The risk of recurrence of depression increases with each episode of depression

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Multiple Recurrences of Major Depressive Disorder

Background: Major depression is an episodic disease with recurrences affecting at least 50% of patients seeking treatment in tertiary referral centers (1). However, most studies only evaluate a single recurrence.

Aim: To study multiple recurrences of unipolar major depression and assess the risk of recurrence after recovery.

Methods: This study is part of the National Institute of Mental Health (NIMH) Collaborative Program on the Psychobiology of Depression, a prospective, naturalistic, longitudinal, multicenter investigation of the episodic course of major depressive disorder. The sample included 366 patients with unipolar depression. Of these patients 318 recovered from their intake episodes and were the subjects of analysis in this study. Recovery was defined as at least 8 consecutive weeks with either no depression symptoms or only 1 or 2 symptoms of mild severity. Recurrence was defined as the reappearance of the full criteria of major depression for 2 weeks.

Main Findings: Of the 318 patients who recovered from their intake episodes, 202 suffered a recurrence. Of those 202 patients who suffered one recurrence, 172 recovered and of those 115 patients had a second recurrence. The cumulative probability of recurrence for a subject with one recurrence at one year after recovery was 25%; two years, 42%; five years 60%. The cumulative probability of recurrence for a subject with two recurrences at one year after recovery was 41%; two years 59%; and five years, 74%. With each succeeding recurrence, the cumulative probability of recurrence increased. The number of lifetime of major depressive episodes was significantly correlated with recurrence during the 10 year follow-up (odds ratio=1.16; 95% CI=1.03-1.31; p=0.02). Conversely, the risk for recurrence progressively decreased as the duration of recovery increased.

It is important to note that out of the original 366, 48 did not recover (13%); 30/202 (14%) did not recover from the first recurrence; and 23/115 (20%) did not recover from the second recurrence.

This was an observational study; while treatment was not controlled, it was documented. During the 4 weeks prior to the first three recurrences, 47-50% of
Conclusions: Major depressive disorder is a chronic illness with a recurring and remitting course for many people. The risk for recurrence goes up with each successive depressive episode. Conversely, the longer the recovery, the lower the risk for recurrence.

Limitations: First the cohort was all Caucasian. Second, the cohort at risk for recurrence progressively shrank. This leads to patients with relatively long intervals of wellness or illness to be disproportionately excluded from successive analyses and underestimating the rates of recurrence over the lifetime of a patient. Only even longer follow-up intervals would eliminate this potential error.

Impact on Internal Medicine: Depression is the most common psychiatric illness. When considering discontinuation of treatment after recovery from a depressive episode, it is important to know the risk for recurrence, incorporate this into the decision analysis and educate the patient about that risk. This study also underscores the frequently chronic nature of depression (those who do not recover from their depressive episode) and the under treatment of those with recurrent depression. This study adds to the literature supporting the prolonged treatment of depression, particularly when in its recurrent form.

Related References:


Major depression is a familial disorder. Most of the familiality results from genetic influences. Environmental influences specific to the individual are also etiological.

3. Clinical Characteristics of Major Depression that predicts risk of depression in relatives

Kendler and colleagues used a large population based twin study to assess the risk for major depression in relatives of people with major depression. In familial major depression an intermediate level of recurrences (<9) long duration of episodes, high level of impairment and recurrent thoughts of death and suicide were associated with a high level of genetic liability in relatives.