Publication bias and 'spin' raise questions about drugs for anxiety disorders

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A new analysis reported in *JAMA Psychiatry* raises serious questions about the increasingly common use of second-generation antidepressant drugs to treat anxiety disorders.

It concludes that studies supporting the value of these medications for that purpose have been distorted by publication bias, outcome reporting

bias and "spin." Even though they may still play a role in treating these disorders, the effectiveness of the drugs has been overestimated.

In some cases the medications, which are among the most widely prescribed drugs in the world, are not significantly more useful than a placebo.

The findings were made by researchers from Oregon State University, Oregon Health & Science University, and the University of Groningen in The Netherlands. The work was supported by a grant from the Dutch Brain Foundation.

Publication bias was one of the most serious problems, the researchers concluded, as it related to double-blind, placebo-controlled clinical trials that had been reviewed by the U.S. Food and Drug Administration. If the FDA determined the study was positive, it was five times more likely to be published than if it was not determined to be positive.

Bias in "outcome reporting" was also observed, in which the positive outcomes from drug use were emphasized over those found to be negative. And simple spin was also reported. Some investigators concluded that treatments were beneficial, when their own published results for primary outcomes were actually insignificant.

"These findings mirror what we found previously with the same drugs when used to treat major depression, and with antipsychotics," said Erick Turner, M.D., associate professor of psychiatry in the OHSU School of Medicine, and the study's senior author. "When their studies don't turn out well, you usually won't know it from the peer-reviewed literature."

This points to a flaw in the way doctors learn about the drugs they prescribe, the researchers said.

"The peer review process of publication allows, perhaps even encourages, this kind of thing to happen," Turner said. "And this isn't restricted to psychiatry - reporting bias has been found throughout the medical and scientific literature."

Craig Williams, a professor in the Oregon State University/Oregon Health & Science University College of Pharmacy, and co-author of the study, said that "most of these drugs are fairly safe and well-tolerated, but if a medication is less effective than believed, this still raises serious questions about its use.

"The level of bias we found did not change the fact that some antidepressants can have value in treating anxiety disorders," Williams said. "However, there is less evidence for value of these drugs than published studies would have you believe. And these concerns are increased when such medications are frequently prescribed by general practitioners with less training in psychiatry."

In this study, the researchers examined a broad body of the evidence and scientific research that had been presented to the Food and Drug Administration, including studies that had been done but were not published in open scientific literature. They found that negative data on drug efficacy tended not to get published, or was de-emphasized when it was published.

Conclusions might have been manipulated or exaggerated because positive results receive more scientific attention, are published sooner, and lead to higher sales of a drug, said Annelieke Roest, the lead author of the publication at the University of Groningen.

"Lots of research is funded eventually by the taxpayer, and that's reason enough to say that scientists should publish all their results," Roest said.

The study reiterated this point, and the need to more routinely publish nonsignificant results.

"There is strong evidence that significant results from randomized controlled trials are more likely to be published than nonsignificant results," the researchers wrote in their study. "As a consequence, the published literature... may overestimate the benefits of treatment while underestimating their harms, thus misinforming clinicians, policy makers and patients."

Antidepressants are now widely prescribed for conditions other than depression, the study noted. They are being used for generalized anxiety, panic disorder, social anxiety, post-traumatic stress disorder and other uses. In both the U.S. and Europe, use of antidepressant drugs has significantly increased in the past two decades, the researchers said, with much of that use driven by non-specialists in primary care settings.

The level of reporting bias in the scientific literature, the researchers wrote, "likely impacts clinicians' perceptions of the efficacy of these drugs, which could reasonably be expected to affect prescription behavior."

More information: Reporting Bias in Clinical Trials Investigating the Efficacy of Second-Generation Antidepressants in the Treatment of Anxiety Disorders *JAMA Psychiatry*. Published online March 25, 2015. DOI: 10.1001/jamapsychiatry.2015.15

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