Drug trials funded by industry are more likely to publish favorable results

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When published results are systematically tracked for drug trials registered with ClinicalTrials.gov, those from industry-funded trials are the likeliest to be favorable to the drug in question, report researchers at Children's Hospital Boston. Publishing in the August 3 issue of the *Annals of Internal Medicine*, the researchers call for more public disclosure about clinical drug trials at their outset to reduce the possibility of bias in the findings.

The research team, led by Florence Bourgeois, MD, MPH, of Children's Division of Emergency Medicine, and Kenneth Mandl, MD, MPH, Laboratory Director in the Children's Hospital Informatics Program, reviewed 546 drug trials conducted between 2000 and 2006 and listed with ClinicalTrials.gov, a comprehensive, web-based federal registry of clinical trials. The analysis focused on five classes of drugs: cholesterol-lowering drugs, antidepressants, antipsychotics, proton-pump inhibitors and vasodilators. The researchers scanned the medical literature for publications associated with each trial, checking four separate databases and contacting trial investigators directly if necessary.

Overall, allowing for a three-year lag time from the completion of the trial, two-thirds of the trials had published results. The industry-funded trials reported positive outcomes 85 percent of the time, as compared with 50 percent for government-funded trials and 72 percent for trials funded by nonprofits or non-federal organizations. In addition, among the nonprofit/nonfederal trials, those that had industry contributions (nearly half) were more likely than those without to report positive

outcomes (85 vs. 61 percent). These differences were all statistically significant.

The researchers acknowledge that the pharmaceutical industry was probably more selective in which trials it funded, helping to account for their greater proportion of favorable outcomes. "Industry is very good at knowing what they want to study, and industry-sponsored studies are more efficient and well funded," says Bourgeois, the study's first author. "But despite these potential biases, this is a stunning result."

The industry-funded trials were in more advanced phases of study; 89 percent were Phase 3 or Phase 4, versus just 51 percent of government-funded trials and 65 percent of nonprofit/nonfederally-funded trials. However, even Phase 1 and 2 trials funded by industry reported the highest percentage of favorable outcomes.

In addition, industry-funded trials were the least likely to have published results within two years of study completion (32 percent) as compared with trials with no industry contributions (54 percent for government trials, and 56 percent for purely nonprofit/nonfederal trials).

As the researchers discuss in the paper, clinical trials can be manipulated in various ways to make the results appear more favorable. Publication bias - a tendency to selectively publish only positive results of a trial, or delay publication of negative results - is one factor that has received much attention, as in a well-publicized 2008 study of antidepressants in The New England Journal of Medicine.

"While we cannot specifically point to which factors contribute to the association between funding source and positive result reporting, our findings speak to the need for more disclosure of all elements of a study," says Bourgeois. "Publication bias is likely a contributing factor, but there may be many more, including biases in study design, patient

selection, data analysis and results reporting."

The use of registries like ClinicalTrials.gov, launched in 1999, was hoped to reduce publication bias by creating a record for all clinical trials. In addition, in 2005, the International Committee of Medical Journal Editors began requiring that a trial be registered before enrolling patients in order to be considered for publication, thus creating a record of the planned study outcomes before the study's initiation. In 2007, the FDA expanded the scope of Clinical Trials.gov, requiring the sponsors of all drug, biologic and device trials to register their studies upon launch (phase I trials excepted).

If trial protocols are made public in advance, a trial sponsor is less able to manipulate or selectively publish the findings, the researchers argue. "Our main call is for transparency, to enable better understanding of the impact of funding source on the study outcomes, and for all study results - good or bad - to be made available," says Mandl, the study's senior investigator, also an Associate Professor at Harvard Medical School.

Provided by Children's Hospital Boston