

Industry and evidence-based medicine: Believable or conflicted? A systematic review of the surgical literature

Chris S. Bailey, MD, MSc*
 Michael G. Fehlings, MD, PhD†
 Y. Raja Rampersaud, MD†
 Hamilton Hall, MD†
 Eugene K. Wai, MD, MSc‡
 Charles G. Fisher, MD, MHSc§

From the *Division of Orthopaedic Surgery, Department of Surgery, University of Western Ontario, London, the †Divisions of Neurosurgery and Orthopaedic Surgery, University of Toronto, Toronto, the ‡Division of Orthopaedic Surgery, Department of Surgery, University of Ottawa, The Ottawa Hospital, Ottawa, Ont., and the §Combined Neurosurgical and Orthopaedic Spine Program, Department of Orthopaedics, University of British Columbia, Vancouver, BC

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Correspondence to:
 Dr. C.S. Bailey
 London Health Science Centre
 E4-120 Victoria Hospital
 800 Commissioners Rd. E
 London ON N6A 5W9
 chris.bailey@lhsc.on.ca

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Background: Over the last few decades medical research and development has come to depend more heavily on the financial support of industry. However, there is concern that financial relations between the medical community and medical industry could unduly influence medical research and therefore patient care. Our objective was to determine whether conflict of interest owing to authors'/investigators' financial affiliation with industry associated with their academic research has been identified in the surgical literature. In particular, we sought to answer the following questions: What is the extent of such conflict of interest? Does conflict of interest bias the results of academic surgical research in favour of industry? What are the potential causes of this proindustry bias?

Methods: We conducted a systematic review of the literature in May 2008 using the OVID SP search engine of MEDLINE, EMBASE, CINAHL, the Cochrane Database of Systematic Reviews, DARE and Health Technology Assessment. Quantitative studies that included a methods section and reported on conflict of interest as a result of industry funding in surgery-related research specifically were included in our analysis.

Results: The search identified 190 studies that met our criteria. Author/investigator conflict of interest owing to financial affiliation with industry associated with their academic research is well documented in the surgical literature. Six studies demonstrated that authors with such conflicts of interest were significantly more likely to report a positive outcome than authors without industry funding, which demonstrates a proindustry bias. Two studies found that the proindustry bias could not be explained by variations in study quality or sample size.

Conclusion: The conflict of interest that exists when surgical research is sponsored by industry is a genuine concern.

Contexte : Au cours des dernières décennies, les activités de recherche-développement en médecine en sont venues à dépendre davantage de l'aide financière de l'industrie. On craint toutefois que les liens financiers entre les milieux médicaux et l'industrie médicale n'exercent une influence indue sur la recherche en médecine et, par conséquent, sur le soin des patients. Nous voulions déterminer si des publications chirurgicales indiquaient l'existence de conflits d'intérêts attribuables aux liens financiers entre les auteurs ou chercheurs et l'industrie associée à leur recherche universitaire. Nous avons cherché plus particulièrement à répondre aux questions suivantes : Quelle est l'étendue de ces conflits d'intérêts ? Les conflits d'intérêts font-ils pencher en faveur de l'industrie les résultats de recherches universitaires en chirurgie ? Quelles sont les causes possibles de biais en faveur de l'industrie ?

Méthodes : Nous avons procédé à une analyse systématique des publications en mai 2008 en utilisant le moteur de recherche OVID SP dans MEDLINE, EMBASE, CINAHL, la Cochrane Database of Systematic Reviews, le Programme DARE et Health Technology Assessment. Nous avons inclus dans notre analyse des études quantitatives comportant une section sur les méthodes et qui ont signalé des conflits d'intérêts à la suite du financement par l'industrie de recherches en chirurgie.

Résultats : La recherche a dégagé 190 études qui répondaient à nos critères. Les conflits d'intérêts des auteurs ou chercheurs qui étaient attribuables à des liens financiers avec l'industrie associée à la recherche universitaire sont bien documentés dans les publications chirurgicales. Six études ont démontré que les auteurs ayant de tels conflits d'intérêts étaient beaucoup plus susceptibles de signaler un résultat positif que ceux qui n'avaient pas reçu de financement de l'industrie, ce qui démontre l'existence d'un biais

en faveur de l'industrie. Les études ont révélé que ce biais ne pouvait être expliqué par les variations de la qualité des études ou de la taille de l'échantillon.

Conclusion : Le conflit d'intérêts qui existe lorsque l'industrie commande des recherches en chirurgie constitue une réelle préoccupation.

Evidence-based medicine has had increasing influence in day-to-day clinical decision-making within the practice of surgery. The best available evidence is founded on the comprehensive and systemic evaluation of the literature, ideally in the form of a meta-analysis or systematic review. The strength of a specific treatment recommendation is based on the quality (level) of evidence within the literature and on clinical experience and patient preference, the latter taking risk, onus and cost into consideration.¹ Clinical experience and patient preference constitute subjective but necessary components of evidence-based medicine in patient care, whereas research is more objectively measured through methodologic evaluation. Good evidence is contingent on good research. The more rigorous the methodology of a study, the better the control of systematic bias and the higher the level of the evidence. However, high-quality research, such as randomized controlled trials, remain challenging, especially in surgery, owing to problems related to blinding, equipoise, patient preference, generalizability and, of particular relevance to this study, prohibitive costs.²

Funding available for medical research can be sought from numerous sources, including government agencies, foundations, academic institutions, medical or surgical societies and industry. Over the last few decades medical research and development has come to depend more heavily on the financial support of industry. In 1980, 32% of total biomedical research was funded by industry; this figure increased to 62% in 2000.³ In 1986, 46% of life science companies supported academic research; within 10 years this figure increased to 92%.³

Although industry funding can lead to medical and technologic advances and provide an opportunity to validate new technologies, the industrial support of biomedical research has come under increasing scrutiny within the scientific community, government, media and public. The major concern is that financial relations between the medical community and medical industry could unduly influence medical research and therefore patient care.⁴ It is well recognized that the collaboration of industry and academic researchers may create a conflict of interest.^{3,5-10}

Conflict of interest, defined as a set of conditions in which professional judgment concerning a "primary interest" tends to be unduly influenced by "secondary interest,"¹¹ introduces a common form of nonscientific bias into biomedical research. Primary interest to a physician is a patient's welfare and to a scientist is the validity of the research. Secondary interest includes personal financial gain, research funding and academic pressure to publish. In

2003, Beckelman and colleagues³ illustrated the scope of this potential conflict: one-quarter of all academic biomedical researchers receive industry funding, one-third of all universities have financial ties with industry sponsors, and one-third of lead authors have personal financial interest in their study topic. Society's perception of this potential conflict is still not clear, especially when the research may not be possible without industry support.¹²

It has been demonstrated in the medical literature that industry funding adversely affects the validity of the research by producing a proindustry result or conclusion.^{3,5-10,13,14} A systematic review of the medical literature reported that the odds of a study having a positive outcome is 3.6 times greater when the research is industry-sponsored.³ Whereas the potential influence of industry funding on the outcomes of medical research has been extensively discussed in the literature, the data related to surgical research are less clear. We undertook a systematic review of the literature to determine whether conflict of interest owing to authors'/investigators' financial affiliation with industry associated with their academic research has been identified in the surgical literature. We sought to examine the extent of this conflict as well as the influence of industry funding on the research results.

METHODS

We performed a systematic review to answer the following questions: What is the extent of author/investigator conflict of interest owing to industry funding of their surgical research or financial affiliation to industry associated with the research (e.g., royalties)? Does author conflict of interest bias the results of academic surgical research in favour of industry? What are the potential causes of the proindustry bias? We conducted a literature search in May 2008 using the OVID SP search engine of the databases MEDLINE (1966-2008), EMBASE (1980-2008), Cumulative Index to Nursing and Allied Health Literature (CINAHL; 1982-2008), the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment. We used the keywords "conflict of interest," "publication bias," "positive outcome bias," "surgery," "research support" and "biomedical research." The search strategy is summarized in Box 1. The review was limited to studies published in English. We further reviewed the bibliographies of the selected studies meeting our inclusion criteria, outlined in the next paragraph, to complement our database search strategy.

We included quantitative studies that contained a methods section and reported specifically on conflict of interest as a result of industry funding in surgery-related research. Studies that included both medical and surgical research were included only if results pertaining to the surgical literature could be analyzed separately. Editorials, narrative reviews, commentaries and letters to the editor were excluded. The abstracts of all articles that matched the search terms and met our inclusion criteria were reviewed. We then obtained the full text version of abstracts that we felt were suitable. These articles were reviewed for data relevant to the research question. Any discrepancy on the selection of articles was resolved by discussion among 2 reviewers.

RESULTS

The literature search identified 190 studies; 8 satisfied our inclusion parameters (Table 1). Six of 8 studied the orthopedic literature,^{4,15,16,18,19,21} 1 the spine literature,²⁰ and 1 the combined literature from the disciplines of orthopedic surgery, neurosurgery, general surgery and plastic surgery.¹⁷

Our systematic review demonstrated that authors' investigators' conflict of interest owing to financial affiliation with industry associated with their academic research was well documented in the surgical literature.^{4,12,15-21} Although specific to orthopedic research, Zuckerman and colleagues⁴ demonstrated that author self-reported conflict of interest involving research presented at a national annual meeting in the United States had substantially increased from 10% in 1985 to 32% in 2002 ($p < 0.001$).

Six studies demonstrated that authors with such conflicts of interest were significantly more likely to report a positive outcome than authors without industry funding, which demonstrates a proindustry bias.^{15-18,20,21} Bhandari and colleagues¹⁷ found that, although not statistically significant, the odds ratio of a proindustry conclusion was 5 times greater in a surgical trial than in an industry-sponsored drug trial.

One potential explanation for this proindustry bias is that industry-funded studies are of higher scientific quality than non-industry funded studies owing to disproportionate funding levels provided by industrial sources. However, 2 studies found that proindustry bias could not be ex-

plained by variations in study quality or sample size.^{17,21} Cunningham and colleagues²¹ found that prospective study design, use of control groups and larger sample size were not more prevalent in industry-sponsored than in non-industry sponsored research, yet the industry-sponsored studies were more likely to conclude with a proindustry outcome. Similarly, Bhandari and colleagues¹⁷ found that neither discrepancy in study quality (assessed using the Detsky Index) nor sample size could explain the proindustry bias associated with industry sponsorship.

A final study included in our review contradicted those mentioned previously. Lynch and colleagues¹⁹ analyzed manuscripts submitted to the *Journal of Bone and Joint Surgery* (the other studies analyzed only research published in journals or presented at meetings) for an association between both scientific and nonscientific factors (including funding source) and outcome bias.¹⁹ They found that industry-funded research was more likely to be published than non-industry funded research but that source of funding was not associated with a positive study outcome and that a positive study outcome was not itself a predictor of acceptance after peer review. However, a low-level form of bias against non-positive outcome studies during peer review was suspected because the quality of the non-positive outcome studies was superior to that of the positive-outcome studies, but the acceptance rate was similar.

DISCUSSION

Our systematic review of the surgical literature suggests that authors' financial conflicts of interest and industry sponsorship of studies examining medical devices or related products exerts a bias toward proindustry results. Furthermore, it appears that the outcome bias in the surgery-related research literature is at least equal to if not greater than that in the medical literature, specifically drug trials.¹⁷ Although the study by Lynch and colleagues¹⁹ used a more robust methodology than the others (examining all submitted manuscripts as opposed to only those published in journals or presented at peer-reviewed meetings), the discrepancy in findings does not negate the significance of the proindustry outcome bias demonstrated by the other studies. Lynch and colleagues¹⁹ themselves state that their methodology included only manuscripts submitted to 1 journal and was specific to hip and knee reconstruction and therefore not necessarily generalizable to other subspecialties in orthopedics, other specialties in surgery or other journals. The fact that submitted, rather than presented or published, manuscripts were analyzed cannot explain the difference among findings in the study by Lynch and colleagues and those of all other studies included in this review. It is unknown if the reason lies in the combination of the low-level bias against non-positive outcome studies in the peer review process and the greater likelihood of manuscript publication for industry-funded research.¹⁹

Box 1. Search strategy

1. Conflict of interest.mp or "conflict of interest"/
2. Publication bias/
3. Positive outcome bias.mp
4. Surgery/or surgery.mp
5. 1 or 2 or 3
6. 4 and 5
7. Research support as topic/or research support.mp
8. Biomedical research.mp or biomedical research/
9. 7 and 8 and 4
10. 6 or 9

Limitations

There are limitations to our study. It is not generalizable beyond the English surgical literature. The true extent of conflict of interest and proindustry bias cannot be determined by the methodology of the included studies because conflict of interest was self-reported. Therefore, it is possible that the true incidence may be higher. Finally, as conflict of interest is self-reported, author compliance with reporting may be increasing and may account for some of the perceived increase in conflict of interest reported by Zuckerman and colleagues⁴ and others.^{3,5,6}

We find it interesting that most of the inquiry into the extent and impact of industry-sponsored research in surgery was in the specialties of orthopedic and spine surgery. Okike and colleagues¹⁶ found that self-reported conflict of interest was common in orthopedic surgery, but mostly for hip and knee reconstruction and spine surgery, and represented about 50% of all research presented at the

2001 and 2002 annual meetings of the American Academy of Orthopaedic Surgeons. In fact, 3 of the 8 reports included in this study investigate research specific to these subspecialties.¹⁸⁻²⁰ Considering that most orthopedic and spine surgeries require the implantation of a surgical device, it is not surprising that the industry-related conflict of interest literature focuses on those disciplines. Although we identified only 1 paper that satisfied our inclusion criteria and investigated conflict of interest in other surgical specialties,¹⁷ we found many editorials discussing concerns in other areas of surgery.²²⁻²⁸

The conflict of interest that exists when surgical research is sponsored by industry seems unavoidable but does not necessarily mean that the research is biased or that the researcher is corrupt.^{15,16,18} Nevertheless, a proindustry bias is a genuine concern in the surgical literature. The challenge is to identify and manage the conflict, hence the author's obligation to disclose his or her conflicts of interest and allow the readers to decide for themselves if a bias exists.

Table 1. Studies included in a systematic review of the literature on conflict of interest owing to authors'/investigators' affiliation with industry associated with their research

Study	Year	Discipline	Purpose	Source	Finding
Leopold et al. ¹⁵	2003	Orthopedic	Assess potential association between research outcome and external factors, including industry funding	Article review in 3 orthopedic journals published between July 1999 and June 2000	Industry-funded studies were significantly more likely to report positive outcome than non-industry funded studies
Okike et al. ¹⁶	2007	Orthopedic	Investigate the association between different types of conflict of interest and study outcome	Podium presentation review at a national orthopedic annual meeting in 2001 and 2002	Authors with a conflict of interest (e.g., royalties, stock options, consulting/employee status) were more likely to report positive outcome
Bhandari et al. ¹⁷	2004	Surgery	Determine whether association between industry funding and conclusions are generalized to surgical specialties	RCTs published between January 1999 and June 2001 in 8 surgical and 5 medical journals	Industry funding was significantly associated with statistically significant proindustry results; variations in study quality or sample size did not explain proindustry findings
Zuckerman et al. ⁴	2004	Orthopedic	Determine the frequency and type of self-reported conflict of interest between orthopedic research and industry	Final program from a national orthopedic annual meeting in 1985, 1988, 1992, 1997, 1999 and 2002	Industrial research support increased significantly between 1995 and 2002; the proportion of support to individual authors rather than to institutions increased significantly
Ezzet ¹⁸	2003	Orthopedic	Define the prevalence of commercial funding in adult lower extremity research and correlation of funding with reported outcomes	Presentations at 2002 national orthopedic meeting and journal articles published in 2001 in 3 orthopedic journals	Research sponsored by industry was more likely to report a proindustry outcome than studies funded independently
Lynch et al. ¹⁹	2007	Orthopedic	Determine if nonscientific variables, including commercial funding, are associated with positive outcomes and acceptance for publication	Manuscripts on hip and knee arthroplasty submitted to <i>JBJS</i> from January 2004 to June 2005, excluding resubmissions, reviews, case reports, editorials and basic science studies	Industry-funded studies were not more likely to conclude a positive outcome, and positive outcome was not more likely to be published; however, non-positive outcome studies were of higher quality, which suggests an insidious bias against publication; industry-funded studies were more likely to be published
Shah et al. ²⁰	2005	Spine	Evaluate association between industry funding and positive research finding	Articles published in <i>Spine</i> from January 2002 to July 2003	Industry-funded studies demonstrated a greater likelihood to report positive results than studies funded independently
Cunningham et al. ²¹	2007	Orthopedic	Assess potential association between nonscientific factors (funding source), scientific factors (study design) and positive study outcome	Abstracts presented at a national orthopedic annual meeting in 2004	Commercial funding was associated with positive outcomes, but those studies did not have better designs or larger samples than non-industry funded studies

JBJS = *Journal of Bone and Joint Surgery*; RCT = randomized controlled trial.

One possible explanation for the apparent bias is a discrepancy in research quality. As industry funding typically provides superior financial support, it has been hypothesized that the result will be improved or higher-level study design with better study administration and an increased sample size, reducing the risk of type- β error. This concept, however, was challenged by the findings of 2 papers included in our review.^{17,21} Clearly, companies are going to be selective in their funding and are more likely to invest in research that will prove beneficial to their products. Bio-medical companies conduct considerable in-house research to preferentially fund academic collaboration that will be successful and result in positive studies.^{6,29,30} We agree with Cunningham and colleagues²¹ that, unlike with drug trials, it is very difficult for a company to perform human in-vivo testing on surgical implants or devices without the involvement of an academic surgeon/researcher. Thus, this explanation is less likely to account for positive outcome bias in surgical trials and warrants further consideration.²¹

Another explanation for the apparent proindustry bias is documented in the medical literature. It has been suggested that trials may be stopped prematurely or a sponsoring company may attempt to obstruct publication of the results if the findings of the study are negative.³¹⁻³⁴ Although these occurrences have not been directly investigated in the surgical literature, 2 publications in our review demonstrated that studies involving researchers with consultant/employee status, royalties or stock options were associated with a higher likelihood of a positive outcome than those involving researchers who received only research support.^{16,18} This implies a more sinister possibility that some investigators may be swayed by secondary interests and, in doing so, disregard the primary interest of study validity.

Even if industry support does not influence investigator behaviour, a negative public perception could jeopardize trust in the scientific community. With this in mind, a recent survey of 245 patients in an orthopedic spine surgeon's office found that "despite adverse publicity in the popular press in the past few years about physicians and conflict of interest issues, the public is overwhelmingly in favour of allowing surgeons to work with industry because of its potential beneficial effect for patients."³⁵

Distinct benefits exist in the collaboration between industry and academic research in surgery for the physician/scientist, industry sponsor and the public. The fact that proindustry bias is present in the surgical literature is worrisome, but the causes behind it are not clear and may be only partially related to true conflict. The findings of our study do, however, imply that the self-reporting of conflicts of interest is not sufficient to ensure integrity in the research and public trust and that further reflection and evaluation by all the key stakeholders is warranted. Further safeguards should be implemented, such as restriction of authorship for surgeons with significant financial conflicts, and partnership between major players, both academic and

industry, to create independent clinical trial groups that minimize actual and perceived bias.

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Contributors: Drs. Bailey and Fisher designed the study and acquired the data, which all authors analysed. Drs. Bailey, Fehlings and Fisher wrote the article, which all authors reviewed and approved publication.

References

- Schünemann HJ, Jaeschke R, Cook DJ, et al. An official ATS statement: grading the quality of evidence and strength of recommendations in ATS guidelines and recommendations. *Am J Respir Crit Care Med* 2006;174:605-14.
- Emanuel EJ, Schnipper LE, Kamin DY, et al. The costs of conducting clinical research. *J Clin Oncol* 2003;21:4145-50.
- Bekelman JE, Li Y, Gross CP. Scope and impact of financial conflicts of interest in biomedical research: a systematic review. *JAMA* 2003; 289:454-65.
- Zuckerman JD, Prasarn M, Kubiak EN, et al. Conflict of interest in orthopaedic research. *J Bone Joint Surg Am* 2004;86-A:423-8.
- Cho MK, Bero LA. The quality of drug studies published in symposium proceedings. *Ann Intern Med* 1996;124:485-9.
- Davidson RA. Source of funding and outcome of clinical trials. *J Gen Intern Med* 1986;1:155-8.
- Kjaergard LL, Als-Nielsen B. Association between competing interests and authors' conclusions: epidemiological study of randomised clinical trials published in the BMJ. *BMJ* 2002;325:249.
- Lexchin J, Bero LA, Djulbegovic B, et al. Pharmaceutical industry sponsorship and research outcome and quality: systematic review. *BMJ* 2003;326:1167-70.
- Als-Nielsen B, Chen W, Gluud C, et al. Association of funding and conclusions in randomized drug trials: A reflection of treatment effect or adverse events? *JAMA* 2003;290:921-8.
- Rochon PA, Gurwitz JH, Simms RW, et al. A study of manufacturer-supported trials of nonsteroidal anti-inflammatory drugs in the treatment of arthritis. *Arch Intern Med* 1994;154:157-63.
- Thompson DF. Understanding financial conflicts of interest. *N Engl J Med* 1993;329:573-6.
- Mirza SK. Accountability of the accused: facing public perceptions about financial conflicts of interest in spine surgery. *Spine J* 2004;4:491-4.
- Finucane TE, Boulton CE. Association of funding and findings of pharmaceutical research at a meeting of a medical professional society. *Am J Med* 2004;117:842-5.
- Montgomery JH, Byerly M, Carmody T, et al. An analysis of the effect of funding source in randomized clinical trials of second generation antipsychotics for the treatment of schizophrenia. *Control Clin Trials* 2004;25:598-612.
- Leopold SS, Warme WJ, Fritz BE, et al. Association between funding source and study outcome in orthopaedic research. *Clin Orthop Relat Res* 2003; (415):293-301.
- Okike K, Kocher MS, Mehlman CT, et al. Conflict of interest in orthopaedic research. An association between findings and funding in scientific presentations. *J Bone Joint Surg Am* 2007;89:608-13.
- Bhandari M, Busse JW, Jackowski D, et al. Association between

- industry funding and statistically significant pro-industry findings in medical and surgical randomized trials. *CMAJ* 2004;170:477-80.
18. Ezzet KA. The prevalence of corporate funding in adult lower extremity research and its correlation with reported results. *J Arthroplasty* 2003;18(Suppl 1):138-45.
 19. Lynch JR, Cunningham MR, Warne WJ, et al. Commercially funded and United States-based research is more likely to be published; good-quality studies with negative outcomes are not. *J Bone Joint Surg Am* 2007;89:1010-8.
 20. Shah RV, Albert TJ, Bruegel-Sanchez V, et al. Industry support and correlation to study outcome for papers published in *Spine*. *Spine* 2005;30:1099-104.
 21. Cunningham MR, Warne WJ, Schaad DC, et al. Industry-funded positive studies not associated with better design or larger size. *Clin Orthop Relat Res* 2007;457:235-41.
 22. Foster RS. Conflicts of interest: recognition, disclosure, and management. *J Am Coll Surg* 2003;196:505-17.
 23. Habal MB. The new science of craniofacial surgery in the form of research and development in the corporate world. *J Craniofac Surg* 2007;18:245-7.
 24. Jones JW, McCullough LB. Surgeon-industry relationships: ethically responsible management of conflicts of interest. *J Vasc Surg* 2002;35:825-6.
 25. McKneally MF. Beyond disclosure: managing conflicts of interest to strengthen trust in our profession. *J Thorac Cardiovasc Surg* 2007;133:300-2.
 26. Rohrich RJ. Plastic surgery journals: a meeting of minds in Berlin. *Plast Reconstr Surg* 2007;120:2101-5.
 27. Sade RM, McKneally M. Responsibilities of investigators. *Ann Thorac Surg* 2002;73:1364-5.
 28. White AP, Vaccaro AR, Zdeblick T. Counterpoint: physician-industry relationships can be ethically established, and conflicts of interest can be ethically managed. *Spine* 2007;32(Suppl):S53-7.
 29. Djulbegovic B, Lacey M, Cantor A, et al. The uncertainty principle and industry-sponsored research. *Lancet* 2000;356:635-8.
 30. Hirsch L. Randomized clinical trials: What gets published, and when? *CMAJ* 2004;170:481-3.
 31. Blumenthal D, Campbell EG, Anderson MS, et al. Withholding research results in academic life science. Evidence from a national survey of faculty. *JAMA* 1997;277:1224-8.
 32. Boyd K. Early discontinuation violates Helsinki principles [commentary]. *BMJ* 2001;322:605-6.
 33. Lièvre M, Menard J, Bruckert E, et al. Premature discontinuation of clinical trial for reasons not related to efficacy, safety, or feasibility. *BMJ* 2001;322:603-5.
 34. Rennie D. Thyroid storm. *JAMA* 1997;277:1238-43.
 35. Khan MH, Lee JY, Rihn JA, et al. The surgeon as a consultant for medical device manufacturers: What do our patients think? *Spine* 2007;32:2616-8.

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