

The Treatment for Adolescents with Depression Study Team. (2003). Treatment for Adolescents with Depression Study (TADS): Rationale, design, and methods. *Journal of the American Academy of Child and Adolescent Psychiatry*, 42(5), 531-542.

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Funded by the National Institute of Mental Health, the Treatment for Adolescents with Depression Study (TADS) is a multicenter, randomized, masked effectiveness trial designed to test the hypothesis that a combined treatment of cognitive-behavioral therapy (CBT) with the selective serotonin reuptake inhibitor (SSRI) fluoxetine (FLX), is superior to either psychotherapy or pharmacological therapy alone, in the treatment of Major Depressive Disorder (MDD) in adolescents (see text box). In this article, the TADS team outlines the design, rationale, and methodology of the trial.

A volunteer clinical sample of 432 youth ages 12-17 will be recruited from site clinics, primary care physicians, mental health providers, schools, juvenile justice facilities, and local media (this stage is expected to conclude by spring, 2003). In order to be eligible for the study, teens must have a DSM-IV diagnosis of MDD, and be antidepressant-free before the start of the study. Teens having other disorders (i.e., bipolar disorder, severe conduct disorder, pervasive developmental disorder, thought disorder, and substance abuse) are ineligible for the study because treatment may require additional or different interventions. Potential candidates for the study who decline to participate or who do not meet eligibility requirements will be offered clinically appropriate treatments outside the study.

Primary outcome measures include the Children's Depression Rating Scale-Revised, and the Clinical Global Impressions-Improvement scale. An independent evaluator will collect primary outcome data at baseline, 6, 12, 18, 24, 30, and 36 weeks. Quality assurance will include: (a) centralized training by the NIMH; (b) a "train the trainers" model whereby site managers monitor local fidelity; (c) mechanisms to provide prompt feedback; (d) teleconferencing; and (e) the extensive use of manuals (11 total). Procedures are also in place to meet clinical emergencies or contingencies that may arise during the course of the trial.

Selected teens will be randomized to receive, on an outpatient basis, one of the following four treatment options: (a) FLX, (b) CBT, (c) FLX and CBT combined (COMB), or (d) placebo (PBO). Stage I (acute) lasts for 12 weeks. During this stage, teens in the FLX group will receive a flexible-dosing schedule devised to achieve normalization (10-40 mg. maximum). Teens in the PBO group will be advised of their medication status at the end of Stage I, and appropriate follow-up efforts will be made, depending upon the teen's response to PBO. Teens receiving CBT will attend required skillbuilding sessions and optional sessions will also be available; this CBT intervention is modified to treat MDD, and includes parent and family sessions. During the first half of Stage I, the CBT intervention includes services such as education about depression and the TADS CBT approach (i.e., psychoeducation), goal setting, mood-monitoring and cognitive restructuring; the latter six weeks focus on issues chosen by the therapist, teen, and parents to meet needs specific to

Specific Aims of TADS

1. To compare the effectiveness of: (a) fluoxetine (FLX); (b) cognitive-behavioral therapy (CBT); (c) a combination of FLX and CBT (COMB), and; (d) placebo (PBO) for reducing Major Depressive Disorder (MDD) symptoms and patient disability over a period of 12 weeks.
2. To compare the effectiveness of the three active treatments (FLX, CBT, and COMB) over nine months of treatment.
3. To compare the acute time-action profiles (speed of response) of FLX, CBT, and COMB.
4. To compare recurrence rates, MDD-associated impairment, and use of mental health/medical services for FLX, CBT, and COMB during long-term maintenance treatment and during open follow-up.
5. To explore predictors of response to treatment, including, among others, characteristics of MDD at baseline, comorbid internalizing and externalizing symptoms, treatment expectations, and family psychopathology and functioning.
6. To examine the acceptability and cost-effectiveness of FLX, CBT, and COMB for the treatment of MDD in adolescents.

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the child and his or her family. Teens in the COMB group will receive both FLX and CBT and, “to allow for limited integration between medication management and CBT in Stages I and II” (p. 538), CBT and medication management will be functionally independent of each other. However, in cases where the teen does not respond as well as expected to the COMB treatment, the FLX clinician and CBT therapist will then consult with each other to evaluate the teen’s overall progress and jointly decide whether changes to the FLX dosing strategy are required.

Stage II (graduated maintenance) lasts for six weeks, and teens continue to receive treatment by the same clinician and/or therapist they saw during Stage I. Depending upon how well teens respond to the intervention, treatments may be leveled or increased. For example, teens who respond well to CBT will be given bi-weekly follow-up visits that are 30-50 minutes long, whereas those who respond only partially will have weekly, 50-60 minute visits. At this stage, teens receiving fluoxetine may have their medication increased to a maximum of 60 mg. Next, Stage III (consolidation) continues for 18 weeks. During this period, no downward adjustments of medication are made (unless there are medically adverse effects), and no new concepts are introduced into the CBT program. Stage IV includes open follow-up for 52 weeks. All teens receive follow-up assessments, including those in the PBO group.

According to the TADS research group, this study represents “the best compromise between the dictates of the RFP, ethical considerations, scientific rigor and credibility, stakeholder concerns, feasibility of implementation, and cost” (p. 535); they expect to publish their results at the conclusion of each stage. While this may be the case, there are several things that are important to note. First, in this traditional randomized design, families are provided no choice of treatment. This is inconsistent with the values expressed in the recently released President’s New Freedom Commission report, which calls for mental health care that “is consumer and family driven.” Given that “choice” alone has been found to be an evidence-based process, it also removes this possible contributor to success.

Second, although there is some flexibility in the CBT intervention, this is basically a study using highly standardized interventions. This is the case despite the fact that the authors report that both interventions – medication and CBT – alone are effective for 60% of the youth served with about half of those relapsing within a year. Given this limited success rate, one would anticipate potentially incorporating a more comprehensive, individualized intervention as part of the study rather than simply combining two highly standardized interventions, each of which has been found to have limited success over a one year period. Within an individualized intervention, medication or CBT could certainly be used if indicated and selected by the adolescent, parents, and treatment team. The traditional approach taken in this study is again inconsistent with the recommendations of the President’s Commission, which calls for “a personalized, highly individualized health management program.” This is particularly important given the high rate of co-occurring problems associated with depression. Nor is there any mention of building on strengths or tailoring interventions to meet the needs of diverse racial or ethnic groups.

In summary, this is a large and important study of a significant mental disorder affecting many adolescents. It has a strong research design from the perspective of internal validity but unfortunately fails to be consistent with recommendations from the President’s Commis-