Critical questions to ask of studies, press releases and scientific reports

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Some basic questions

- **What type of study?**
  They are not all created equal

- **Was it peer-reviewed?**
  If “yes,” be wary; if “no,” be very wary

- **Who paid for the work to be done?**
  Studies have shown that it can make a difference to the reported findings

What type of study?

Confidence in the findings

- **Observational**
- **Experimental**
- **Double-blind, randomized controlled trial (RCT)**
- **Systemic review/meta-analysis of RCTs**

Was it peer reviewed?

"We portray peer review to the public as a quasi-sacred process that helps to make science our most objective truth teller. But we know that the system of peer review is biased, unjust, unaccountable, incomplete, easily fixed, often insulting, usually ignorant, occasionally foolish, and frequently wrong."

Richard Horton, editor-in-chief, *The Lancet*

Who paid for the work to be done?

Pharmaceutical industry sponsorship and research outcome and quality: systematic review

Joel Lexchin, Lisa A Bero, Benjamin Djulbegovic, Otavio Clark

Abstract

Objective To investigate whether funding of drug studies by the pharmaceutical industry is associated with outcomes that are favourable to the funder and whether the methods of trials funded by pharmaceutical companies differ from the methods in trials with other sources of support.

Methods Medline (January 1966 to December 2002) and Embase (January 1980 to December 2002) searches were supplemented with material identified in the references and in the authors' personal files. Data were independently abstracted by three of the authors and disagreements were resolved by consensus.

Results 30 studies were included. Research funded by drug companies was less likely to be published than research funded by other sources. Studies sponsored by pharmaceutical companies were more likely to have outcomes favouring the sponsor than were studies with other sponsors (odds ratio 4.05; 95% confidence interval 2.98 to 5.51; 18 comparisons). None of the 13 studies that analysed methods reported that studies funded by industry was of poorer quality.

Conclusion Systematic bias favours products which are made by the company funding the research. Explanations include the selection of an inappropriate comparator to the product being investigated and publication bias.

Introduction

favourable outcome may result in biases in come, and reporting of industry sponsored

A recent systematic review of the financial conflicts on biomedical research studies financed by industry, although as other studies, always found outcomes favou sponsoring company.[5] However, this review papers published only in English, excluded letters and abstracts, and looked at studies other industries. We reviewed the relation b source of funding of the research and th outcomes and investigated whether qua methods in studies funded by pharmaceuti nies differs from that in other studies.

Methods

Study selection

We included only studies that specifically stat analysed research sponsored by a pharmace pany, compared methodological quality or with studies with other sources of funding, ar the results in quantitative terms. Outcomes were conclusions about differences in drug ef adverse effects, cost outcomes, or publica between industry funded trials and other published in any language was eligible for in

Some studies analysed both pharmaco non-pharmacological trials and combine funded by drug companies and other ind one group. In these cases, if most pharmaceutical trials and were funded industries they were excluded.

Financial ties and concordance between results and conclusions in meta-analyses: retrospective cohort study

Veronica Yank, clinical instructor,[1] Drummond Rennie, professor,[2] Lisa A Bero, professor[3]

ABSTRACT

Objective To determine whether financial ties to one drug company are associated with favourable results or conclusions in meta-analyses on antihypertensive drugs.

Design Retrospective cohort study.

Setting Meta-analyses published up to December 2004 that were not duplicates and evaluated the effects of antihypertensive drugs compared with any comparator on clinical end points in adults. Financial ties were categorised as one drug company compared with all others.

Main outcome measures The main outcomes were the results and conclusions of meta-analyses, with both outcomes separately categorised as being favourable or not favourable towards the study drug. We also collected data on characteristics of meta-analyses that the literature suggested might be associated with favourable results or conclusions.

Results 124 meta-analyses were included in the study, 49 (40%) of which had financial ties to one drug company. On univariate logistic regression analyses, meta-analyses of better methodological quality were more likely to have favourable results (odds ratio 1.16, 95% confidence interval 1.07 to 1.27). Although financial ties to one drug company were not associated with favourable results, such ties constituted the only characteristic significantly associated with favourable conclusions (4.09, 1.30 to 12.83). When controlling for other characteristics of meta-analyses in multiple logistic regression analyses, meta-analyses that had financial ties to one drug company remained more likely to report favourable conclusions (5.11, 1.54 to 16.92).

Conclusion Meta-analyses on antihypertensive drugs and with financial ties to one drug company are not associated with favourable results but are associated with favourable conclusions.

Meta-analyses pool data from multiple studies identified through a systematic review of the literature to provide summary statistics on the efficacy of a given treatment. Such meta-analyses represent the highest level of research evidence in the hierarchy of study types.[14] They also may equal, if not surpass, randomised controlled trials in their cost effectiveness[15] and in their influence on patient care and healthcare policy.[16,17] Drug companies have started to reference meta-analyses in their advertisements.[18]

In the 1990s and early 2000s concerns were expressed about the influence of the pharmaceutical industry on meta-analyses.[19,20] Between 2003 and 2005 the Cochrane Collaboration debated whether its systematic reviews should be funded by drug companies; its current policy statement states that "The sponsorship of a Cochrane review by any commercial source or sources. . . is prohibited."[21] More recently a study compared matched pairs of Cochrane meta-analyses and industry sponsored meta-analyses published in print journals and found evidence that the industry sponsored meta-analyses were more likely to recommend the experimental drug.[22] The study was, however, unable to control for the possible confounding effects of the Cochrane methodology. In addition, the study examined only eight pairs of meta-analyses and so was unable to comment on the characteristics of meta-analyses not represented in its sample.

Some antihypertensive drugs have been shown to dramatically improve mortality and morbidity. The market for these and other antihypertensive drugs is highly competitive and lucrative. According to market research, both angiotensin receptor blockers and calcium channel blockers were in the top 10 list of global therapeutic drug classes by sales in 2005, equating to earnings of over $26b (£13b; €18b).[23] Concern exists about the effect of such profits on doctors. The

More questions

- **What was actually measured?**
  Deaths from heart attack, or levels of "bad" cholesterol? (Also beware "mice cured" stories)

- **How large, and how long?**
  Beware of small studies with short duration

- **Was the main finding statistically significant?**
  The bar in many disciplines is low

- **How large was the effect?**
  Or: How significant is this in the real world? You may need help with this …

Questions for your expert sources

- **Do the results justify the conclusions?**
  Or is there an alternative explanation?

- **Was the analysis performed correctly?**
  Ask about flaws in statistical analysis or in the design of the study

- **How does this result fit with those from other studies?**

- **How large is this effect?**
  Get them to help you put measures like "odds ratio," "relative risk" and "number needed to treat" into phrases that everyone can understand.

(And don't forget to ask all sources about their financial and other conflicts)

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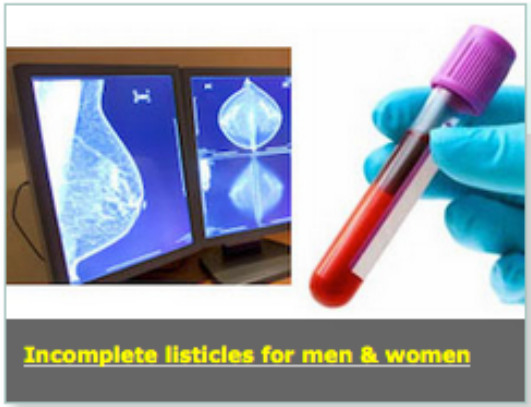

Incomplete listicles for men & women

CBS promotes screening but never mentions harms

5-star score for HealthDay story

Fear-mongering & fawning in the same story

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+ What's the total cost?
+ How often do benefits occur?
+ How often do harms occur?
+ How strong is the evidence?
+ Is this condition exaggerated?
+ Are there alternative options?
+ Is this really a new approach?
+ Is it available to me?
+ Who's promoting this?
+ Do they have a conflict of interest?

http://www.healthnewsreview.org//about-us/review-criteria/

REPORTING ON CANCER RESEARCH

Welcome to **Reporting on Cancer Research,** a Web site for science writers and the public with definitions of terms and brief overviews of how things work in the world of oncology research.

Explaining Study Findings

Tips from the Center for Medicine and the Media, The Dartmouth Institute for Health Policy and Clinical Practice, developed by Steven Woloshin and Lisa M. Schwartz, Professsors of Medicine.

* Number glossary(absolute risk, relative risk)

* Statistics glossary (p values, confidence intervals, survival)

* Questions to guide reporting (e.g., how important are the outcomes?)

* How to highlight study cautions(useful phrases)

To learn more about statistics:

Know Your Chances: Understanding Health Statistics, Steven Woloshin, Lisa M. Schwartz, H. Gilbert Welch, University of California Press, 2008.

Statistics With Confidence (second edition), Douglas Altman, BMJ Books. London, UK. 2000, Oxford University Press, Oxford, UK, 2000.

http://www.oxfordjournals.org/our_journals/jnci/resource/reporting_on_cancer.html

You should read this essay

(Even if you don't show it to your editor)

Essay

Why Most Published Research Findings Are False

John P. A. Ioannidis

Summary

There is increasing concern that most current published research findings are false. The probability that a research claim is true may depend on study power and bias, the number of other studies on the same question, and, importantly, the ratio of true to no relationships among the relationships probed in each scientific field. In this framework, a research finding is less likely to be true when the studies conducted in a field are smaller; when effect sizes are smaller; when there is a greater number and lesser preselection of tested relationships; where there is greater flexibility in designs, definitions, outcomes, and analytical modes; when there is greater financial and other interest and prejudice; and when more teams are involved in a scientific field in chase of statistical significance. Simulations show that for most study designs and settings, it is more likely for a research claim to be false than true. Moreover, for many current scientific fields, claimed research findings may often be simply accurate measures of the prevailing bias. In this essay, I discuss the implications of these problems for the conduct and interpretation of research.

Published research findings are sometimes refuted by subsequent evidence, with ensuing confusion and disappointment. Refutation and controversy is seen across the range of research designs, from clinical trials and traditional epidemiological studies [1–3] to the most modern molecular research [4,5]. There is increasing concern that in modern research, false findings may be the majority or even the vast majority of published research claims [6–8]. However, this should not be surprising. It can be proven that most claimed research findings are false. Here I will examine the key factors that influence this problem and some corollaries thereof.

The Essay section contains opinion pieces on topics of broad interest to a general medical audience.

Modeling the Framework for False Positive Findings

Several methodologists have pointed out [9–11] that the high rate of nonreplication (lack of confirmation) of research discoveries is a consequence of the convenient, yet ill-founded strategy of claiming conclusive research findings solely on the basis of a single study assessed by formal statistical significance, typically for a *p*-value less than 0.05. Research is not most appropriately represented and summarized by *p*-values, but, unfortunately, there is a widespread notion that medical research articles

It can be proven that most claimed research findings are false.

should be interpreted based only on *p*-values. Research findings are defined here as any relationship reaching formal statistical significance, e.g., effective interventions, informative predictors, risk factors, or associations. "Negative" research is also very useful. "Negative" is actually a misnomer, and the misinterpretation is widespread. However, here we will target relationships that investigators claim exist, rather than null findings.

As has been shown previously, the probability that a research finding is indeed true depends on the prior probability of it being true (before doing the study), the statistical power of the study, and the level of statistical significance [10,11]. Consider a 2 × 2 table in which research findings are compared against the gold standard of true relationships in a scientific field. In a research field both true and false hypotheses can be made about the presence of relationships. Let R be the ratio of the number of "true relationships" to "no relationships" among those tested in the field. R is characteristic of the field and can vary a lot depending on whether the field targets highly likely relationships or searches for only one or a few true relationships among thousands and millions of hypotheses that may be postulated. Let us also consider, for computational simplicity, circumscribed fields where either there is only one true relationship (among many that can be hypothesized) or the power is similar to find any of the several existing true relationships. The pre-study probability of a relationship being true is $R/(R + 1)$. The probability of a study finding a true relationship reflects the power $1 - \beta$ (one minus the Type II error rate). The probability of claiming a relationship when none truly exists reflects the Type I error rate, α. Assuming that c relationships are being probed in the field, the expected values of the 2 × 2 table are given in Table 1. After a research finding has been claimed based on achieving formal statistical significance, the post-study probability that it is true is the positive predictive value, PPV. The PPV is also the complementary probability of what Wacholder et al. have called the false positive report probability [10]. According to the 2 × 2 table, one gets $PPV = (1 - \beta)R/(R - \beta R + \alpha)$. A research finding is thus

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Abbreviation: PPV, positive predictive value

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