Industry Sponsorship and Research Outcome

A Cochrane Review

SOURCE OF REVIEW

This review is an update of an earlier review of studies examining the association of pharmaceutical industry sponsorship of drug studies and research outcomes. The review was converted to a Cochrane Methodology Review, updated to double the number of included studies, and the scope was expanded to include device studies. The review also examines whether industry-sponsored studies have different risks of bias compared with non–industry-sponsored studies. Two of the authors of the review were supported by grants for their work on the review; Octavian A. Busuioc, from the Canadian Institutes of Health Research, and Andreas Lundh, from the Julie von Mullens Foundation and Kontorchef Gerhard Bronsteds Travel Grant, Denmark. The full review is available at http://onlinelibrary.wiley.com/doi/10.1002/14651858.MR000033.pub2/pdf.

BACKGROUND

An increasing number of clinical drug trials are funded by the pharmaceutical industry. These drug trials may be included in systematic reviews and clinical practice guidelines that form the basis for treatment recommendations. Thus, results and conclusions that are unfavorable to the sponsor (ie, studies that find a drug no more effective than placebo or clinically less effective or safe than other drugs used to treat the same condition) can pose considerable financial risks to companies.

Systematic reviews have documented that pharmaceutical industry sponsorship of drug studies is associated with findings that are favorable to the sponsor’s product. There are several potential ways that industry sponsors can influence the outcome of a study, including how the question is framed, how the study is designed and conducted, the way data are analyzed, selective reporting of favorable results, and spin in conclusions. It is not clear which, if any, of these methodological considerations explain the association of industry sponsorship and favorable outcomes.

The objective of this Cochrane Review was to investigate whether industry-sponsored drug and device studies have more favorable outcomes and differ in risks of bias, compared with studies having other sources of sponsorship. Cross-sectional studies, cohort studies, systematic reviews, and meta-analyses that quantitatively compared primary research studies of drugs or medical devices sponsored by industry with studies sponsored by other sources were included.

SUMMARY OF FINDINGS

Forty-eight studies met the inclusion criteria for the Cochrane Review. The drugs and devices examined in the included studies were prescribed for a wide range of illnesses and conditions, from heart disease to psychiatric conditions, and were compared with placebo or other treatments. Studies sponsored by industry reported greater benefits than the other studies (risk ratio [RR], 1.24 [95% CI, 1.14-1.35]). This means that the number of studies with favorable results is approximately 24% higher among industry-sponsored studies compared with non–industry-sponsored studies. Industry-sponsored studies also had more favorable harm results (RR, 1.87 [95% CI, 1.54-2.27]), meaning that the industry-sponsored studies showed less evidence of harm. The reports of industry-sponsored studies also presented more favorable overall conclusions (RR, 1.31 [95% CI, 1.20-1.44]) compared with non–industry-sponsored studies, and the results and conclusions sections in these articles were less likely to be in agreement with each other. In addition, when 2 drugs were compared head to head in studies sponsored by different companies, the drug that compared favorably in terms of efficacy or harm was most often the drug manufactured by the sponsor of that study.

There are a number of ways that industry sponsors can influence the design, conduct, and reporting of trials to make the results and conclusions favor their product. The Cochrane Review did not find a difference between industry and non–industry-sponsored studies in methodological characteristics that may increase the risk of bias, such as randomization sequence, allocation concealment, and follow-up, although industry-sponsored studies generally reported adequate blinding more often than non–industry-sponsored studies. This analysis suggests that industry-sponsored drug and device studies are more often favorable to the sponsor’s products compared with non–industry-sponsored drug and device studies because of biases that cannot be explained by standard “risk of bias” assessment tools. Instead, the bias in industry-sponsored studies may be partially mediated by factors such as the choice of comparators, dosing and timing of comparisons, selective analysis, and selective reporting.
LIMITATIONS ON THE EVIDENCE

The majority of included articles were coded as having a high risk of bias. Many lacked information on how the study was conducted and did not control for confounders that could influence the relationship between industry sponsorship and research outcomes. However, most of the studies did conduct a comprehensive search. When the analyses in the Cochrane Review were restricted to the 9 studies with low risk of bias, the relationship between sponsorship and outcomes was stronger. The review was conducted according to a prespecified protocol that included a comprehensive search, but it included only published studies, since the previous review found problems with the completeness and quality of the data in unpublished reports. Data on the association of sponsorship and outcomes of device studies are sparse, with only 2 studies reporting separate data on devices.

IMPLICATIONS FOR TREATMENT

This Cochrane Review provides convincing and consistent evidence for the existence of an “industry bias” in drug studies; the evidence for device studies is insufficient. The findings of the review have important implications for making decisions about drug treatments. Decision makers must take sponsorship into account when evaluating whether they should base clinical practice and reimbursement on the results of a study. Clinical practice guidelines, which are increasingly based on systematic reviews, should be made more transparent by disclosing the sponsorship of studies included in the guideline and by regarding industry sponsorship as a factor that increases the risk of bias. However, the sponsorship of studies included in systematic reviews and clinical practice guidelines is rarely reported. Even Cochrane Reviews do not consistently assess and report industry sponsorship as a source of bias in included studies. While improved transparency about sponsorship will alert decision makers to the potential for industry bias, it will not identify the specific reasons for the bias or eliminate it. The findings of this Cochrane Review support the need for better access to trial protocols, to information on how trials are actually conducted, and to crude data to evaluate sources of bias in industry-sponsored studies. Governments and noncommercial sponsors also need to respond by increasing funds for independent drug and device trials. Independently sponsored trials should focus on testing innovative and essential treatments, as well as comparisons with existing effective treatments, thus shifting the resources spent on drug and device trials away from trials with a marketing purpose to those that are clinically important. Although clinical trial registries are a step toward improving access to trial data, governments should consider incentives to improve the public availability of trial protocols and results. Governments should consider making submission of data from previous trials sponsored by a company a mandatory requirement for ethics approval for future trials to be conducted by that company or for gaining regulatory drug and device approval for products from that company.

Lisa Bero, PhD

REFERENCES


Publisher Online: February 25, 2013. doi:10.1001/jamainternmed.2013.4190

Author Affiliation: Department of Clinical Pharmacy and Health Policy, University of California, San Francisco.

Correspondence: Dr Bero, Department of Clinical Pharmacy and Health Policy, University of California, San Francisco, 3333 California St, Ste 420, San Francisco, CA 94118 (bero@pharmacy.ucsf.edu).

Conflict of Interest Disclosures: None reported.