Optimum length of continuation phase treatment

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In the acute phase treatment of major depression, remission of symptoms is the goal. After this the goal of treatment then becomes the prevention of relapse. This phase of treatment is referred to as the continuation phase. Many patients want to stop antidepressants shortly after a positive response. The AHCPR Depression Practice Guidelines states the continuation phase should proceed for four to nine months. This is a broad time span derived from studies of variable design with a relatively small number of patients. Reimherr and colleagues prospectively assessed for relapse in 395 of 839 outpatients diagnosed with major depression who had a symptomatic remission after treatment with fluoxetine 20 mg./day for 12 weeks. Those patients achieving remission were randomized to be switched to placebo after 12, 26 and 50 weeks of treatment, creating time intervals 1 (12-24 weeks), 2 (26-38 weeks), and 3 (50-62 weeks) respectively. Relapse rates were assessed in each time interval. Significant differences in relapse rates occurred between treatment and placebo at interval 1 (26.4% vs. 48.6%) and interval 2 (9.0% vs. 23.2%). The difference between relapse rates continued into time interval 3 (10.7% vs. 16.2%) but did not reach statistical significance. These data suggest that treatment should continue for at least 26 weeks (6.5 months) after remission, for a total of 38 weeks of treatment (9 months) and possibly longer.

The majority of prescriptions for antidepressants are filled for no more than 3 months or about 13 weeks. This suggests that many patients stop, presumably after a favorable response and do not proceed with the continuation phase of treatment. This results in a high risk for relapse. Successful treatment of depression lies in a sustained course of antidepressants. Even with continued treatment with fluoxetine, the relapse rate in the first time interval after 12 weeks
of treatment was 26.4%, and 9.0% in the second time interval (26 weeks of treatment).

One limitation of this study is that patients who met criteria for depression were included without regard for whether the depressive episode was a first occurrence or a reoccurrence. This could bias the sample and skew the relapse rate (i.e. recurrent depression, higher relapse rates or single episode depression, lower relapse rate). Also only 359/839 (43%) had a full response after 12 weeks of treatment with 20mg of fluoxetine. This could indicate a more severely depressed cohort or one with more recurrent depression. In practice, the physician may be uncertain if the episode being treated is the first episode or a recurrent one. Frequently, the depressive episode is the first one to be treated. The authors argue that the study more closely resembles real clinical practice because no distinction was drawn. Nevertheless, this study strongly demonstrates the need for continued treatment with antidepressants after remission of symptoms for at least 26 weeks, making the total treatment period 38 weeks. Even with treatment the potential for relapse remains a significant risk for patients with depression.