

PSYCHIATRY

COMMENTARY

Most guidelines suggest that the most suitable pharmacological treatment for unipolar psychotic depression is a combination of an antipsychotic and an antidepressant. Wijkstra et al's systematic review challenges that wisdom. They found no difference in outcomes of patients treated with a combination of antidepressant and antipsychotic drugs, compared with antidepressant alone. However, it is still too soon to recommend a global change in clinical practice.

Several studies have highlighted the risk of increased suicidal thoughts and behaviours in children and adolescents taking SSRIs in recent years. Juurlink et al's study has highlighted the almost five-fold risk of completed suicides in the elderly within the first month of starting SSRIs compared to other antidepressants. The absolute risk is low, however, suggesting that there is a small group who are more vulnerable.

Depression and dementia often co-exist in older adults and it is sometimes difficult to differentiate the two. This meta-analysis by Ownby et al shows that depression may be an independent risk factor for developing Alzheimer's disease later in life.

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Br J Psychiatry. 2006 May;188:410-5.

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PHARMACOLOGICAL TREATMENT FOR UNIPOLAR PSYCHOTIC DEPRESSION: SYSTEMATIC REVIEW AND META-ANALYSIS

BACKGROUND: The optimal pharmacological treatment of unipolar psychotic depression is uncertain. **AIMS:** To compare the clinical effectiveness of pharmacological treatments for patients with unipolar psychotic depression. **METHOD:** Systematic review and meta-analysis of randomised controlled trials. **RESULTS:** Ten trials were included in the review. We found no evidence that the combination of an antidepressant with an antipsychotic is more effective than an antidepressant alone. This combination was statistically more effective than an

antipsychotic alone. **CONCLUSIONS:** Antidepressant monotherapy and adding an antipsychotic if the patient does not respond, or starting with the combination of an antidepressant and an antipsychotic, both appear to be appropriate options for patients with unipolar psychotic depression. However, clinically the balance between risks and benefits may suggest the first option should be preferred for many patients. Starting with an antipsychotic alone appears to be inadequate.

Am J Psychiatry. 2006 May;163(5):813-21

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THE RISK OF SUICIDE WITH SELECTIVE SEROTONIN REUPTAKE INHIBITORS IN THE ELDERLY

OBJECTIVE: The authors explored the relationship between the initiation of therapy with selective serotonin reuptake inhibitor (SSRI) antidepressants and completed suicide in older patients. **METHOD:** The authors linked population-based coroner's records with patient-level prescription data, physician billing claims, and hospitalization data for more than 1.2 million Ontario residents 66 years of age and older from 1992 to 2000. For each suicide case, four closely matched comparison subjects were selected using propensity score methods. The authors determined the odds ratio for suicide with SSRIs versus other antidepressant treatment, calculated at discrete monthly intervals from the start of treatment. **RESULTS:** Of 1,329 suicide cases, 1,138 (86%) were each fully matched to four comparison subjects using propensity scores. During the first month of therapy, SSRI antidepressants were associated with a nearly fivefold

higher risk of completed suicide than other antidepressants (adjusted odds ratio: 4.8, 95% confidence interval=1.9-12.2). The risk was independent of a recent diagnosis of depression or the receipt of psychiatric care, and suicides of a violent nature were distinctly more common during SSRI therapy. Numerous sensitivity analyses revealed consistent results. No disproportionate suicide risk was seen during the second and subsequent months of treatment with SSRI antidepressants, and the absolute risk of suicide with all antidepressants was low. **CONCLUSIONS:** Initiation of SSRI therapy is associated with an increased risk of suicide during the first month of therapy compared with other antidepressants. The absolute risk is low, suggesting that an idiosyncratic response to these agents may provoke suicide in a vulnerable subgroup of patients.

Arch Gen Psychiatry. 2006 May;63(5):530-8

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DEPRESSION AND RISK FOR ALZHEIMER DISEASE: SYSTEMATIC REVIEW, META-ANALYSIS, AND METAREGRESSION ANALYSIS

CONTEXT: A history of depression may increase risk for developing Alzheimer disease (AD) later in life. Clarifying this relation might improve understanding of risk factors for and disease mechanisms in AD. **OBJECTIVE:** To systematically review and complete a meta-analysis on the relation of depression and AD. **DATA SOURCES:** We conducted electronic bibliographic searches of MEDLINE, PsychLit, EMBASE, and BIOSIS using search terms sensitive to studies of etiology combined with searches on terms related to depression and AD and reviewed reference lists of articles. **STUDY SELECTION:** Studies with data contrasting depressed vs nondepressed patients who did and did not later develop AD were included. Studies that related continuous measures of depression and cognitive status were excluded. **DATA EXTRACTION:** Numerical data were independently extracted by 3 reviewers. They also rated studies on a scale that

assessed quality indicators for observational studies. Data on the interval between observation of depression and the diagnosis of AD were collected when available. **DATA SYNTHESIS:** Meta-analytic evaluation with random-effects models resulted in pooled odds ratios of 2.03 (95% confidence interval, 1.73-2.38) for case-control and of 1.90 (95% confidence interval, 1.55-2.33) for cohort studies. Findings of increased risk were robust to sensitivity analyses. Interval between diagnoses of depression and AD was positively related to increased risk of developing AD, suggesting that rather than a prodrome, depression may be a risk factor for AD. **CONCLUSIONS:** A history of depression may confer an increased risk for later developing AD. This relation may reflect an independent risk factor for the disease.