



Worldwide, an estimated one million people die by suicide each year.

Upwards of 20 million people attempt suicide. More than 90 percent of people who die by suicide had a diagnosable mental illness or substance abuse disorder.¹ Psychiatric disorders are a major underlying factor in suicide. Logically, effective treatments for these disorders will help to reduce the risk that suicide might occur. Physicians are on the front line of detecting psychiatric illnesses and helping people with treatment options.

As with all medications that work through the brain, antidepressants can cause uncomfortable and disruptive side effects, particularly early in treatment. Recent reports suggest that one such side effect is an increased risk of suicidality (thoughts about suicide and suicide-related behaviors) in some patients. This prompted the Food and Drug Administration (FDA) to issue a Black Box warning regarding a potential link between antidepressants and suicidality in 2004.² In the years since, some researchers have challenged the existence of such a link, causing widespread confusion among physicians regarding the potential risks of using antidepressants in their practices.

In this brief guide, we will examine myths about the relationship between anti-depressants and suicide and discuss the implications for physicians.

Myths About Antidepressants and Suicide

Myth:

The Black Box warning issued by the FDA indicates that antidepressants cause children, adolescents and young adults to become suicidal.

Fact:

The Black Box warning issued by the FDA reads, "Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders."²

IMPLICATIONS FOR PHYSICIANS

It appears that children, adolescents and young adults who are treated with antidepressants, especially early in treatment, might be more likely to think about suicide and perhaps exhibit behaviors consistent with the intention of suicide. For adolescents, the risk of suicidality doubled in those treated with antidepressants relative to placebo-treated controls (4 percent vs. 2 percent). Importantly, the research did not reveal an increase in suicides.

Myth:

The Black Box warning issued by the FDA regarding antidepressants and suicidal behaviors applies to all age groups.

Fact:

The FDA Black Box warning is specific only to children, adolescents, and young adults.²

IMPLICATIONS FOR PHYSICIANS

At present, data warrant concerns about increased suicidality during treatment with antidepressants in children, adolescents and young adults, but not the general adult population. However, suicidality should always be considered a possibility when treating with medications that influence brain function.

Myth:

The FDA warned that suicidal behaviors increased with antidepressant use in the elderly.

Fact:

Exactly the opposite. FDA labeling suggests that adults ages 65 and older taking antidepressants might exhibit a decreased risk of suicidality.²

IMPLICATIONS FOR PHYSICIANS

For unclear reasons, it appears that elderly patients are more likely to experience decreased suicidality during treatment.

Myth:

All antidepressant medications are approved for use in children and adolescents.

Fact:

Fluoxetine (Prozac[®]) and escitalopram (Lexapro[®]) are the only medications approved for use in children and adolescents for the treatment of major depressive disorder.³

IMPLICATIONS FOR PHYSICIANS

The fact that fluoxetine and escitalopram are the only drugs approved for use in children and adolescents does not necessarily mean that they are the most effective or the safest. Such information should be weighed carefully before prescribing antidepressants to young people. Most of the practice parameters reference fluoxetine as the first-line medication for adolescent depression.⁴ Escitalopram will probably be added to the guidelines.

Myth:

Antidepressants are the only medication class associated with suicidal thoughts and behaviors in patients.

Fact:

A long list of medications, including montelukast (Singulair[®]), isotretinoin (Accutane[®]), zolpidem (Ambien[®]/Ambien CR[®]), mefloquine (Lariam[®]), varenicline (Chantix[®]), atomoxetine (Strattera[®]), antiepileptic medications and even the antiviral oseltamivir (Tamiflu[®]) have been associated with increased risk of suicidal behavior or ideation in clinical reports and randomized clinical studies.⁵

IMPLICATIONS FOR PHYSICIANS

A wide range of prescription medications influence thoughts, mood and behavior. For unclear reasons, in some patients these influences manifest in increased suicidal thoughts and behaviors. Patients should be monitored accordingly.

Physicians can help patients understand that treating conditions such as depression requires time, patience, and more than one medication might need to be tried to find the appropriate match.

Myth:

Antipsychotics like clozapine (Clozaril), risperidone (Risperdal), olanzapine (Zyprexa), quetiapine fumarate (Seroquel), aripiprazole (Abilify) and ziprasidone (Geodon) are all safe alternatives to traditional antidepressants for children and adolescents.

Fact:

Used primarily for schizophrenia and bipolar disorder in adults (only risperidone and aripiprazole have FDA approved indications for patients below age 18), these medications are sometimes given off-label for suspected depression and behavioral disorders in children and adolescents. No substantive research supports their use for depression in adolescents.⁶

IMPLICATIONS FOR PHYSICIANS

The lack of data regarding the effectiveness of antipsychotics for depression and their poor safety profile (including weight gain, lethargy, problems concentrating, immune dysfunction, facial tics and even depression) makes them poor choices for depression in young people.⁶ Their influence on suicidality and suicide are not known, though they can decrease the risk of suicide in adults with schizophrenia and bipolar disorder.



Practical steps to improving clinical outcomes

Clinical depression is one of the major risk factors for suicide. Treating conditions such as depression in practice requires time, patience, and often a lot of trial and error. Recent evidence that antidepressants can increase the risk of suicidal thoughts and behaviors in some patients, particularly adolescents, makes prescribing decisions more complicated. Here are some steps that can help doctors minimize the risk of suicide when treating patients for depression.

1. Patients being treated with antidepressants (or the parent if a patient is a child or adolescent) should be instructed to call if they experience (or observe) any of the following symptoms – particularly if they are new or worse than before filling the prescription.⁷
 - Thoughts about suicide or dying
 - Attempts to commit suicide
 - New or worse depression
 - New or worse anxiety
 - Feeling very agitated or restless
 - Panic attacks
 - Insomnia
 - New or worse irritability
 - Acting aggressive, being angry, or violent
 - Acting on dangerous impulses
 - An extreme increase in activity and talking (mania)
 - Other unusual changes in behavior or mood
2. Doctors should be aware that most antidepressants are ineffective as short-term (weeks rather than months) treatments for depression and that several months are required for clinical improvements in most cases. Barring troublesome side effects, patients should be urged to commit to at least an eight week course, on par with most clinical trials. Patience is needed here, as more than one medication might need to be tried before a suitable match is found.
3. Ensure that an antidepressant is appropriate. Antidepressants can be effective in cases of clinical (diagnosable) depression. However, of the nearly 10 percent of Americans taking prescription antidepressants, estimates suggest perhaps 40 percent do not suffer from clinical depression.⁸ Such off-label use is increasingly common. However, antidepressants should not be used as a quick response to signs of distress and they do not provide immediate relief for significant anxiety or acute episodes of depression. For some patients, lifestyle changes, counseling or investigation into underlying medical conditions might be recommended instead, or in addition. The risk of side effects is the same regardless of whether the antidepressants are being prescribed for an approved indication or an off-label use. Given the risk of suicidality alone, always ensure the potential benefits are carefully weighed against the potential risk of their use.
4. It is important to recognize that antidepressants affect adolescents and adults differently. Recent trials assessing the effectiveness of antidepressants for adolescent depression have revealed mixed results.⁹ Only fluoxetine and escitalopram are approved by the FDA for use in adolescent depression. Care should be exercised in decisions regarding antidepressants for those 18 and under.¹⁰⁻¹²

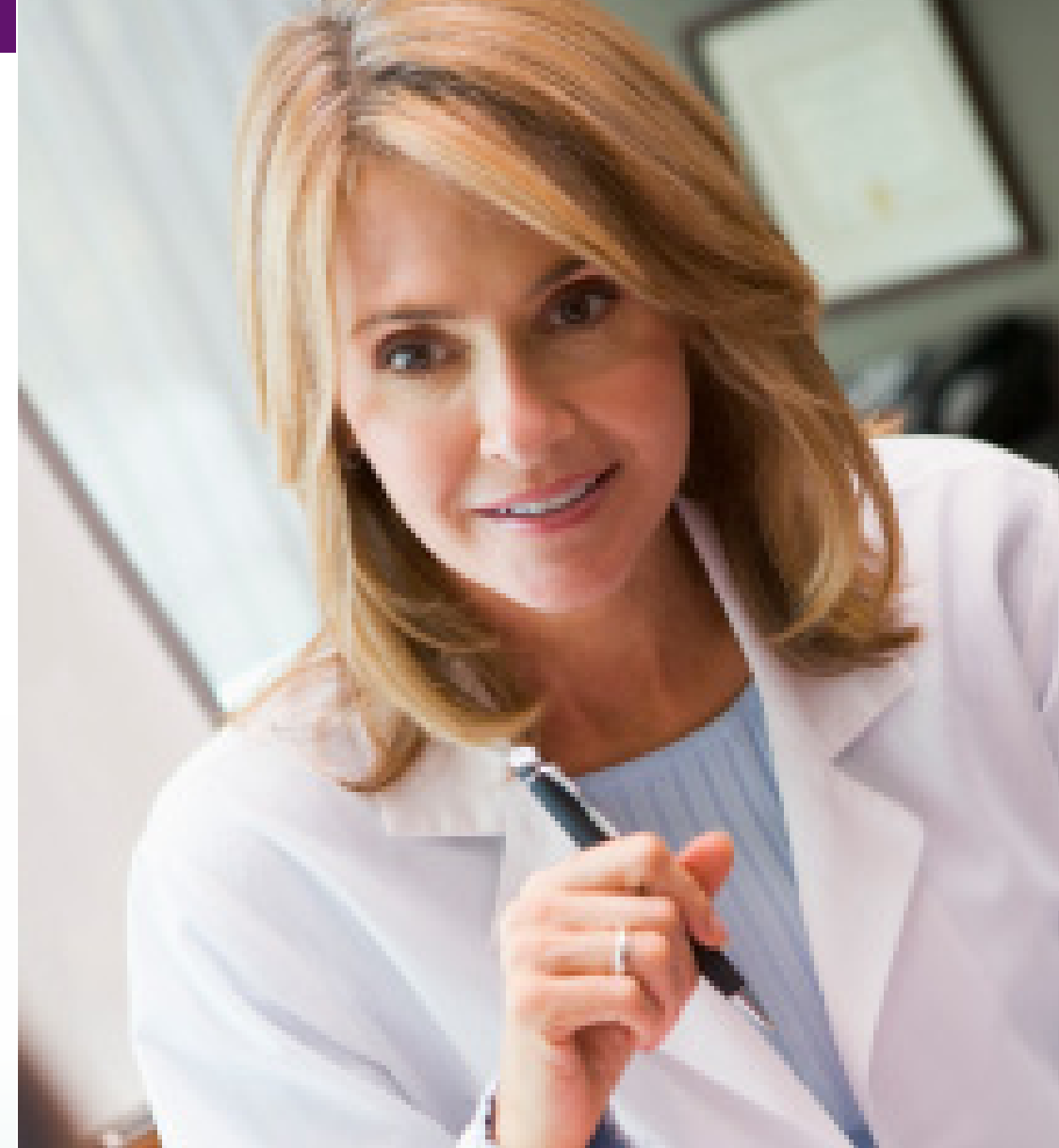
5. When dealing with adolescents, depression is difficult to assess even with standardized measurements. Decisions about antidepressants should be made carefully. Patients and their parents should be encouraged to educate themselves about the medications. As with adults, lifestyle changes (increased exercise, improved diet and sleep), treating underlying medical conditions and psychotherapy are often effective as primary approaches.
6. Often depression is related to conditions like fibromyalgia, hypothyroidism, HIV and Lyme disease. These conditions are also associated with increased risk of suicide. An estimated 15 percent of MS sufferers die by suicide.¹³ Antidepressants should not be relied on as the only treatment for these conditions, but are often useful in treating clinical depression associated with them.
7. Be aware that an estimated 20 percent of patients prescribed antidepressants will experience significant psychological (e.g., anxiety, restlessness, delusions) and neurological (e.g., vertigo, “brain zaps”) symptoms if they stop taking the medication abruptly.¹⁴ Physicians should instruct patients not to stop the medication abruptly and to work with the physician to develop a tapering schedule at the appropriate time. The relationship between suicidality and the discontinuation syndrome associated with antidepressants is unclear. Patients should be instructed to call if any of the symptoms listed in step #1 emerge when discontinuing an antidepressant.
8. If concerned about a patient’s risk for suicide, physicians should reach out to the patient’s emergency contact or a close family member to stay with the patient until the crisis is over. If the patient’s life is in imminent danger, have them escorted to the nearest emergency department by a family member or emergency services. Call 911 if there is an immediate need for crisis intervention or involuntary evaluation.

This information is provided by the National Alliance on Mental Illness (NAMI) - Florida and the Florida Psychiatric Society. NAMI-Florida and FPS thank Daniel Castellanos, MD of Florida International University, Abbey Strauss, MD of Boca Raton, FL, Rajiv Tandon, MD of University of Florida, and Wayne Goodman, MD and Jane Pearson, PhD of NIMH for their input into the development of this material. The development was funded in part by a grant through the Statewide Office of Suicide Prevention, Executive Office of the Governor from Noven Therapeutics, LLC, which had no control over its content. Printing and distribution of the information was funded in part by grants from the Eli Lilly Company and the Bristol-Myers Squibb Company.

References

Facts referenced were correct as of June 1, 2009 and web sites referenced.

1. NIMH. The Numbers Count: Mental Disorders in America. 2008. www.nimh.nih.gov/health/publications/the-numbers-count-mental-disorders-in-america/index.shtml#Suicide
2. FDA. Antidepressant use in children, adolescents, and adults. www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm096321.htm
3. FDA. Highlights of Prescribing. www.accessdata.fda.gov/drugsatfda_docs/label/2009/021323s030s031_021365s021s022tbl.pdf
4. USF FMHI Med Guidelines. <http://fmedicaidbh.fmhi.usf.edu/>
5. FDA. Public health advisory: Important information on Chantix (varenicline). www.fda.gov/oc/drug/advisory/varenicline.htm
6. Elias M. Adult antipsychotics can worsen troubles. USA Today, May 2, 2006. www.usatoday.com/news/health/2006-05-01-adult-antipsychotics-kids_x.htm
7. FDA. Medication guide - Antidepressant medicines, depression and other serious mental illnesses, and suicidal thoughts or actions. www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/ucm100211.pdf
8. Barber C. The medicated Americans: Antidepressant prescriptions on the rise. Scientific American. February, 2008. www.sciam.com/article.cfm?id=the-medicated-americans
9. Antidepressant medications in children and adolescents. Therapeutics Letter. April/May/June 2004. www.ti.ubc.ca/PDF/52.pdf
10. Jureidini JN et al. Efficacy and safety of antidepressants for children and adolescents. BMJ. 2004; 328:879-883. (Abstract available online at www.ncbi.nlm.nih.gov/sites/entrez?term=Jureidini&search=Find%20Articles&db=pmc&cmd=search)
11. Bailey D. Benefits and risks of using antidepressants in children and adolescents. Expert Opin Drug Saf, 2008; 7(1):9-27. (Abstract available online at www.informapharmascience.com/doi/abs/10.1517/14740338.7.1.9?journalCode=eds)
12. Papanikolaou K, Richardson C, Pehlivanidis A, Papadopoulou-Daifoti Z. Efficacy of antidepressants in child and adolescent depression: a meta-analytic study. J Neural Transm, 2006; 113(3):399-415. (Abstract available online at www.ncbi.nlm.nih.gov/pubmed/16075184)
13. Feinstein A. Multiple sclerosis, depression, and suicide. BMJ 1997;315:691-692. (Abstract available online at www.bmj.com/cgi/content/extract/315/7110/691)
14. Warner CH, Bobo W, Warner C, Reid S, Rachal J. Antidepressant discontinuation syndrome. American Family Physician. 2006;74(3):449-56. (Abstract available online at www.ncbi.nlm.nih.gov/pubmed/16913164)



What physicians need to know about
depression, medications
and suicide

