Are we cherry picking participants for studies of antidepressants?

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Findings from clinical studies used to gain Food and Drug Administration approval of common antidepressants are not applicable to most patients with depression, according to a report led by the University of Pittsburgh Graduate School of Public Health. Published in the May issue of the *American Journal of Psychiatry*, the study suggests only a small percentage of people with depression qualify for these studies, and those who do not qualify are often treated with the same medications but may suffer poorer clinical outcomes.

A part of the National Institute of Mental Health-funded Sequenced Treatment Alternatives to Relieve Depression (STAR*D) project - the largest study of the treatment of depression conducted in the United States - researchers compared symptoms and outcomes in depressed patients who met phase III study inclusion criteria to those who did not. Phase III studies for antidepressants determine the effectiveness of the drug in comparison to a placebo. The inclusion criteria for these studies are not standardized nor subject to federal guidelines, resulting in some variation from study to study in the profile of eligible patients. Typically excluded are patients with milder forms of depression, who might be more likely to respond to a placebo drug, and those who may have chronic depression or psychiatric and medical co-morbidities - additional illnesses or conditions.

After assessing 2,855 patients treated with citalopram, a commonly prescribed selective serotonin reuptake inhibitor for mood disorders, study authors concluded that fewer than one in four, or 22.2 percent, of

the patients met the usual criteria for inclusion in phase III antidepressant trials.

"Only a small percentage of depressed patients in our study would have qualified for inclusion in phase III efficacy trials of depression drugs," said study lead author, Stephen Wisniewski, Ph.D., professor of epidemiology and co-director of the Epidemiology Data Center, University of Pittsburgh Graduate School of Public Health. "This raises major concerns about whether results from traditional phase III studies can be generalized to most people with depression, who also often suffer from anxiety, substance abuse and other medical and psychiatric problems."

When Dr. Wisniewski and colleagues further assessed how well patients did on treatment, they found that those who met the eligibility criteria for phase III trials had better outcomes, including higher remission rates, less severe side effects and serious adverse events. The depression remission rate in the patients who met the criteria was 34.4 percent, compared to only 24.7 percent in the ineligible group. Additionally, the drug response rate also was higher in the eligible group - 51.6 percent compared to 39.1 percent of the ineligible group.

"Results from research studies suggest more optimistic outcomes than may exist for real-world patients receiving treatment for depression," said Dr. Wisniewski. Although phase III eligibility criteria could be changed to include a broader population of patients, Dr. Wisniewski cautions that this could come at the cost of more serious side effects in patients who have co-morbidities and are generally sicker. These patients may not be able to safely tolerate the drugs being tested. Instead, he suggests medical care providers who treat patients with depression use their professional judgment by noting that most phase III findings are based on patients who may be very different than those under their care.

Source: University of Pittsburgh Schools of the Health Sciences (news : web)