The Use of Medication in Treating Childhood and Adolescent Depression: Information for Patients and Families

Prepared by the American Psychiatric Association and the American Academy of Child and Adolescent Psychiatry in consultation with a National Coalition of Concerned Parents, Providers, and Professional Associations

This revision of the original 2005 Parents Medical Guide to the treatment of depression in children and adolescents is a joint project of the American Psychiatric Association and the American Academy of Child and Adolescent Psychiatry. It has been updated to include important research that has added to our knowledge about effective treatments for child and adolescent depression. Its goal is to help parents and families make informed decisions about getting the best care for a child with depression. For easy use, it is presented in Frequently Asked Questions (FAQ) format.

This updated version was developed by a workgroup of members selected by the American Psychiatric Association and the American Academy of Child and Adolescent Psychiatry. A list of workgroup members and their disclosures of any competing interests can be found at the end of the guide.

FAQ's

How can I advocate effectively for my child who has depression?
Where can I get additional information?
Members of the Parents Medical Guide Workgroup

What is major depression and how is it recognized in children?
Depression is a serious illness that can affect nearly every part of a young person's life and significantly impact his or her family. It can disrupt relationships among family members and friends, harm school performance and limit other educational opportunities. It can lead to other health problems through its effects on eating, sleeping, and physical activity. Because it has so many consequences, it is important that depression is recognized and treated successfully. When it is, most children can get back on track with their lives.

Major depression, or clinical depression, is a mood or "affective" disorder, a category of disorders that includes unipolar depressive disorder, dysthymia and bipolar disorder. Although depression can occur in young children, it is much more common in adolescents. Depression before puberty occurs equally in boys and girls. After puberty, depression is more common in girls.

Depression is not always easy to recognize in children. In children, symptoms of depression are often hidden by other behavioral and physical complaints—examples of which are listed below. Many young people who are depressed will also have a second psychiatric condition at the same time which can complicate diagnosis.

For a diagnosis of depression, at least five of the following symptoms must be present for a period of at least two weeks. These symptoms must also represent a change in behavior and interfere with the child's ability to function at school, at home, or with their friends.

Symptoms of Major Depressive Disorder in Adults	**Signs of Depression Frequently Seen in Youth**
Depressed mood most of the day	Irritable or cranky mood
Decreased interest/enjoyment in once-favorite activities	Boredom, loss of interest in sports, video games; giving up favorite activities
Significant weight loss/gain	Failure to gain weight as normally expected; overeating and weight gain especially in teens
Insomnia or hypersomnia	Changes in sleep patterns; delays in going to or falling asleep; refusal to wake for school; early morning awakening

Psychomotor agitation/retardation	Difficulty sitting still, pacing, or very slowed down with little spontaneous movement
Fatigue or loss of energy	Persistently tired, feels lazy
Low self-esteem; feelings of guilt	Self-critical; blaming oneself for things beyond one's control; "no one likes me, everyone hates me"; feels stupid
Decreased ability to concentrate; indecisive	Decline in performance in school due to decreased motivation and ability to concentrate; frequent absences
Recurrent suicidal ideation or behavior	Frequent thinking and talking about death; writing about death; giving away favorite toys or belongings

Other disorders that fall in the spectrum of mood disorders include dysthymia and bipolar disorder. Dysthymia is a disorder that usually has less severe symptoms than major depression, but it is more chronic and persistent. Instead of shifting into well-defined periods of depression, the child with dysthymia lives in an ongoing joyless and gray world.

Another mood disorder is bipolar disorder. It is very important to recognize and diagnose bipolar disorder because it may first appear as an episode of depression. In bipolar disorder, periods of depression may alternate with periods of mania. During these periods of mania the child will show unnaturally high levels of energy, and/or irritability. If there is a family history of bipolar disorder, it should be discussed with your child's physician as your child may require special treatment considerations. Some children and adolescents may develop mania without a family history of bipolar disorder.

Further information about bipolar disorder in children and adolescents is available on the American Academy of Child and Adolescent Psychiatry website:
http://www.aacap.org/cs/root/facts_for_families/bipolar_disorder_in_children_and_teens

What are the treatments for depression?

There are a number of different treatments for depression. These include various forms of psychotherapy, medication, working with the family or a combination of these.

Treatment can also include work with the child's school and/or having the child get involved with peer support or self-help groups.

Your child's physician should develop a comprehensive treatment plan that deals with your specific situation, your child's needs, and the recommended treatment approaches. Your physician should also fully discuss with you and your child the risks and benefits of the treatment plan.

Are antidepressant medications effective for the treatment of child/adolescent depression?

Yes, antidepressant medications can be effective in relieving the symptoms of depression for some children and adolescents. One antidepressant--fluoxetine, or Prozac–a medicine in the category of selective serotonin reuptake inhibitors, or SSRI's, has been approved by the FDA for treating depression in children 8 years of age and older. Escitalopram, or Lexapro has also been approved by the FDA for treating adolescents 12 years of age and older. Your physician may prescribe other antidepressant medications as well. You should know that prescribing an antidepressant that has not been approved by the FDA for use with child and adolescent patients (referred to as off-label use or prescribing) is common and consistent with general clinical practice. Atypical antipsychotics, however, are not approved by the FDA for the treatment of depression in children and adolescents and are not considered appropriate for first-line treatment. As generally used, tricyclic antidepressants (e.g. imipramine, amitriptyline) have not been shown to be effective for pediatric depression and they should not be used as the first treatment.

About 60 percent of children and adolescents will respond to initial treatment with medication. Of those who don't, a significant number will respond to another medication and/or to the addition of a form of psychotherapy called cognitive behavioral therapy (CBT).

An important study--the Treatment for Adolescents with Depression Study (TADS) funded by the National Institute of Mental Health (NIMH), and published in 2004 examined three different treatments for adolescents with moderate to severe depression.

• One treatment used the antidepressant medication fluoxetine, or Prozac.

• Another effective treatment used CBT. CBT helps a patient recognize and change negative patterns of thinking and behavior that are associated with depression.

• The third approach used a combination of medication and CBT.

Each of these treatments was compared to taking a placebo or sugar pill. After 12 weeks of treatment, 71 percent of the patients who received the combination of medication and CBT were much improved. This combined treatment was nearly twice as good in

relieving depression as taking a placebo. About 35% of people who took a placebo showed improvement and 43% of those who received psychotherapy improved. In those who received medication alone, 61% improved. Combined treatment also resulted in better functioning and quality of life. It is the preferred treatment for speedier responses across a broad range of outcomes such as remission and recovery of function. [1,2]

Although all three treatment approaches reduced the frequency of suicidal thinking and behavior, fluoxetine treatment alone was associated with increased suicidal thoughts and behavior when compared to treatment with placebo or psychotherapy alone. However, after three months of treatment, the number of young people experiencing such thoughts and behaviors dropped substantially. There were no completed suicides by any of the adolescents who received one of the three treatments.

This research shows that medication can be an important and valuable treatment for depression in children and adolescents. Importantly, combined treatment may also protect against suicidal thoughts and/or behaviors in patients taking an antidepressant. This effect, however, has not been shown in all the studies that have tested combination treatment against medication treatment alone. [3,4,5]

Are treatments other than medication available for children with depression?
Various forms of psychotherapy, including cognitive behavioral therapy (CBT) and interpersonal therapy (IPT) are helpful for treating mild to moderate forms of depression. CBT tries to help a patient recognize and change negative patterns of thinking and behavior that may contribute to depression. IPT guides the patient to problem solving approaches to damaged interpersonal relationships that can both cause and result from depression.

What is cognitive behavioral therapy (CBT)?
Depressed people think in ways that contribute to their depression and they avoid activities that could reduce their depression. This can make depressive symptoms worse. CBT tries to help patients recognize their negative thoughts and help them to participate in activities that can reduce their symptoms. CBT uses techniques such as problem solving, managing negative emotions, and improving social effectiveness.

CBT has been studied more with depressed adolescents than with depressed children. Several of these studies have shown that CBT is superior to some other forms of psychotherapy in relieving depression. One study that compared treatment with CBT and treatment with medication showed that while medication worked faster, by 16 weeks those treated with CBT were doing just as well as those treated with medication. Most studies have found that for more severe or ongoing depression, the combination of CBT and medication is the fastest and most effective approach.

CBT may be particularly helpful for depressed adolescents who have other psychiatric problems such as anxiety disorders. It may not work as well for those with a history of trauma or abuse. It also does not work as well if the child's parent is currently depressed,

unless that parent is also treated. Older adolescents seem to do better with a treatment approach that is based on the treatment of adults.

CBT has been used with younger children, but mostly to prevent depression or to treat children with milder symptoms. Because CBT is helpful for children with anxiety disorders, it may--with some modifications--also help younger children with depression.

CBT requires specific training. If a therapist presents him or herself as a CBT therapist, parents should ask what type of CBT training the therapist has had.

Will my child's depression pass without treatment?
If depression is untreated, it often lasts from six to nine months, an entire school year for most children. But, if it is not treated it can have serious consequences. It increases the risk for substance abuse, eating disorders, adolescent pregnancy, and suicidal thoughts and behaviors. Children are also likely to have ongoing problems in school, at home, and with their friends. Also, the child runs the risk of developing a chronic and more difficult-to-treat depression. Once a child or adolescent has one period of depression he or she is more likely to get depressed again. For further information, AACAP's Practice Parameters on Depression may be accessed at the website: http://www.aacap.org/galleries/PracticeParameters/Vol%2046%20Nov%202007.pdf

How long should my child continue taking antidepressant medication?
Even when a patient is in remission (having no or minimal depressive symptoms) the same treatment should be continued for another 6 to 9 months. This is to help prevent relapse. This recommendation is based on a National Institute of Mental Health sponsored study of depressed children and adolescents. Patients in this study who improved after 12 weeks of fluoxetine treatment and who continued their treatment relapsed less often than patients who were switched to placebo. (Forty-two percent of the fluoxetine treatment group had a return of depressive symptoms compared to 69% for the placebo group). [(6)] If depressed teens who improved with fluoxetine continued on a combination of fluoxetine plus CBT, even a higher proportion of them remained well compared to those who got fluoxetine alone. [(7)]

Because the risk of relapse remains high even with continued antidepressant treatment, it is very important for patients, families, and doctors to see if depressive symptoms begin again after remission, and to take appropriate steps if they do.

Some young people may need treatment for longer than 6-9 months. Youth who have a family history of mood disorders, severe and complex episodes of depression, a slow and difficult response to treatment, a history of chronic depression, and/or multiple depressive episodes may benefit from continuing treatment for 1-2 years or more. In one study, 38% of depressed adolescents who were in remission, but who continued to receive the SSRI sertraline (Zoloft), for an additional year remained well. None of the adolescents in remission who stopped the medication and received a placebo instead stayed well. [(8)] We don't know yet which patients are most likely to benefit from longer treatment. Your

child's doctor will work with you and your child to determine the best time to stop antidepressant treatment.

What can be done if my child does not improve with medication?
Most young people with depression (about 60 percent) will improve when treated with an SSRI antidepressant. But about 40% of them will not improve when first treated in this way.

The Treatment of SSRI-Resistant Depression in Adolescents (TORDIA) study examined other treatment options for adolescents who do not get better when first treated with an SSRI. Four different treatment groups were studied. One group received a SSRI that was different from the first one they tried, the second group received an antidepressant medication that was not an SSRI (venlafaxine-Effexor), the third group received the different SSRI combined with cognitive behavioral (CBT) therapy, and the fourth group, the non-SSRI medication and CBT. The teenagers who were switched to another medication combined with CBT psychotherapy showed the most improvement. The combined medication-CBT treatment was also more effective than medication-alone treatments. A switch to another SSRI was just as effective as a switch to venlafaxine, but with fewer side effects. [(9)]

These results are encouraging for adolescents who do not initially respond to treatment with an SSRI. Their symptoms may improve if they are switched to another SSRI combined with CBT. There may be less improvement if they are switched to just another antidepressant. Before trying a different treatment, though, it is important to give enough time to see if the initial treatment works, at least 6-8 weeks.

If there is not enough of a positive response to the first treatment, changing medication, adding psychotherapy, or combining both should be considered. For many adolescents, the best treatment will be a combination of individual psychotherapy and medication.

Further information on the Treatment of SSRI-resistant Depression in Adolescents is available on the NIMH website:
http://www.nimh.nih.gov/trials/practical/tordia/treatment-of-ssri-resistant-depression-in-adolescents-tordia.shtml

Do antidepressants increase the risk of suicide?
Suicidal thoughts and behaviors are more common during adolescence than at any other time, but suicide is more common among adults. In any year about 16 percent of high school students think about suicide and about 3-8 percent show suicidal behaviors. Fortunately, very few of them commit suicide. Children and adolescents with depression are much more likely to think about suicide and to attempt it than other children. Although not all suicidal children have depression, untreated depression increases the risk of suicide.

The Food and Drug Administration (FDA) described an increase in reports of suicidal thoughts and/or behaviors in children and adolescents taking antidepressants. But, there were no suicides in the cases they studied. Autopsies of teenagers who have committed suicide show that very few of them had traces of an antidepressant, making the link between antidepressant use and suicide even weaker.

Between 1992 and 2001, there was a large increase in the number of adolescents being prescribed SSRI antidepressants. But, during that time the rate of suicide among American youth ages 10–19 actually dropped by more than 25 percent. This was the first time in nearly 50 years that the suicide rate declined in young people.

What factors other than depression increase the risk of suicide in children and youth?

There are risk factors for suicide besides depression, although depression is the most common diagnosis in adolescents with completed suicide. Often, particularly in boys, completed suicide is associated with depression, conduct disorder, and substance abuse. Sometimes, boys who commit suicide have the latter two without a mood disorder. Anxiety disorders are also common in youth who commit suicide, but almost always in combination with a mood disorder. Depression alone is a bigger contributor to suicide in girls than in boys.

Youth who commit suicide often have difficulty managing their emotions and they commonly make impulsive and risky decisions. Other risk factors for completed suicide include having access to a gun in the house, having made a previous suicide attempt with high suicidal intent and having combinations of a mood disorder along with conduct disorder or substance abuse. (10)

Repeated suicide attempts increase the risk for a completed suicide. Parents should be very alert to repeated attempts. Suicide attempts that are discovered by accident are very serious. They suggest that the young person had a strong wish to die and timed their suicide attempt to decrease the chance of it being discovered.

Another group of teenagers who commit suicide appear to be hard working, careful, and popular. They may do well at their studies and in sports. Often, they appear to be perfectionists. Even though they perform well, they may become very anxious and pessimistic before taking a test or before important events. These young people may be

suffering from an undiagnosed anxiety disorder. They are afraid of doing badly and before a feared event they may go without sleep and seem very preoccupied. Because they seem to perform so well, their death by suicide is often deeply puzzling to their family, teachers, and friends.

Treatment for children and adolescents with depression must include frequent monitoring for suicidal thoughts or behavior, especially during the first 6 weeks of treatment, when suicidal events are most likely to occur. Any child or adolescent who admits to thoughts about suicide or who attempts suicide should receive a comprehensive psychiatric assessment, which should be included in an overall treatment plan. Parents should not be in the position of deciding whether their child's suicidal thoughts or actions pose an imminent danger.

The death of a child by suicide is always a tragedy, but it is important to remember that suicidal thoughts and actions lessen with appropriate treatment. Early recognition and access to effective treatment are essential keys to reducing suicide in children and youth. Since depression is often a major contributor to completed suicide, it is worth considering treating depression with antidepressant medication particularly if combined with cognitive behavioral therapy (CBT), since the combination treatment results in the fastest and most complete response.

Does talking about suicide increase the likelihood that a child will hurt him/herself?
Any expression of suicidal thoughts or feelings by a child or adolescent is a clear signal of distress and should be taken very seriously by health care professionals, parents, family members, teachers, and others.

When a young person talks about suicidal thoughts, there is an opportunity to discuss the need to take special precautions and/or protective measures. Any treatment approach that increases discussion of previously unspoken suicidal thoughts or impulses is helpful. It is much more worrisome and dangerous for a young person with depression to hide the fact that he or she is having suicidal thoughts. The data demonstrate that asking a youth about suicidal ideas does not increase the risk for suicide. Indeed, such questions can help identify adolescents at risk so that appropriate interventions can be implemented. (11)

How can I help monitor my child during treatment?
Since some children and teens may have physical and/or emotional reactions to antidepressants, parents should be attentive to signs of increased anxiety, agitation, panic, aggressiveness, or impulsivity. Your child may experience involuntary restlessness, or an unwarranted elation or energy accompanied by fast, driven speech and unrealistic plans or goals. These reactions are more common at the start of treatment, although they can occur at any point in treatment. If you see these symptoms, consult your doctor immediately. It may be necessary to adjust the dosage, change to a different medication, or to stop using medication.

In a small number of instances, a child or adolescent might have extreme reactions to antidepressants as a result of genetic, allergic, drug interactions, or other unknown factors. Whenever you observe any unexpected symptoms in your child, immediately

contact the child's doctor.

Some children and adolescents may experience weight gain while taking antidepressants and as a result, may want to stop taking their medication. If weight gain becomes a concern, it should be discussed with your child's doctor.

While regular doctor's appointments are important, the frequency of monitoring should be suited to the needs of the child and family. If you and your child's physician do not see evidence of improvement in your child's health within 6-8 weeks, your doctor should reevaluate the treatment plan and consider changes.

Since depression increases the risk for suicide, precautions for suicide prevention should be put in place if a child, or any family member, has depression.

• Lethal means of suicide, such as guns should be removed from the house, and large quantities of dangerous medications, including over-the-counter drugs, should not be left in an accessible location.

• Families should work in consultation with their child's physician or other mental health professional to develop an emergency action plan, called a "safety plan," that is a planned set of actions for you, your child, and your doctor to take if and when your child has increased suicidal thinking. This should include access to a 24-hour number available to deal with crises.

• If your child voices new or more frequent thoughts of wanting to die or to hurt him- or herself, or takes steps to do so, you should implement the safety plan, and contact your child's doctor immediately.

What is a black box warning?

A "black box warning" is a cautionary label placed on some medications. The Food and Drug Administration (FDA) uses it to alert prescribing doctors and patients that special care should be taken using a medication. Black box warnings may apply to patients with particular medical conditions, or to patients within a certain age range.

The FDA decided to attach such a "black box warning" to all antidepressant medications used to treat depression and other disorders such as anxiety and obsessive-compulsive disorder (OCD) in children and adolescents.

In 2007 this warning was extended to young adults 18-24 years of age. This label states that antidepressant medications are "associated with an increased risk of suicidal thinking and/or behavior in a small proportion of children and adolescents, especially during the early phases of treatment."

The FDA did not ban the use of antidepressant medications for youth. The purpose of the warning was to alert physicians and parents to watch children and adolescents to see if their symptoms got worse, or if they showed unusual changes in behavior. The FDA also specifically said that "depression and other serious mental illnesses are the most important causes of suicidal thoughts and actions".

Why did the FDA issue a black box warning?
In 2004, the FDA reviewed 23 clinical trials involving more than 4,300 child and adolescent patients. These patients received any of nine different antidepressant medications. No suicides occurred in any of these studies.

All of the studies the FDA reviewed measured suicidal thinking and behavior by using "Adverse Event Reports." These report the spontaneous sharing of thoughts about suicide or potentially dangerous behavior made by a patient (or reported by the patient's parent). Such "adverse events" were reported by approximately 4 percent of all children and adolescents taking medication, compared with 2 percent of those taking a placebo.

A more recent study found that the risk was even smaller—around 3% in those on medication and 2% in those on placebo. Most of these events were increases in suicidal thoughts. Only a few were actual suicide attempts, and NONE were suicide completions. [12)]

Through careful monitoring, the development of a safety plan, and the combination of medication with psychotherapy, the risks for increased suicidal thoughts can be managed. For moderate to severe depression, there is benefit in the use of medication because of a higher rate of relief, and more complete relief, from depressive symptoms than not using any medication.

Since the FDA issued the black box warning, there has been a decline in antidepressant use, but an increase in completed suicides in adolescents in both the US and the Netherlands. Although it is not yet clear how these trends may be related, this has been the first increase in the adolescent suicide rate reported in over a decade. [(13)]

Can my child continue taking prescribed antidepressant medication?
If your child is being treated with a medication and is doing well, he or she should continue with the treatment for at least 6-9 months under the guidance of the prescribing physician. Research suggests that any increased risk of suicidal thoughts or behaviors is most likely to occur during the first three months of treatment, with some studies showing that the risk is highest in the first 3-6 weeks. Teens especially should know about this possibility, and the patient, parents, and physician should discuss a safety plan – for example, whom the child should immediately contact – if thoughts of suicide occur.

No patient should abruptly stop taking antidepressant medications. Suddenly stopping

medication raises the possibility of negative withdrawal effects such as agitation or increased depression. If you are thinking of changing or stopping your child's antidepressant treatment you should always consult with your child's physician before taking such action.

How can I advocate effectively for my child who has depression?
You have the right to any and all information available about the nature of your child's illness, the treatment options, and the risks and benefits of treatment. Make sure your child receives a comprehensive evaluation. Ask lots of questions about the diagnosis and any proposed course of treatment. If you are not satisfied with the answers or the information you receive, it is perfectly acceptable to seek a second opinion. Help your child or teenager learn about depression, in an age-appropriate way, so he or she can be an active partner in treatment.

It is always important to discuss and develop a personalized treatment approach with your health care provider and to weigh and balance the various risks and benefits of treating your child for depression.

ENDORSERS:
American Academy of Child and Adolescent Psychiatry (www.aacap.org)
American Association of Suicidology (www.suicidology.org)
American Foundation for Suicide Prevention (www.afsp.org)
American Psychiatric Association (www.psych.org)
American Society for Adolescent Psychiatry (www.adolpsych.org)
Child and Adolescent Bipolar Foundation (www.cabf.org)
Depression and Bipolar Support Alliance (www.dbsalliance.org)
Families for Depression Awareness (www.familyaware.org)
National Alliance for the Mentally Ill (www.nami.org)
National Association of Psychiatric Health Systems (www.naphs.org)
Mental Health America (www.mentalhealthamerica.net)
Society for Adolescent Medicine (www.adolescenthealth.org)
Suicide Awareness Voices of Education (www.save.org)
Suicide Prevention Action Network (www.spanusa.org)

Where can I get further information?
You may want to visit the AACAP Resource Center on Depression website, http://www.aacap.org/cs/Depression.ResourceCenter and/or the National Institute of Mental Health website, http://www.nimh.nih.gov/index.shtml

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Disclaimers:
The information contained in this guide is not intended as, and is not, a substitute for professional medical advice. All decisions about clinical care should be made in consultation with a child's treating physician.

No pharmaceutical funding was used in the preparation and maintenance of this guide or the Web site ParentsMedGuide.org.

After reviewing the Medication Guide for Treating Depression, please help us better serve your needs and the needs of others by completing a brief opinion survey. Your feedback on the guide is essential for us to provide accurate and helpful information about child and adolescent depression. Click **HERE** to begin the survey. Thank you!

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APPENDIX
List of Disclosures