Sequenced Treatment Alternatives to Relieve Depression
(STAR*D) Study

The NIMH-funded Sequenced Treatment Alternatives to Relieve Depression (STAR*D) Study was conducted to determine the effectiveness of different treatments for people with major depression who had not responded to initial treatment with an antidepressant. This was the largest and longest study ever conducted to evaluate depression treatment.

The Sequenced Treatment Alternatives to Relieve Depression (STAR*D) Study, funded by the NIH National Institute of Mental Health, was a nationwide public health clinical trial. The purpose of the trial was to determine the effectiveness of different treatments for people with Major Depressive Disorder (MDD) who had not responded to initial treatment with an antidepressant. Over a seven-year period, the study enrolled more than 4,000 outpatients, aged 18-75 years. The participants were individuals who came to their doctors for care and who had other psychiatric and medical conditions like those regularly seen in typical clinical practices. Patients from both mental health (specialty care) and non-mental health (primary medical care) practices in diverse racial, ethnic, and socioeconomic populations were enrolled in the study.

How is the STAR*D study different from other studies of depression?

STAR*D had a unique study design that mimicked clinical practice and ensured high levels of patient participation, making the results directly applicable to practitioners and their patients. This study was conducted by psychiatrists and primary care physicians in both private practice and public clinics to reflect the treatments patients typically receive in community settings. The study reflected what was done in clinical practice by allowing the study participants to choose what treatments were acceptable to them, and then limited randomization of each participant only to his/her range of acceptable treatment strategies. No prior studies had evaluated the acceptability of different treatment strategies in broadly defined participant groups treated in diverse care settings.

Why was the STAR*D study important?

Each year, 9.5 percent of the population, or about 20.9 million American adults, struggle with depressive illness. MDD is a recurring and chronic illness, frequently returning for two or more episodes, with episodes that often last two years or more. Depression is currently the fourth most disabling illness worldwide, and according to the World Health Organization, it will be the second leading cause of disability by the year 2020. About 10 percent of men and up to 25 percent of women will experience depression in their lifetime. People with depression do even more poorly at work, socially, and with their families than do people with a variety of general medical conditions. Depression is responsible for up to 70 percent of psychiatric hospitalizations and about 40 percent of suicides. The cost of depression in the United States in the year 2000 was estimated to be $83 billion, including both $26 billion in costs of treatment and $57 billion in losses such as absenteeism, reduced productivity at work, and the value of lifetime earnings lost due to suicide-related deaths.

There is only limited information about how to successfully treat people with depression, especially how to treat people with depression who have not gotten better with the first treatment tried. Depression is considered “treatment-resistant” when at least one adequately delivered treatment does not lead a person to reach a “remission” of their depressive symptoms, that is, to become symptom-free. About half the participants who were treated with a first medication or talk therapy in prior studies showed a reduction in their symptoms to at least half the level of intensity. Of those, about two-thirds actually became symptom-free.
The results of STAR*D have provided data needed to inform the practice guidelines that doctors and other practitioners use for treating people who have depression. The results have provided descriptive information about specific treatment strategies, such as, at what dose a medication should be prescribed and how long a treatment should be tried before deciding that it is ineffective and moving on to another treatment strategy. Results have also provided much needed information on the long-term course of depression in terms of the frequency, nature, and timing of relapses (return of depressive symptoms less than 6 months after a remission) as well as information about the cost effectiveness of various treatments. Furthermore, the results have helped determine whether there are characteristics of patients, their depressive symptoms and/or their responses to different treatments that might help doctors and other practitioners prescribe the most effective treatment for a particular patient at the outset.