

Long term treatment of depression with selective serotonin reuptake inhibitors and newer antidepressants

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The introduction of fluoxetine in 1987 marked the arrival of the selective serotonin reuptake inhibitors (SSRIs) for the treatment of depression. In the United States antidepressant prescriptions accounted for 2.6% of primary care visits in 1989, rising to 7.1% in 2000.¹ This pattern was reflected across Europe, where SSRIs are now the most commonly prescribed antidepressants. Newer antidepressants, such as the serotonin norepinephrine reuptake inhibitors, including venlafaxine and duloxetine, also contributed to the remarkable increase in antidepressant prescribing.²

Several reasons were put forward for this trend: improved tolerability; reduced lethality in overdose; the aggressive marketing of newly patented drugs; the wider range of available antidepressants; and ease of prescription. An analysis of the UK general practice research database showed that prescriptions almost doubled from 1993 to 2005.³ However, the increase in antidepressant prescribing was not accounted for by new diagnoses but rather a rise in the number of prescriptions given for long term treatment: although the proportion of patients receiving short term treatment declined, the proportion of patients receiving continuing prescriptions for over five years increased. Another primary care study found that the mean duration of antidepressant prescriptions for depression was 4.8 years and 48% of the sample received treatment for more than two years.⁴

The early optimism accompanying SSRIs has faded amid controversy over their effectiveness and safety.⁵ Recent meta-analyses have concluded that antidepressants have only a modest advantage over placebo, with the magnitude of benefit increasing with severity of depression.⁶⁻⁷ Debate has persisted about the association between SSRIs and suicidal behaviour,⁸ considerable disquiet has been expressed about the perceived medicalisation of social problems that really require social solutions. In this review we examine the evidence for the benefits and harms of long term use of SSRIs and newer antidepressants in adults with major depression.

Do SSRIs reduce the risk of relapse or recurrence of depression?

Depression is commonly a recurrent illness: over half of people with a diagnosis of major depression will go on to have a further episode, and the risk of future relapse rises, with 80% of those having a second episode going on to have a third.⁹ Most clinical guidelines recommend that treatment with antidepressants should be continued

SOURCES AND SELECTION CRITERIA

To identify relevant articles, we searched the Cochrane Library, Clinical Evidence, the National Institute for Health and Clinical Excellence's website, and Medline. We combined the search terms "major depressive disorder" and "antidepressant" with terms for adverse events ("adverse events", "harms", "drug reactions", "toxicity") and benefit ("efficacy", "effectiveness"). We gave priority to systematic reviews, meta-analyses, and evidence based clinical guidelines published within the past 10 years. When no report of those types was available, we considered individual randomised controlled trials or observational studies.

for four to six months after recovery to reduce the risk of relapse (re-emergence of original symptoms) and recurrence (new episode of depression).¹⁰⁻¹¹ However, the benefits of long term or maintenance treatment are considered, particularly by clinicians, to be less certain.¹²

A systematic review included 31 randomised trials (4410 participants) investigating whether continuing treatment with antidepressants (of all classes, although most included either a tricyclic antidepressant or an SSRI) reduced the risk of relapse.¹³ These trials were mainly discontinuation studies in which participants with depressive disorders who had responded to acute treatment were randomly assigned to continue drug treatment or receive a placebo.

Pooled results found that, compared with placebo, continuing antidepressant treatment after recovery markedly reduced the proportion of patients who relapsed over one to three years (pooled odds ratio for

SUMMARY POINTS

The rise in the prescribing of antidepressants is largely accounted for by an increase in long term treatment.

Half of people with a diagnosis of major depression will go on to have a further episode, and risk of recurrence increases with each episode.

Evidence for the benefits of long term prescribing of antidepressants comes almost exclusively from secondary care settings.

Continuing antidepressant treatment roughly halves the absolute risk of relapse.

The increased risk of suicidal behaviour associated with selective serotonin reuptake inhibitors (SSRIs) is restricted to people aged under 25.

People with risk factors for relapse of depression should be advised to continue with SSRIs for at least 12 months and consider long term treatment.

Long Term Treatment Of Depression

Raffaela Di Napoli



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