

1. Ottawa Citizen (April 9, 2004)  
'No evidence' popular antidepressants help children  
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Study slams anti-depressant research  
Report finds 'disturbing shortcomings' in earlier trials on drugs for kids  
By ROD MICKLEBURGH

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Ottawa Citizen (April 9, 2004)  
'No evidence' popular antidepressants help children  
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The benefits of antidepressants prescribed to thousands of Canadian toddlers, children and teens have been exaggerated and the risks downplayed, according to a disturbing new report that's raising concerns about the drugs' potential for harm.

And the researchers who wrote it conclude there is no evidence to justify prescribing these drugs to children.

The Australian team reviewed six published studies of Prozac, Paxil and Zoloft -- drugs known as SSRIs, or selective serotonin reuptake inhibitors -- as well as Effexor.

According to the study, published in today's edition of the British Medical Journal:

- Children who took a placebo showed strong improvement and those who took the real drugs didn't do significantly better. Two small studies found no advantage for the antidepressants over the placebo.

- In one study, 11 of 93 adolescents taking Paxil had a serious adverse event, compared to two of 87 children taking a placebo. The Australian team says that, despite this striking difference, the study's authors concluded Paxil was "generally well tolerated."

The authors also said most side effects were not serious, even though seven of the youth on Paxil had to be admitted to hospital during treatment. Five were admitted with side effects that have been linked with SSRIs, including suicidal thinking. But "only one serious event (headache) was judged by the treating investigator to be related to paroxetine (Paxil) treatment."

- Drug companies paid for the trials and "otherwise remunerated" the authors of at least three of the four bigger studies. Two of the authors of one study testing Paxil in teens were employees of GlaxoSmithKline, which makes the drug. In another study of the Pfizer drug Zoloft, Pfizer paid all the authors, and the study supervisor held stock options in Pfizer. Funding for another study of Prozac was originally attributed to the U.S. National Institute of Mental Health, but U.S. Food and Drug Administration records show Eli Lilly, manufacturer of Prozac, paid for the study.

- The authors of the four larger studies "exaggerated the benefits, downplayed the harms, or both," raising serious concerns over whether the medical journals that published their work bothered to properly scrutinize their data.

- Overall, the numbers of children studied were small, the followup period short and the dropout rates high. The Australian team fears biased reporting and "overconfident recommendations" are misleading doctors, patients and their families and that many are overlooking non-drug treatments that are "probably both safer and more effective."

"The fact that serious adverse effects with newer antidepressants are common enough to be detected in randomized controlled trials raises serious concerns about their potential for harm," the authors report in the British Medical Journal.

"The magnitude of benefit is unlikely to be sufficient to justify risking those harms, so confidently recommending these drugs as a treatment option, let alone as first-line treatment, would be inappropriate."

The study, led by researchers at the Women and Children's Hospital in North Adelaide, comes on the heels of a U.S. report showing that the number of children and adolescents taking Paxil and other antidepressants increased 49 per cent between 1998 and 2002, with the biggest jump in preschoolers.

None of the drugs has been approved in Canada for anyone under 18, but doctors are prescribing them "off-label" -- which they are allowed to do -- to children as young as three for depression, anxiety, social phobia, attention problems and obsessive-compulsive disorder.

In a statement, Pfizer said that it plans to send a detailed response to the British Medical Journal, regarding "inaccuracies and omissions" in the report.

Health Canada issued a public advisory in January about the increased risk of suicide in children taking SSRIs. In February, an expert advisory panel asked Health Canada to require drug makers to add new warnings in materials provided to doctors.

British health officials have gone further, warning doctors last winter to stop prescribing the newer antidepressants to children. The only exception was Prozac. The UK Committee on Safety of Medicines argued studies have shown the drug is safe and effective in children.

Dr. Robert Milin, clinical director of the youth program at the Royal Ottawa Hospital, said he finds "a bit offensive" the suggestion investigators might not have been doing their job properly. He also said a recent study showed some evidence that the use of SSRIs may be lowering the suicide rate in adolescents.

He urged parents not to be alarmed and said no patients should stop their drugs without consulting their doctor. "That's the last thing you want to do because there is potential for withdrawal symptoms from some of these medications."

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Globe and Mail (April 9, 2004)

Study slams anti-depressant research

Report finds 'disturbing shortcomings' in earlier trials on drugs for kids

By ROD MICKLEBURGH

A team of medical researchers has issued a strong call for doctors to reconsider prescribing widely used anti-depressant drugs to children, after finding "disturbing shortcomings" in a number of clinical trials on their effectiveness. In a study published today in the British Medical Journal, the team of five Australian university researchers concludes that anti-depressant drugs cannot confidently be recommended as a treatment option for childhood depression.

Their powerful recommendation adds to the growing clamour against the routine prescription of drugs known as SSRIs (selective serotonin reuptake inhibitors) to troubled young patients.

Critics charge that SSRIs show little benefit over placebos in treating childhood depression, while increasing suicidal thoughts in some.

Yet, they are increasingly popular. Last year, more than 450,000 Canadians 19 years and under were treated by doctors for depression. Anti-depressant medication was prescribed to 75 per cent of them.

Some estimate that the number of annual SSRI prescriptions for young people has risen 58 per cent in Canada since 1998. At the same time, in the United States, the use of anti-depressant drugs by preschoolers nearly doubled from 1998 to 2002.

The most well-known SSRIs include Prozac, Zoloft, Luvox, Paxil, Effexor, Celexa and Remeron.

Britain has effectively halted prescription of all SSRIs except Prozac to those under 18, while Health Canada issued a warning earlier this year that advised anyone under 18 taking an SSRI anti-depressant to consult their doctor.

Dr. Jane Garland, head of the Mood and Anxiety Disorders Clinic at the Children's Hospital in Vancouver, said she agreed "absolutely" with the BMJ study.

She said it echoes her own observations in a recent edition of the Canadian Medical Association Journal.

"There is a possibility of small benefits for some patients, but the majority of the time, SSRIs demonstrate no benefit over placebos. I think we should be alarmed at such an uncritical acceptance of SSRIs by supposedly scientific practitioners," she said. "This is another nail in the coffin for SSRIs . . . but even as the evidence mounts, it doesn't seem to change prescription practices."

The researchers examined six previously published, randomized controlled trials involving the use of SSRIs by depressed children. They noted that the authors of three of the trials were paid for their work by pharmaceutical companies.

Benefits were exaggerated and harms were downplayed, according to the BMJ study, which also noted that placebos had virtually the same positive impact on young patients as SSRIs.

In one trial looked at by the researchers, 9 per cent of those being treated with the SSRI drug Zoloft withdrew because of adverse affects, compared with a 3-per-cent withdrawal by those taking a placebo. Despite these results, the BMJ report stated: "The authors [of the Zoloft study] concluded that [Zoloft] is an effective, safe and well tolerated short-term treatment for children and adolescents."

These, and other suspect trials, "raise the question of whether the journals that published the research reviewed the studies with a sufficient degree of scrutiny, given the importance of the subject," the Australian researchers said.

"We are concerned that biased reporting and overconfident recommendations in treatment guidelines may mislead doctors, patients and families.

"It is vital that authors, reviewers and editors ensure that published interpretations of data are more reasonable and balanced than is the case in the industry-dominated literature on childhood anti-depressants."

Despite accumulating evidence against the efficacy of SSRIs, however, Dr. Garland said there is still a place for them in treating childhood depression. She said they have been proven effective in treating anxiety disorders, and doctors continue to prescribe them for depression "because they work."

Dr. Garland explained that about 80 per cent of patients improve after taking SSRIs, even if 60 per cent taking a placebo also improve and some patients would have become better without medication.

But Dr. Garland added physicians must be more aware of possible adverse side effects to young patients and should understand that the clinical benefit isn't high.