUH has a limited accuracy rating of 80% (Lu, 2019). Secondly, approximately 1-2% of the surveys had missing information regarding mental health. Lastly, self-reporting was also a limitation to this study (Lu, 2019). The strengths of this cross-sectional survey were that it evaluated a five-year time period, and it was one of the few studies that focused on analyzing the use of mental health care providers.

In a cross-sectional study performed by Moitabai, Olfson, and Han (2016), the prevalence of depression in the adolescent population was investigated. A yearly survey was utilized to gain data. Depression in this study was defined as the occurrence of a major depressive episode. This

study also examined differences in sociodemographic sets, noting any trends over the course of a year. Mojtabai et al. (2016) used data collected from the NSDUH from 2005 to 2014. Subjects involved were ages 12-25 years from the United States who responded to an annual survey. Responses from a total of 351, 250 adolescents and young adults were calculated, and it was determined that 31, 132 met the criteria for the study (Mojtabai et al., 2016).

Results revealed the prevalence of depression in the United States general population of adolescents and young adults increased by (2.6%) between the years of 2005-2014 (Mojtabai et al., 2016). Furthermore, the results showed a significant increase in the prevalence of depression in subjects who are 12-20 years old. The additional information gained from this study shows that along with the increased prevalence, there was also an increase in the use of mental health providers, medications, and overnight hospital stays (Mojtabai et al., 2016). There was also a significantly higher incidence of depression in female adolescents compared to males, whites compared to minorities, and lower socioeconomic standards (Mojtabai et al., 2016).

The most noteworthy limitation of this study was self-reporting by adolescents in which accuracy is unable to be determined. Other limitations include differences in reporting sources and limiting the study to major depressive episodes. The strengths of the study are that it looked at the prevalence of depression in adolescents over a broad span of eight years and that it examined many sociodemographic characteristics.

### **Efficacy of Antidepressants in Adolescents.**

One method used for the treatment of depression in the adolescent population is the use of antidepressant medications. Over the years, there have been significant differences in opinions regarding the efficacy of antidepressants in adolescents. One study, in particular, was a systematic review and meta-analysis conducted by Locher et al. (2017) to determine the efficacy

and safety of selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and placebo for treating certain psychiatric disorders in adolescents. The disorders evaluated included depression, anxiety, obsessive-compulsive disorder (OCD), and posttraumatic stress disorder (PTSD). Multiple databases such as: Cochrane, EMBASE, PsycINFO, PubMed, and Web of Science were utilized to search for applicable studies. Based on the searching methods, they were able to identify 36 applicable studies with a total of 6,778 subjects. The types of studies included in this project were double-blind, controlled trials, and randomized. The authors evaluated 17 studies on depression, 10 for anxiety, 8 for OCD, and 1 for PTSD.

According to the data collected, treatment with SSRIs and SNRIs are more effective than placebo in all patients except pediatrics, where efficacy was equal to placebo (Locher et al., 2017). Based on these findings, there is not good evidence to support the pharmacologic treatment of depression in the pediatric population. Also, when looking at depression, there was only a subtle improvement noted in adolescents. Overall, SSRIs and SNRIs were more effective at treating anxiety than depression, which is consistent with previous studies. The results also demonstrate a much higher incidence of adverse events such as suicidality with the use of antidepressants when compared to placebo. Therefore, Locher et al. (2017) concluded that the results carry concerns regarding the safety of antidepressant use in all patients less than 18 years old.

There were a few key strengths and limitations for this study. The strengths of this study are that it utilized a large sample size and it focused on two different classes of antidepressants. The main limitation is the fact that the article was a systematic review and meta-analysis of other

author's studies, which allows for the possibility that the works reviewed could have inaccuracies or bias.

The goal of another experiment performed by March et al. (2007) was to determine the efficacy and safety of treatment in adolescents with depression. This study was a controlled clinical trial that involved 13 different sites in the United States, where randomized treatments were evaluated over a period of nine months. A total of 327 participants between the ages of 12-17 who had been diagnosed with major depressive disorder were involved in the trial. Proper parent approval and consents were obtained, allowing participation in this double-blind study. The trial remained double-blind for the first 12 weeks only. The clinical trial evaluated treatment outcome with fluoxetine therapy, placebo therapy, CBT, and a combination of fluoxetine therapy with CBT.

The results of the efficacy of treatment for this clinical trial were calculated at 12, 18, and 36 weeks. The response rate at week 12 was a 73% response to combination therapy with fluoxetine and CBT, a 62% response with treatment with fluoxetine only, and a 48% response with CBT alone (March et al., 2007). At week 18, combination therapy produced an 85% response, fluoxetine a 69% response, and CBT a 65% response (March et al., 2007). Results at the conclusion of the trial at 36 weeks demonstrated an 86% response to combination therapy, 81% to fluoxetine, and 81% with CBT only (March et al., 2007). Surprisingly, the results showed the same efficacy with CBT compared with fluoxetine alone for the treatment of depression in the adolescent population. However, the combination of both fluoxetine and CBT was the most effective. As the safety of fluoxetine was analyzed, it was found that overall there was less suicidality with fluoxetine. Interestingly, it was far more common to have suicidal events in

patients who were being treated with fluoxetine (14.7%) compared to 8.4% for combo therapy, and 6.3% for CBT (March et al., 2007).

One limitation of this double-blind clinical trial was eliminating the placebo group after week 12. The authors decided to make the trial unblind at that time, which has the potential to affect the outcomes. Other limitations were the use of a relatively small sample size and only one specific antidepressant medication was analyzed. The strength of this study was the fact that it is an actual controlled clinical trial with real results that were evaluated by trained medical staff.

Zhou et al. (2015) evaluated the efficacy of antidepressants in adolescents and young adults. This study was unique because the authors included patients with substance abuse in their research. They performed a systematic review and meta-analysis utilizing multiple different databases to search for relevant data dating from 1970 to 2013. A total of five clinical trials consisting of a total of 290 patients were analyzed. The age of the patients included in the review was restricted to 25 years or younger. The degree of depression was evaluated using the Childhood Rating Depression Scale or the Hamilton Depression Rating Scale. A total of 2,055 reports were acknowledged; however, only five studies met the full criteria.

The results of this study showed that the use of antidepressants for the treatment of depression in adolescents was superior when compared to placebo (Zhou et al., 2015). However, results concluded no improvement in outcomes when antidepressants were used to treat patients with substance-use disorders when compared to placebo. The authors concluded antidepressant medications are not indicated to treat a substance use disorder. Also, that further research is needed to prove its efficacy for patients with both substance use disorder and depression (Zhou et al., 2015).

Limitations associated with this research are that only five studies met the author's criteria and half of the efforts were evaluating substance-use disorders. The strength of this study was that research included all studies that met the criteria for the past 49 years. Another strength is that the study was not only able to report on efficacy, but it also demonstrated no evidence of decreased tolerability of antidepressant medication in adolescents and young adults.

### **Safety of Antidepressants in Adolescents.**

Antidepressants, much like all medications, have the risk of side effects ranging from mild to severe. There has been a great deal of attention directed towards the safety of antidepressant use in the adolescent population. A study performed by Anderson, Pace, Libby, West, and Valuck (2012) was to determine the safety of the five most commonly prescribed antidepressants in adults and adolescents. The goal of this particular study was to calculate the extensiveness of multiple antidepressant side effects. Furthermore, the study aimed to analyze the efficacy as well. The authors utilized LifeLink to locate claims over 11 years, ranging from 1998 to 2008. The study focused on patients who were at or above 13 years old and was recently diagnosed with depression. Several different classes of antidepressants were studied including: selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), tetracyclic antidepressants, phenylpiperazine, and bupropion. Side effects that were evaluated include nausea, vomiting, headache, sedation, agitation, and sexual dysfunction. A retrospective claims study was conducted involving a total of 40,017 patients in which 3,617 were considered to be adolescents between the ages of 13 and 18.

According to the results, nausea and headaches were the two most common side effects in both adolescents and adults. Headaches were most frequently reported with an estimated



occurrence rate of up to 11% for adults and adolescents (Anderson et al., 2012). The second most common was nausea or vomiting, up to 4% (Anderson et al.). In the adult population, nausea was more prevalent with the use of SNRIs compared to the use of SSRIs. Bupropion therapy had significantly fewer reports of headaches for both populations compared to SSRI therapy (Anderson et al., 2012). Also, headaches were more prevalent with tetracyclic antidepressants than with SSRIs in adolescents. The presence of all other side effects that were included in this study was relatively insignificant across the board in the adolescent population. Overall, the study suggests fewer side effects were associated with SSRIs than with SNRIs or tetracyclic therapy in adolescents (Anderson et al., 2012).

There were some notable limitations observed in this study. First, adolescents under the age of 13 were excluded from the study. Secondly, the sample size for TCAs and MAOIs was small. Lastly, although safety was the focus of this study, the authors failed to include suicidality in the side effects profile. The strengths of this investigation are that it included a large sample size and that many different classes of antidepressants were evaluated.

Bushnell et al. (2015) utilized the LifeLink Health Plan Claims Database to obtain data sets for the purpose of evaluating prescribing practice of antidepressants in children and adults. Specifically, the study focused on patients who were started on a selective serotonin reuptake inhibitor (SSRI) before and after 2004. The material collected was between the years 2000 and 2009. Their theory was that perhaps lower, safer doses of SSRIs were prescribed after 2004 when the FDA issued a black box warning suggesting a risk of suicidality. A total of 51,948 children aged 5-17 who fit the criteria of the study were evaluated. In addition, young adults ages 18-24 and adults ages 25-64 were also included for comparison. The authors excluded

escitalopram from the study stating that a lack of research relating to its use not being approved until late 2002.

The results of the data collected from the study showed that treatment in children was initiated most often with sertraline in 38% of subjects (Bushnell et al., 2015). The rate of use for other antidepressants was as follows: fluoxetine 35%, citalopram 15%, and paroxetine 11% (Bushnell et al., 2015). Of the children studied, 50% of them had a diagnosis of depression and 21% of them received their prescription from a psychiatrist (Bushnell et al., 2015). According to the data, the number of children and adolescents who began treatment with a low dose of antidepressants increased over time; predominantly after the 2004 warning by the FDA. In fact, there was an impressive 116% increase in the number of lower doses amongst adolescents ages 13-17 (Bushnell et al., 2015). Other pertinent findings revealed that patients who were started on antidepressant therapy by a psychiatrist were prescribed a lower initial dose compared to those initiated by a general provider (Bushnell et al., 2015). In conclusion, the black box warning for increased suicidality issued by the FDA in 2007 helped to ensure patients were being started on a safer dose of antidepressant (Bushnell et al., 2015).

One limitation in this literature work is that records that were studied were subject to human error or inaccuracies. Also, initial doses could have inaccuracies due to the possibility that some patients were initially started on a free sample of a different dose of medication. The dominant strength of this study is that it took into consideration the FDA black box warning issued in 2007 evaluating cases before and after that time.

### **Suicide Risk Associated With Antidepressant Use in Adolescence.**

The suicide risk associated with antidepressant use in adolescents has been surrounded by controversy stemming back to the release of a black-box warning by the FDA in 2004. The

black-box warning linked the use of several antidepressants with suicidal thoughts and behavior in adolescents. A few years later, the FDA elaborated on that warning by adding depression itself can lead to suicidal thoughts and behaviors. These statements by the FDA sparked the need for further studies.

Research analysis performed by Gibbons, Hur, Bhaumik, and Mann (2006) was conducted with the intent to examine the relationship between suicide in children ages 5-14 and the use of antidepressants. Data regarding the United States suicide rates among children aged 5-14 were collected via the National Vital Statistics database maintained by the CDC. The authors choose to focus on younger adolescents because they believed that there is less information available on the safety and efficacy of antidepressants in the younger population. Suicide rates and demographic characteristics were examined between the years of 1996-1998. The Poisson regression model was utilized to help determine the relationship between SSRIs and the rate of suicide and other demographics.

Based on the results, a total of 933 childhood suicides were found over the studied three-year period. Results revealed higher rates of suicide in children and young adolescents who were not taking an SSRI (Gibbons et al., 2006). Utilizing the Beyes model, it was estimated that there was an 81% increase in the suicide rate in the absence of SSRIs (Gibbons et al., 2006). As the rate of SSRI prescriptions decreased, the rate of suicide increased from 0.7 per 100,000 to 1.7 per 100,000 (Gibbon et al., 2006). The author's findings support the idea that SSRI use may help reduce suicide in younger adolescents (Gibbons et al., 2006).

This study on suicide rates in young adolescents had some apparent limitations. The most significant limitation is that the sample population only included children between the ages of 5-

14. The sample size is significant because, it is widely known that the rate of suicide is much higher in older adolescents. Another weakness of this study is that only a three-year period that took place over ten years ago was analyzed. The strength of this study is that it studied actual suicide rates and compared them to SSRI use.

Gordon and Melvin (2014) performed a review of the literature to study the risks with antidepressants in children and adolescents. They intended to gather information that would help inform providers about the risk of prescribing antidepressants. The authors evaluated relevant studies from 1991-2013. The studies included were randomized control trials, meta-analyses, toxicological studies, and pharmacoepidemiologic studies. The age of adolescents evaluated was between 6-18 years-old. The initial medical database search found 153 articles; however, 35 remained after exclusions were made.

The results of the available randomized controlled trials that were studied by Gordon and Melvin (2014) shows an overall increase in suicidality with many different types of antidepressants. The most notable increase in suicidality was observed in the early stages of treatment. Based on the research, fluoxetine was associated with the lowest rates of suicidality, whereas venlafaxine was found to have the highest risk (Gordon & Melvin, 2014). Children and adolescents who were treated with antidepressants for depression had a higher incidence of suicidality than those who were being treated for anxiety (Gordon & Melvin, 2014). The authors also studied suicidal ideation risk with newer generation antidepressants. They discovered a 58% increased risk of suicidality with the use of newer-generation antidepressants when compared to placebo (Gordon & Melvin, 2014). Oddly, no increase was noted in the 13-18 year-old population. The results of the study suggest an overall small increase in suicidality with antidepressant use in the adolescent population (Gordon & Melvin, 2014).

The limitations of the study are that it is comprised of other author's work which makes it difficult to fully determine the accuracy and limitations of each study. The strength of the study was that a long time period was evaluated. The study included all relevant articles from 1991-2013.

Olfson, Marcus, and Shaffer (2006) performed a matched case-control study to measure and define suicide risk with antidepressant therapy in children and adults. The data examined was collected from the Centers for Medicare and Medicaid Services from 1999 up to 2001. The data included claims, medications, and demographics from all 50 states. The study evaluated patients between the age of 6-64 years who met the criteria. The authors carefully searched for suicide attempts in cases related to antidepressant therapy. They eliminated 12 suicide deaths and 107 attempts by excluding patients who underwent inpatient treatment for 15 days or more within two months prior to the suicide attempt. There was a total of 784 suicide attempts cases that met criteria.

The results of this study demonstrate that white males were likely common to commit suicide in both adult and children population (Olfson et al., 2006). Secondly, white females were most likely to attempt suicide (Olfson et al., 2006). No suicide or suicide attempts were found in patients aged 12 or younger. Based on the findings, 25% of adults and 10% of adolescents who attempted suicide were also treated for substance abuse (Olfson et al., 2006). Half of the adult patients were treated with hypnotic medications before their death by suicide (Olfson et al., 2006). However, none of the child or adolescents studied were treated with hypnotics. According to the results, there was a significant increase in suicide attempts in children and adolescents who were treated with antidepressants.

Additionally, there was also a modest increase in suicide deaths in children and adolescents who were on antidepressant therapy. Suicide attempts were fewer when antidepressants were used in the adult population compared to adolescents. The study concludes that the risk of a suicide attempt is 1.52 times higher amongst children and adolescents who take antidepressants (Olfson et al., 2006).

Although this study proves very informative, there were some limitations. The study was limited to a small data range that only studied a two-year period. Also, the cases evaluated were dated back to 1999-2001. The strength of the study is that it directly examined suicide attempts and deaths related to antidepressant use in all populations.

### **Efficacy of Cognitive Behavior Therapy for Depression in Adolescents**

An alarming number of adolescents are living with depression. These individuals need a way to cope with depressive symptoms. Talking to a trained professional counselor is a popular tool used to help cope with symptoms of depression. The efficacy of cognitive-behavioral therapy (CBT) has been widely studied. In fact, a randomized clinical trial conducted by Brent et al. (2015) set out to determine the efficacy of CBT for the treatment of depression in adolescents. The study involved four different clinical sites and a total of 316 patients for evaluation. The data analyzed was from August 2003 to February 2006. The effects of CBT were evaluated during the course of treatment and up to 75 months post-therapy. At the beginning of the trial, all participants were 13-17 years old who had an established diagnosis of depression but were not currently having a depressive episode. Data was obtained by performing patient assessments at baseline, three months, nine months, 21 months, 33 months, and 75 months.

The findings demonstrated that CBT is effective in treating depression in the adolescent population. Outcomes were calculated using the Depression Symptoms Rating scale. During the last assessment, 88% of the initial participants underwent assessment. 29 patients that were not examined during the 33-month assessment were assessed at the conclusion of the trial.

According to results, there was a significant decrease in depression in patients who underwent CBT (Brent et al., 2015). Also, a much lower incidence of depressive episodes was explicitly noted during the first nine months of enrollment. The most substantial benefits of CBT were seen early on (Brent et al., 2015).

A limitation of the study is that 12% of the initial sample size was not retained throughout the length of the study and those patients had to be excluded. The strengths of this study are that it included a large sample size and that all participants shared similar characteristics at baseline. Another strength was the high number of assessments that were performed throughout the entire study.

An investigation by Cox et al. (2014) was to determine the efficacy of different types of treatment therapy for depression in children and adolescence. The objective was to compare antidepressants and psychological therapy alone and in combination. The authors performed a systematic review of multiple medical databases to find randomized controlled trials that met their criteria, dating all the way back to 1950. Patients who met the criteria were between six and 18 years of age with a documented diagnosis of MDD. A total of 11 studies and 1,307 subjects met the criteria and were analyzed in this study.

The results showed no significant differences in statistics comparing psychological therapy to antidepressant drug therapy (Cox et al., 2014). Based on limited data, results for antidepressant use was slightly more efficacious compared to psychotherapy alone (Cox et al.,

2014). Similarly, limited available data also showed better outcomes with the combination of psychotherapy and antidepressant medication for the treatment of depression in adolescence than antidepressants alone (Cox et al., 2014). In addition, the findings revealed no evidence to support that combination therapy was more efficacious when compared to psychotherapy alone (Cox et al., 2014).

A significant limitation for this study was that there was limited data available for review. All results of this study were based on limited evidence and the authors concluded that more evidence is needed to determine the most efficacious treatment of depression in adolescences.

## **DISCUSSION**

Based on the current literature, there has been a significant increase of depression in the adolescent population. A 2016 study estimated that approximately 1.9 million children in the US are affected by depression (Ghandour et al., 2019). In fact, there was a 52% increase from 2005-2017 in the rate of adolescents aged 12-17 who reported having a major depression episode based on the results of the National Survey on Drug use and Health (Twenge et al., 2019). The significant increase in depression is worrisome and rightfully has gotten the attention of medical providers across the country. As the rate of depression in the adolescent population continues to rise, so does the demand for accessibility to mental healthcare specialists. In recent years, mental health specialists have become increasingly more accessible. The work of Avenevoli et al. (2015) highlights the need for quality awareness and prevention around the country when it comes to depression in the adolescent population. The review of the literature revealed an obvious need for prevention in adolescents, especially those who are more likely to be affected by depression. Specifically, those who are more likely to experience depression are older adolescents, females, those from low-income families, and those being raised by a single parent



(Ghandour et al., 2019). According to the study performed by Locher et al. (2007) there is no good evidence to support the treatment of depression at all in the pediatric population.

According to literature, the use of antidepressant medication for depression in adolescents is efficacious. Several studies showed positive results with the use of antidepressants when compared to placebo. Of the studies reviewed, results did vary from mild to significant improvements observed when antidepressants were being administered. The majority of studies show that the use of an antidepressant alone and the use of CBT alone are both effective at treating depression in adolescents. The observed results of antidepressants compared to CBT were comparable at treating depression in adolescents. However, all research studies analyzed demonstrate the use of antidepressants combined with CBT was the most efficacious at treating depression in adolescents. In fact, March et al. (2007) showed that SSRIs and CBT were both equally effective at 81%. That same study also demonstrated that the combination of SSRI and CBT was the most effective at 86% (March et al., 2007).

The research shows that the use of antidepressants in adolescents is relatively safe, with a low risk of mild to moderate side effects. Based on the literature, the majority of the side effects of antidepressants are mild. The most common side effects noted were headaches, nausea, and vomiting. The works of Anderson et al. (2012) revealed that headaches were most frequently reported with an estimated occurrence rate of up to 11% for adults and adolescents. The second most common was nausea or vomiting, up to 4% (Anderson et al., 2012). Of the studies reviewed, there was a significantly low incidence of severe side effects noted with the use of antidepressants in the adolescent population. Although the use of antidepressants in adolescents appears to be relatively safe, the safest treatment for depression that has been proven effective is CBT. In fact, in some studies CBT was equally effective as antidepressant therapy. When

confronted with the challenge of treating depression in an adolescent, CBT is safe and efficacious. Therefore, CBT should always be considered when treating depression in adolescents. The literature work of Brent et al. (2015) also shows there was a significant decrease in depression in patients who underwent CBT.

The most noteworthy unwanted side effect of antidepressant use in adolescents was suicidality. According to literature, although there is an overall risk of suicidality in adolescents who are taking an antidepressant, that risk is very low. The risk of suicide itself is even lower, in the same data sample. However, the current research shows conflicting results when attempting to determine the suicidality risk with antidepressants amongst the youths. For example, the results of the available randomized controlled trials that were studied by Gordon and Melvin (2014). showed an overall increase in suicidality with many different types of antidepressants. Based on the research, fluoxetine was associated with the lowest rates of suicidality and venlafaxine was found to have the highest risk (Gordon & Melvin, 2014). Contrarily, the results of a study by Gibbons et al. (2006) revealed higher rates of suicide in children and young adolescents who were not taking an SSRI (2006). In that particular study, there was an overwhelming 81% increase in the suicide rate in the absence of SSRIs (Gibbons et al., 2006). Other studies showed that combination therapy is the most effective method of reducing the risk of suicidality. The work of March et al (2007) showed that treating depression with the combination of an SSRI and CBT significantly reduced the risk of suicide in adolescents.

In conclusion, the rate of depression in adolescents and the number of patients seeking depression treatment continues to rise. Even more concerning is the substantial increase in the rate of suicide among adolescents. Although there are conflicting studies, some studies show a connection between antidepressant use in adolescents and suicidal thoughts and tendencies.

However, the literature does not illustrate a clear correlation between increased antidepressant use causing the increase in suicide among adolescents. Therefore, I can conclude that treating depression in the adolescent population with an antidepressant medication has a very low risk of resulting in suicide. Based on a thorough analysis of the literature, the use of antidepressants for treating depression in the adolescent population is mostly safe and effective.

### **Applicability to Clinical Practice**

Given a significant number of children are negatively affected by depression, the safety and efficacy of depression treatment deserves investigation. As the prevalence of depression continues to grow in the adolescent population, it is the medical provider's responsibility to provide the safest and most effective care possible. The evidence-based research provides insight into the treatment of depression in adolescents and its associated risks.

Antidepressant use may be associated with an increased risk of suicidal behavior, especially in adolescents, and should be prescribed with caution. However, based on the current research, that risk is insignificant. Also, there is no clear evidence in the literature that the increase in youth suicide is related to dosing. According to the literature, there was a decrease in dosage and overall usage for antidepressants prescribed to adolescents after the release of the black-box warning by the FDA for suicidal thoughts and behavior (Cheung et al., 2008). Additionally, the study conducted by Cheung et al. (2008) concluded that there was an increase in suicide among adolescents after the release of the warning by the FDA.

Overall, the research confirms the importance of developing prevention and monitoring programs for adolescents who have depression, especially if they are being treated with an antidepressant. It can be determined that a systematic screening process prior to medication

administration is essential for prevention. A final conclusion taken from the review of literature is there is a need for further research to determine the cause or causes of the alarming increase in suicide rate among adolescents. Furthermore, once other possible causes are identified, a plan of prevention should be implemented to aide in decreasing youth suicide.

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