UT SOUTHWESTERN MEDICAL CENTER NEWS

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Successfully treating depression often requires trying different drugs, new research shows

DALLAS – March 22, 2006 – If a first antidepressant medication doesn't work, try a different one, UT Southwestern Medical Center researchers report.

New research shows that one in three to four people who do not achieve a full remission of symptoms from an initial antidepressant became symptom-free after changing to or adding a second antidepressant. Phase two results of the four-phase study on treatments for depression – the largest of its kind – appear online in two companion articles in today's *New England Journal of Medicine*.

"The message to the patient is: 'Hang in there. If the first treatment does not relieve your symptoms, consider changing or adding another medication. Follow instructions from your doctor, and don't give up,' " said Dr. A. John Rush, vice chairman of clinical sciences and professor of psychiatry at UT Southwestern. He is principal investigator of the study and lead author of one of the articles. "For a depressed individual, it may not matter so much what drug is being prescribed, but that the person moves forward and keeps trying."

Designed to assess the effectiveness of various treatments for depression in "real-world" settings for people who also have other medical and psychiatric conditions, the $35 million, six-year study – designated STAR*D (Sequenced Treatment Alternatives to Relieve Depression) and funded by the National Institute of Mental Health (NIMH) – involved nearly 3,000 patients at 41 primary-care and psychiatric clinics. Researchers at 14 medical institutions worked together under the direction of UT Southwestern as the national coordinating center.

In phase one of the study, participants were treated with the antidepressant citalopram hydrobromide (Celexa) for up to 14 weeks. A "measurement-based care" approach was used, whereby patients' symptoms and medication side effects were evaluated at each visit based on certain guidelines, with dosages modified as needed.

At the end of phase one, about one-third of the participants were symptom-free. The two-thirds who didn't achieve remission could select from several treatment options – including whether to change medications or continue using citalopram and add a second medication. Of those, 1,429 continued in the study.

The patients who chose to switch medications were randomized into three groups receiving one of three popular antidepressants: bupropion hydrochloride-SR (Wellbutrin-SR), sertraline hydrochloride (Zoloft) or venlafaxine hydrochloride-XR (Effexor-XR). Of those, approximately 25 percent achieved remission of symptoms within 14 weeks, with no significant differences in efficacy, safety or tolerability

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between the three drugs.

Participants who decided to add a medication were given either bupropion hydrochloride-SR or buspirone hydrochloride, along with citalopram, which they were already taking. Within 14 weeks, 30 percent of these patients became symptom-free, with neither medication combination statistically different in its effectiveness on primary outcomes.

"These results show that augmenting a first antidepressant with a second one may be worthwhile for some patients and might be considered even earlier for some people," said Dr. Madhukar Trivedi, professor of psychiatry at UT Southwestern and lead author of one of the studies.

"If you add together the people who achieved remission in both phase one and phase two of STAR*D, you see that more than 50 percent of participants become symptom-free after one or two treatments," Dr. Trivedi said. "That is exciting. If you compare this to the vast majority of other chronic medical diseases, getting to remission in this large percentage is good news."

Each year, about 19 million American adults – or 9.5 percent of the population – struggle with depression, a recurring and chronic illness. It frequently returns two or more times, each episode usually lasting two years or more. Depression, the fourth-most disabling illness worldwide, cost the United States an estimated $83 billion in the year 2000.

"The bottom line is, 'If you can hang in there for at least two different treatments, you have better than a 50 percent chance of not just getting better, but getting well,' " said Dr. Rush.

"The bad news is that we still have a way to go with the 40 percent of people who've had two different drug treatments and still haven't achieved remission – which means that we need better treatments," he said. "For a person walking into a doctor's office with depression, that could mean that your first treatment may not be your last. But it does suggest that it's worthwhile to keep on trying."

Dr. Trivedi said the study also points to the need for further research to help customize treatments to individual patients. Results of phases three and four of the STAR*D study are expected to be published later this year, he said.

Also participating from UT Southwestern in the study were Dr. Diane Warden, assistant professor of psychiatry, Dr. Kathy Shores-Wilson, adjunct assistant professor of psychiatry, and Dr. Melanie M. Biggs, associate professor of family and community medicine and psychiatry. In addition, researchers from the University of Pittsburgh; the New York State Psychiatric Institute and the College of Physicians and Surgeons of Columbia University; Massachusetts General Hospital; the University of Pittsburgh School of Medicine; NIMH; and the STAR*D study team were included.

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