

## Should we use SSRIs to treat adolescents with depression?

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### Evidence-based answer

Yes. Based on current evidence, fluoxetine is the most effective selective serotonin reuptake inhibitor (SSRI) for treatment of major depressive disorder in adolescents. It is the only agent approved by the US Food and Drug Administration (FDA) for use in children (strength of

recommendation [SOR]: **A**, based on meta-analysis of RCTs).

All SSRI medications increase the risk of suicidal behavior in adolescents, but do not increase the risk of completing suicide (SOR: **A**, based on meta-analysis of RCTs).

### Clinical commentary

#### First, we must spot those at risk

Family physicians are often the primary providers of healthcare for adolescents. Most health issues affecting this unique population are social and behavioral in origin. By routinely incorporating prevention and screening techniques into the adolescent visit, we can detect at-risk individuals. We need to inquire about sleep, personal interests, eating behaviors, future plans, friends and social activities, school performance, mood, and drug and alcohol use so that we can

detect early symptoms of depression.

For those family physicians who like reminders, there are mnemonics and questionnaires that evaluate the social and behavioral aspects of the adolescent visit. Family physicians should also educate parents and family members about depressive signs and symptoms and the potential warning signs of suicidality.

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### FAST TRACK

**A combination of fluoxetine and cognitive therapy was better than either alone for treatment of adolescent depression**

### Evidence summary

Major depressive disorder is common among adolescents and is associated with significant morbidity, including substance abuse and eating disorders. One study of survey data from 1769 adolescents found a lifetime prevalence of 15.3% for major depression. The majority of those reporting episodes of major depression in this study had recurrent symptoms and impairment in work or school.<sup>1</sup>

### Fluoxetine and therapy together have the best results

A large, multicenter, randomized controlled trial evaluated the effectiveness of fluoxetine (Prozac), cognitive behavioral therapy (CBT), or the combination of the 2. Researchers evaluated improvement with the Children's Depression Rating Scale-Revised (CDRS-R). The CDRS-R uses adolescent and parent interviews to rate 17 symptom areas: impaired schoolwork, difficulty

**FAST TRACK****AACAP concluded that fluoxetine is effective for the treatment of depression in children and adolescents**

having fun, social withdrawal, appetite disturbance, sleep disturbance, excessive fatigue, physical complaints, irritability, excessive guilt, low self-esteem, depressed feelings, morbid ideas, suicidal ideas, excessive weeping, depressed facial affect, listless speech, and hypoactivity. Combination treatment with fluoxetine and CBT was statistically superior to placebo, CBT alone, or fluoxetine alone. In addition, fluoxetine alone was superior to CBT alone.<sup>2</sup>

A meta-analysis including both published and unpublished trials of SSRI medications found that fluoxetine was more likely than placebo to cause remission of symptoms after 7 to 8 weeks of treatment (number needed to treat [NNT]=6). Fluoxetine treatment was also associated with a reduction in symptom scores as measured with the CDRS-R (NNT=5).<sup>3</sup>

Data were conflicting for the efficacy of paroxetine (Paxil), sertraline (Zoloft), and citalopram (Celexa).<sup>3,4</sup> No data were available for escitalopram (Lexapro).

**But are SSRIs safe for adolescents?**

Considerable controversy surrounds the safety of SSRIs in children due to reports of increased suicidal behavior. In 2004, the FDA conducted a meta-analysis of the suicide related adverse events from the published and unpublished trials of SSRIs including fluoxetine, sertraline, paroxetine, fluvoxamine (Luvox), and citalopram. A team of experts reviewed the adverse events from each trial to evaluate for suicidality including suicidal ideation, preparatory acts, self-injurious behavior, or suicide attempts. They found a risk ratio of 1.66 (95% confidence interval, 1.02–2.68) for suicidality in the treatment arms compared with placebo. There were no completed suicides in any study.<sup>5</sup>

This review led to the FDA's October 2004 "black box" warning regarding suicidality and antidepressant medication in adolescents. However, an ecological analysis of prescription data and US Census data found an overall decline in suicide rates as the rate of prescriptions for SSRI medications increased, suggesting a beneficial correlation of SSRI medications on suicide rates.<sup>6</sup>

**Recommendations from others**

The American Academy of Child and Adolescent Psychiatry (AACAP) recommends psychosocial and pharmacologic intervention for depression, with psychotherapy as the preferred initial treatment for most adolescent patients.<sup>4</sup> This organization reviewed the current published and unpublished data including the FDA analysis to formulate its conclusions regarding safety and efficacy. AACAP concluded that fluoxetine is effective for the treatment of depression in children and adolescents. ■

**References**

1. Kessler R, Walters E. Epidemiology of DSM-III-R major depression and minor depression among adolescents and young adults in the National Comorbidity Survey. *Depression Anxiety* 1998; 7:3–14.
2. March J, Silva S, Petrycki S, et al. Treatment for Adolescent Depression Study Team. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents with Depression Study (TADS) randomized controlled trial. *JAMA* 2004; 292:807–820.
3. Whittington CJ, Kendall T, Fonagy P, Cottrell D, Cotgrove A, Boddington E. Selective serotonin reuptake inhibitors in childhood depression: systematic review of published versus unpublished data. *Lancet* 2004; 363:1341–1345.
4. Report 10 of the Council on Scientific Affairs. *Safety and Efficacy of Selective Serotonin Reuptake Inhibitors (SSRIs) in Children and Adolescents*. Available at: [www.aacap.org/galleries/Psychiatric-Medication/CSA\\_Report\\_10\\_final.pdf](http://www.aacap.org/galleries/Psychiatric-Medication/CSA_Report_10_final.pdf). Accessed August 6, 2007
5. Hammad TA, Laughren T, Racoosin J. Suicidality in pediatric patients treated with antidepressant drugs. *Arch Gen Psychiatry* 2006; 63:332–339.
6. Olfson M, Shaffer D, Marcus SC, Greenberg T. Relationship between antidepressant medication treatment and suicide in adolescents. *Arch Gen Psychiatry* 2003; 60:978–982.