

# Questions and Answers about the NIMH Treatment for Adolescents with Depression Study (TADS)

## 1. Q. What is TADS and why is it important?

The Treatment for Adolescents with Depression Study (TADS) is a multi-site clinical research study examining the short- and long-term effectiveness of an antidepressant medication and psychotherapy alone and in combination for treating depression in adolescents ages 12 to 17. Thirteen academic and community clinics across the country were involved in the \$17 million trial.

TADS is important because major depression is one of the most common disorders of adolescence and occurs in both girls and boys. Experts estimate that in the United States, about 5 percent—or one in 20 teens—have moderate to severe major depression. This means that in a high school of 1,000 adolescents, 50 are likely to have major depression on any given day.<sup>1</sup> Adolescents with major depression suffer greatly and have difficulty with peer relationships and in school. The illness also imposes a significant burden on the teen's family. Many, but not all, adolescents with depression have suicidal thoughts. Without effective treatment, some may die by suicide.

The [initial findings](#) published in the August 18, 2004, issue of the *Journal of the American Medical Association (JAMA)*, provide data from the first 12-week treatment period. The 36-week results were published in the *Archives of General Psychiatry* in October 2007.

## 2. Q. Who participated in TADS?

A. TADS included 439 participants ages 12 to 17 from various geographic regions in the United States who were diagnosed with major depression. Recruitment for the trial began in Spring 2000 and ended in Summer 2003.

## 3. Q. What treatments were used in TADS?

A. For the first 12 weeks of their study participation (Stage 1), participants were randomly assigned to receive one of four treatments

- Fluoxetine (Prozac) alone
- Placebo (sugar pill) alone, with clinical management
- Cognitive-behavior therapy (CBT) (talk therapy) alone
- Combination of fluoxetine and CBT

At the end of the first 12 weeks, participants taking pills were informed if they were taking placebo or the active medication fluoxetine. Those taking the placebo who were not improved could choose to receive any one of the other three treatments in the study—fluoxetine alone, CBT alone, or

combination therapy. Participants who did improve while taking placebo were followed by the researchers for up to 12 weeks and offered active treatment if their depression worsened during that time.

Participants in any of the three active treatment groups (fluoxetine, CBT, or the combination treatment) who improved during the first 12 weeks continued with their assigned treatments for six more weeks (Stage 2). Participants who continued to do well in Stage 2 progressed to Stage 3, which lasted another 18 weeks for a total of 36 weeks of study participation.

Fluoxetine is the only antidepressant medication approved by the U.S. Food and Drug Administration (FDA) for use in treating adolescents with depression.

CBT is a talk therapy that teaches a person how to better cope with the challenges of depression and life in general. Specifically, a therapist may educate his or her patient about depression, the possible causes of it and how to manage it. He or she may also help the patient set realistic and positive personal goals, encourage participation in pleasant activities, learn to solve social problems, discourage negative thinking, learn how to negotiate and compromise when conflicts arise, and foster assertiveness.

#### **4. Q. What were the results of the study?**

A. After the first 12 weeks, 71 percent of participants receiving the combination treatment were much or very much improved. Among those receiving fluoxetine alone, 61 percent improved, and among those receiving CBT alone, 44 percent improved. Among those receiving a placebo, 35 percent improved.

Results remained consistent at the end of 18 weeks and 36 weeks. At 18 weeks, combination treatment still outpaced the other treatments with an 85 percent response rate, compared to 69 percent for fluoxetine alone and 65 percent for CBT alone.

By 36 weeks, the response rate to combination treatment still remained the highest (86 percent), while response rates to fluoxetine and CBT essentially caught up, at 81 percent each.

It is important to note that suicidal thinking decreased substantially in all active treatment groups. However, during treatment, those taking fluoxetine alone had higher rates of new and alarming suicidal thinking or behavior (15 percent) than those in combination treatment (8 percent) and those in CBT alone (6 percent), particularly in the early stages of treatment. There were no suicides in the TADS study.

#### **5. Q. What do the results of the study mean for children who have depression?**

A. The results suggest that combination treatment is the safest and most effective treatment overall for adolescents with depression. Fluoxetine alone or in combination with CBT accelerates recovery from major depression compared to CBT alone. Although the response rate of CBT alone “catches

up” to the response rate of fluoxetine alone several weeks later and to the combination therapy several months later, those few months in the life of an adolescent with depression can seem like a very long time. Further, adding CBT also appears to lessen the risk of suicidal thinking and behavior in patients given fluoxetine, and helps them develop new skills to contend with difficult, negative emotions.

However, every child or adolescent is different, and no one-size-fits-all treatment approach exists. Decisions about treatment for adolescents with depression must be made on a case-by-case basis. Before starting treatment, each child should be carefully and thoroughly evaluated by a doctor to determine if medication is appropriate. Those who are prescribed an antidepressant should be monitored regularly and frequently by a health care professional, especially during the first few weeks.

For more information about treating depression in adolescents, visit the NIMH [Depression in Children and Adolescents Web page](#).

## **6. Q. What happened after the initial 36-week treatment period?**

A. Following the end of the treatment period, the TADS team recommended ways in which participants could maintain treatment on their own, depending on the specific needs of the individual. Recommendations included continuing to take medication and see the doctor periodically, or continuing to work with a therapist and apply the behavioral techniques learned in CBT. Participants then were asked to return for an assessment every three months, for one year. At these visits, participants were interviewed about their symptoms and administered questionnaires similar to those used at the beginning of the study. In addition, the TADS doctors met with the family when needed or requested during that year to discuss recommendations for treatment options available in the community. Results of this year-long follow-up period will be available in the future.

## **7. Q. Can results of TADS be generalized to the general population?**

A. Because the trial sample included a mix of younger and older teens; both genders; and ethnic, racial, and socioeconomic diversity, the TADS results can be applied broadly to the adolescent population.

## **8. Q. Who sponsored TADS?**

A. TADS was sponsored by the National Institute of Mental Health and coordinated by the Department of Psychiatry and the Duke Clinical Research Institute at Duke University Medical Center. The principal investigator for the study was John March, M.D., MPH. The principal statistician was Susan Silva, Ph.D., also of Duke University.

Eli Lilly and Company provided the fluoxetine and matching placebo to Duke University under an independent educational grant. Eli Lilly had no role in the design or implementation of the study, analysis of the data, or writing of the manuscripts.

TADS was monitored for safety by the NIMH Data Safety and Monitoring Board.

## **9. Q. Are there additional studies on treating depression in adolescents?**

A. NIMH has funded other studies involving adolescents with depression, including the [Treatment of Resistant Depression in Adolescents \(TORDIA\)](#) study and the [Treatment of Adolescent Suicide Attempters \(TASA\)](#) study. Results for these trials are pending. NIMH has also funded the [Antidepressant Safety in Kids \(ASK\)](#) study, in which short and long-term risks of antidepressant use among children and adolescents will be assessed. For a complete list of all NIMH clinical trials, visit the [Clinical Trials page](#) on the NIMH Web site or [ClinicalTrials.gov](#).

## **10. Q. How can I obtain access to the TADS protocols, manual and data set?**

A. The TADS materials are available on the [TADS Web site](#)  
<https://trialweb.dcri.duke.edu/tads/index.html>

For a complete listing of TADS publications, see the [ClinicalTrials.gov TADS record](#).

## **Reference**

1. Essau C, Dobson K. Epidemiology of depressive disorders. In: Essau C, Petermann F, eds. *Depressive Disorders in Children and Adolescents: Epidemiology, Course and Treatment*. Northvale, NJ: Jason Aronson Inc; 1999:69-103.

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