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**Two Papers from Landmark STAR*D Study Offer New Guidance
on Treatment-Resistant Depression**

Arlington, Va. – Hope for remission remains, even for patients with treatment-resistant depression who have been through at least two trials of antidepressant medication. Two papers in the September 2006 issue of *The American Journal of Psychiatry (AJP)*, the official journal of the American Psychiatric Association (APA), suggest preferred strategies for these patients and are the latest results from the landmark “Sequenced Treatment Alternatives to Relieve Depression” study (STAR*D).

In the first of the two papers, the patients’ current antidepressant treatment was augmented with either lithium or triiodothyronine (T₃), a thyroid hormone. The rate of remission over 14 weeks for patients who received T₃ (25 percent) was higher than the rate for those who received lithium (16 percent), a difference that was not statistically significant. The percentage of patients who dropped out of the study because of side effects was lower for T₃ (10 percent) than for lithium (23 percent), which was statistically significant.

Andrew A. Nierenberg, M.D., of Massachusetts General Hospital, reported the findings in the article, “A Comparison of Lithium and T₃ Augmentation Following Two Failed Medication Treatments for Depression: A STAR*D Report.”

“The study documents that the patient who has not responded to two or even three previous treatments still has reason for hope for a remission from his or her depression,” said Robert Freedman, M.D., *AJP* editor-in-chief. “Furthermore, the results offer rational guidance for the choice of treatment based on data that were not previously available to physicians.”

In the second paper, another treatment approach was explored for patients who had failed to achieve remission on at least three prior medications. The antidepressant tranylcypromine – part of a class of medications not previously tried in STAR*D, the monoamine oxidase inhibitors (MAOIs) – was compared to a combination treatment consisting of venlafaxine and mirtazapine, two antidepressants that enhance norepinephrine and serotonin transmission but in different ways. In this trial the rates of remission were 7 percent for tranylcypromine and 14 percent for the combination – a difference that was not statistically significant. The percentage reduction in depressive symptoms, however, was significantly greater with the venlafaxine-mirtazapine combination (25 percent versus 6 percent).

Patrick J. McGrath, M.D., of New York State Psychiatric Institute, presented the results in the article, “Tranylcypromine Versus Venlafaxine Plus Mirtazapine Following Three Failed Antidepressant Medication Trials for Depression: A STAR*D Report.”

“The results are more generalizable than previous findings on depression treatments because STAR*D included the broad range of depressed outpatients seen in typical psychiatric and family practices, many of whom have coexisting medical and psychiatric disorders,” said Darrel A. Regier, M.D., M.P.H., director of the APA’s Division of Research.

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In an accompanying editorial, Marcia Valenstein, M.D., of the University of Michigan, wrote, “All clinicians should pay close attention to the results of these well-executed trials. While the STAR*D project could not address all complex treatment sequencing decisions, it has provided important evidence applicable to clinical decision making by ordering treatments by relative efficacy or tolerability at specific therapeutic junctures.”

These studies were funded by the National Institute of Mental Health. Medications for the STAR*D trials were provided at no cost by Bristol-Myers Squibb, Forest Pharmaceuticals, GlaxoSmithKline, King Pharmaceuticals, Organon, Pfizer, and Wyeth-Ayerst Laboratories. Additional financial disclosures appear at the end of each article.

(*Am J Psychiatry*. 2006; 163: 1519-1541).

Note to Editors: Contact APA’s Office of Communications and Public Affairs at 703-907-8640 or press@psych.org for an embargoed copy of the article and editorial.

Earlier STAR*D results were reported in the following:

American Journal of Psychiatry 2006; 163:28–40, January 2006

New England Journal of Medicine 2006; 354:1231–1242, March 23, 2006

New England Journal of Medicine 2006; 354:1243–1252, March 23, 2006

American Journal of Psychiatry 2006; 163: 1161-1172, July 2006

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