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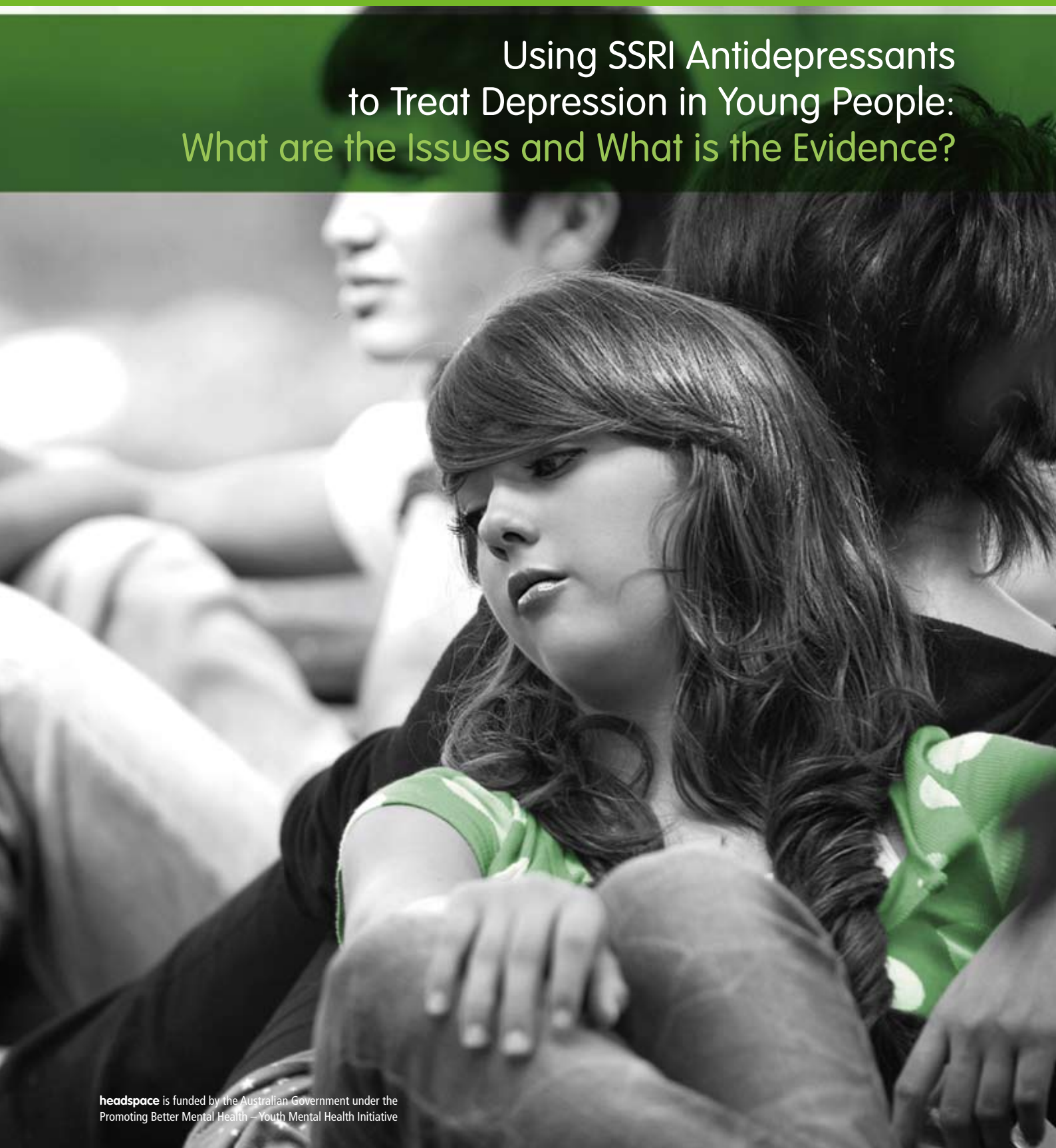
National Youth Mental Health Foundation

Evidence Summary:

Using SSRI Antidepressants to Treat Depression in Young People: What are the Issues and What is the Evidence?



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What are the issues and What is the evidence?

Why is there so much debate on this issue?

The controversy about using Selective Serotonin Reuptake Inhibitors (SSRIs) first emerged in light of evidence indicating an increase in both suicidal ideation and suicidal behaviour among children and adolescents aged 12-18 years prescribed SSRIs for the treatment of depressive illnesses (1). This culminated in a black box warning in the United States to clinicians about using this class of medication for young people aged up to 24 years. In Australia, no antidepressants (including any SSRIs) are currently approved by the Therapeutic Goods Administration (TGA) for the treatment of major depression in children and adolescents aged less than 18 years (2). The controversy has resulted in declining rates of SSRI prescriptions to young people in many countries (3). However, an association has recently been drawn between these declining rates of prescriptions and an increased suicide rate over the same period of time (3). One study has shown that there has been no increase in psychotherapy referrals to compensate for the decreasing prescription rates, (4) suggesting that there has been **a reduction in interventions generally for young people with depression,** rather than SSRI prescriptions specifically.

There continues to be strong debate on this topic, with many clinical researchers arguing that SSRIs are essential for treating depression in this age group, (5-9) while others claim the contrary (10-11). What further complicates this issue is the potential for bias to be introduced into this debate if only positive findings from SSRI drug trials are published in peer reviewed journals, which was certainly the case in the past (9).

Are SSRIs Effective for Young People? What is the Evidence?

The results of a recent Cochrane systematic review (12) are consistent with earlier findings (6), which indicate that the only SSRI with **consistent evidence of its effectiveness** in young people is fluoxetine. Paroxetine does not appear to be more effective than placebo. There are inconsistent outcomes for citalopram and sertraline.

The effectiveness of fluoxetine however **is modest.** The rate of those who respond (ie. whose symptoms improve) while on fluoxetine is between 41%-61%, compared to 20%-35% on placebo. The rates of remission from depression, a potentially more clinically meaningful outcome, are less and range between 31% -41%. The overall change in depression severity scores on the Children's Depression Rating Scale-Revised (CDRS-R) between fluoxetine and placebo groups is small at 5.63 points (from a possible range of 17-113) and unlikely to indicate significant clinical change. Young people on fluoxetine do not appear to be functioning better in their daily lives at the end of the trials.

It is important to note however, that the majority of clinical trials have **excluded young people with more severe forms of depression,** including those with comorbid mental health disorders (including substance use disorder) and those **with suicidal ideation or deliberate self harm.** The extent to which SSRIs are effective for treating depression in these patients – who make up the majority of young people seen in public clinical services – is unknown.

Based on the available evidence, current clinical practice guidelines highlight fluoxetine as the only SSRI with FDA approval (in the US) and more consistent evidence of effectiveness in this age group. In Australia however, no SSRIs are currently approved for the treatment of major depressive disorder in those aged less than 18 years (2). Guidelines indicate that **if medication is to be considered, it should only be prescribed to young people with moderate to severe depression (not mild depression)** (13). Guidelines also recommend weekly monitoring visits with the young person in the first 4 weeks of commencing medication, and then fortnightly thereafter (13-14).

What is the Evidence Regarding the Risks of using SSRIs?

The results of several systematic reviews (1,7,12) demonstrate that there is an increased risk of both suicidal ideation and suicidal behaviour for young people treated with an SSRI compared to those receiving placebo. However, no deaths have been reported that are attributable to SSRI prescription.

What does All this Mean about Treating a Young Person with Depression?

There is evidence that fluoxetine is modestly effective for reducing symptoms of depression in young people, however there is also evidence of an increased risk of suicidal ideation and behaviour. Balanced against these findings are the **even greater risks of not treating depression with any type of intervention** (eg. pharmacological or psychological).

There is a clear imperative to engage young people who are experiencing a depressive disorder in good clinical care. Clinicians can **consider a range of evidence-based interventions,** including those that are relatively simple. For example in the recent ADAPT trial, which compared fluoxetine with fluoxetine plus cognitive behaviour therapy (CBT), 21% of young people accepted into the trial **responded to a brief psychosocial intervention** and subsequently had to be excluded from the study before randomisation (15). Trials such as ADAPT demonstrate that a high level of 'standard care', which may or may not include medication, is sufficient for many young people, including those experiencing moderate to severe depression (15-17). There is also evidence that psychological therapies, such as CBT and interpersonal therapy (IPT) can be effective for some young people, at least in the short term (18).

Overall, a stepped model approach is recommended for the treatment of depression in young people (13), whereby clinicians consider commencing treatment with a psychological therapy, such as CBT or IPT. This is especially the case for young people with **mild depression.** In cases of **moderate to severe depression,** SSRI medication may be considered within the context of comprehensive management of the patient, which includes regular careful monitoring for the emergence of suicidal ideation or behaviour (13).

Irrespective of the treatment chosen, it is essential that there is close monitoring of the young person's symptoms, and any side effects if medication is prescribed. This also helps to form the basis of **ongoing collaborative discussions** with the young person and their families and supporters where appropriate, about further treatment options for those who do not respond to initial treatment (including the use of increasingly complex interventions or medication).

Keeping up with new findings?

There are a number of sources of up-to-date information about the effectiveness of interventions for treating depression. The Centre of Excellence in Youth Mental Health will continue to update information about effective interventions for youth mental health disorders (http://www.headspace.org.au/knowledge-centre/). Other useful sites include:

The Cochrane Library - Australian Access (http://www.cochrane.org.au/)
The Centre for Evidence Based Mental Health (http://cebmh.warne.ox.ac.uk/cebmh/cebmh.htm)
The York Centre for Review and Dissemination (http://www.york.ac.uk/inst/crd/)

For more general information about principles and practice of evidence based medicine go to: The Centre for Evidence Based Medicine in Oxford (http://www.cebm.net/).

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