

Not the Last Word

Everyone (Else) is Conflicted

Joseph Bernstein MD

“It is tempting if all you have is a hammer, to treat every problem as a nail,” the psychologist Abraham Maslow said.

Note from the Editor-in-Chief: We are pleased to present to readers of Clinical Orthopaedics and Related Research® the next installment of “Not the Last Word,” a bimonthly column. The goal of this section is to explore timely and controversial issues that affect how orthopaedic surgery is taught, learned, and practiced. We welcome reader feedback on all of our columns and articles; please send your comments to eic@clinOrthop.org.

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Orthopaedic surgeons have more than just hammers — they have saws, clamps, and chisels too. Nonetheless, they may be tempted to see all musculoskeletal complaints as problems amenable to surgical treatment; that is just a byproduct of their training and socialization. They earn their pay by treating musculoskeletal complaints with hammers. For some, fame and academic advancement comes with writing papers exalting the hammer. In short, orthopaedic surgeons are under the sway of “competing interests” long before they accept a free meal, a free pen, or a free vacation. The disclosure policies of many journals and organizations (emphasizing cash and swag from industry) tend to miss that point.

Consider the biases that may affect an orthopaedic surgeon who invents a surgical procedure such as the percutaneous fixation of the lumbar facet joints to treat mechanical low back pain. The operation is touted on television and Twitter; the surgeon builds a large practice and the country house that comes with it. The surgeon lectures around the world and publishes scores of articles describing the procedure. For all of these spoils, however, a declaration of competing interests is not required unless the surgeon accepts money from a

commercial firm. Clearly, this process of disclosure is inadequate.

The process of disclosure may even be counterproductive. Research has shown that the very act of disclosing a conflict could liberate a reporter to skew his presentation. This phenomenon has been termed “moral licensing” [8].

In their 2012 study, Loewenstein and colleagues [8], divided research participants into two groups: Estimators (asked to guess the number of coins in a jar, after viewing the jar briefly and from a distance) and Advisors (subjects who were allowed unlimited time to view the coin jars up close, and in turn, asked to provide advice to the Estimators). In one scenario, the researchers rewarded both the Estimators and the Advisors when the Estimators correctly guessed the number of coins in the jar. For the second iteration, the researchers created a conflict. They rewarded Estimators for accurate guesses, whereas the Advisors were told privately that they would be paid more with each inaccurate guess. Not surprisingly, the Advisors offered bad advice. Interestingly, when the second form was repeated with public acknowledgement that the Advisors were conflicted, the quality of the advice worsened. “The bias was substantially greater when the

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conflict of interest was disclosed,” Loewenstein and colleagues wrote [8].

Current measures aimed at limiting bias need improvement. Although it may be tempting to treat every problem of bias with an even stronger disclosure process, there are, in fact, better options on the table. Stronger disclosures do not address the moral licensing problem. Exceptionally stringent disclosure policies could even dissuade researchers from publishing in peer-reviewed literature altogether.

Biases cannot be eliminated, but they can be balanced. Hence, the proper approach to a potentially biased paper such as “The Bernstein Procedure: Percutaneous Lumbar Facet Fixation for Treatment of Mechanical Low Back Pain” by J. Bernstein MD, is not necessarily to reject it. It is likewise not helpful to inundate the reader with a list of conflicts, real or imagined. The best approach is to publish the paper, “The Safe and Inexpensive Treatment of Mechanical Low Back Pain with NSAIDs and Exercise.”

Beyond the issue of personal conflicts of interest, the real bias in the literature is that journal reviewers favor positive results, studies that echo the prevailing paradigms, and findings that support greater clinical activity. In a better world, journals would publish all valid studies regardless of topic, potential interest to readers, or findings [2]. PLoS ONE, a peer-reviewed open access journal, uses this model — although it is

far from the publishing standard. For now, editors can do more to combat bias by publishing papers that refute prior studies; papers that investigate “orphan” interventions not generally supported by industry (nonoperative care, generic drugs, off-patent devices); and papers that report negative results [6], even with low power (such that they may be available for meta-analysis).

Overall, the best response to potentially biased work is not to festoon it with lengthy and stifling disclosure statements (though if disclosures are to be made, the dollar amounts received should be included as well, as there is a qualitative difference between, say, five hundred dollars and five million dollars). The best response to biased work is to rebut it. As Supreme Court Justice Louis Brandeis said in a case involving potentially dangerous teaching, “The remedy to be applied is more speech, not enforced silence.”

Commentary

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We are all conflicted at some level. This issue is not whether we have a conflict or not, but how we manage the conflict in our daily work and academic

interactions. All of us are influenced, to some extent, by our environments, our industry, and our peers. In academics, the current approach taken by most associations and journals has been to impose mandatory, exhaustive reporting of our conflicts, and to do so each year. This process has its origins in the belief that greater transparency in academics will allow improved translation of knowledge; it has been fueled by recent negative publicity of surgeon-industry relationships in orthopaedics.

As part of a 2007 settlement with the US Department of Justice, Biomet Inc (Warsaw, IN, USA), DePuy, a Johnson & Johnson company (Warsaw, IN, USA), Smith & Nephew Inc (Memphis, TN, USA), Stryker Orthopaedics (Mahwah, NJ, USA), and Zimmer Inc (Warsaw, IN, USA) were required to report publicly all physician payments related to hip and knee arthroplasty [11]. More than 40% of the payments to surgeons exceeded USD 100,000 [11]. We have shown that positive study findings are more common in studies authored by individuals with a conflict of interest related to royalties [10]. The result of all this been a growing mistrust of researchers and surgeons who report industry funding or related conflicts in a study favoring an industry product. I believe, though, that the problem lies not the fact that conflicts exist, but rather how they are managed and interpreted by the community at large.

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In support of Dr. Bernstein's position, stronger and lengthy disclosures do not solve the problem. The absolute test of a strongly positive claim of the treatment effectiveness of a new drug, device or technique, is its "staying power." The more investigators can independently confirm, or refute, a clinical trial, the greater the validity of a study finding. Multiple clinical trials on a study question should be encouraged and widely published, especially those that challenge a previous trial.

This is especially true in orthopaedic surgery, where average trial sizes are small; studies in our literature often enroll fewer than 100 patients, and so are extremely prone to Type II (false negative) or spurious Type I (false positive) errors [13]. These small trials, which often report few total outcome events are highly correlated with very large and generally implausible treatment effects [13]. Studies with fewer than 50 total outcome events that favor a new drug or device should be viewed with considerable skepticism until confirmed by other independently conducted clinical trials. Even a small change in distribution of outcome across the treatment and control arms could change the significance of the results.

One poignant example involves research on BMP-2 and its possible effect on reoperation rates in open tibial shaft fractures [1, 7]. The original and pivotal industry-funded trial of 450 patients (which contained 41 total

outcome events, specifically, reoperations) identified a significant reduction in the risk of reoperation with BMP-2 treatment compared to controls (12/135 versus 29/139, $p = 0.02$) [7]. But this trial's main finding could have been reversed by simply three outcome events moving from one group to another. As it turns out, a subsequent randomized trial of 277 patients (23 reoperations with BMP versus 21 reoperations in controls; total outcome events: 44) refuted the improved treatment effect of BMP-2 in open fractures of the tibia. Additional followup studies are needed to validate or disprove a single, positive study with a small number outcome events that concludes in favor of a new treatment [1].

Conflicts of interest are ubiquitous. Whether reported extensively or not, assume investigators are conflicted. The mere presence of industry funding and reported conflicts should not be the reason to disbelieve a study. Rather, the mere presence of just a single positive (or negative) small trial should create more concern.

Commentary

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There is good reason to share Dr. Bernstein's skepticism regarding

the negative effects of required disclosures. Although disclosures are a popular response to the conflicts of interest present in the practice of modern medicine, evidence suggests that they do not represent a panacea. On the contrary, they may even exacerbate the ills that they are designed to treat.

Journals implement disclosure requirements because they want readers to understand the incentives that may have shaped the views represented in published evidence. However, my research with Loewenstein and Cain [4, 5] suggests that disclosure may actually increase the bias it is intended to address. In our studies, when people knew that their advice to customers would come with a disclosure of how they would get paid, they felt licensed by that honest revelation to indulge in giving more self-serving advice. The implication is that doctors who disclose financial conflicts of interest may be morally freed to indulge in offering advice and conclusions that serve their financial self-interest [3].

Disclosure falls short of an ideal solution for consumers of expert advice as well. How should a patient respond to her physician's honest disclosure of a conflict of interest? Let us say your doctor tells you that she is on the board of, and owns stock in, the firm that sells the medical device she is prescribing you. Suddenly, to consider

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other treatments implies that you suspect your doctor's motives. The disclosure that was meant to protect consumers turned into a burden that makes them feel obligated to follow their doctor's advice — or even to help the doctor out [12].

I wholeheartedly support Bernstein's call for more research on orphan interventions and well-designed studies with negative results that might question the efficacy of a common treatment. The inevitable move to open-access publishing is an essential and highly overdue step toward increasing the speedy availability of research results [9]. But making it easier to publish this sort of research will not do much if there are no papers to publish. If no firm, institution, or agency is ready to sponsor research showing the lack of a therapeutic difference between costly branded drugs and their cheaper generic alternatives, then there will be no papers to publish. The truth is that profits drive not just what research gets put into practice, but what research gets done in the first place.

The stronger solution to conflicts of interest is divestiture. It is not enough to disclose payments from drug manufacturers. Many of those payments should be prohibited. Hospitals, medical schools, and professional societies can do much more to demonstrate their commitment to truth, honesty, and the well-being of patients by restricting

the corrupting influence of outside payments. These divestitures will be costly: it means me saying no to enticing benefits. But they are the responsible thing to do.

References

1. Aro HT, Govender S, Patel AD, Hernigou P, Perera de Gregorio A, Popescu GI, Golden JD, Christensen J, Valentin A. Recombinant human bone morphogenetic protein-2: a randomized trial in open tibial fractures treated with reamed nail fixation. *J Bone Joint Surg Am.* 2011;93:801–808.
2. Bernstein J, Ahn J, Veillette C. The future of orthopaedic information management. *J Bone Joint Surg Am.* 2012;94:e95.
3. Cain DM, Detsky AS. Everyone's a little bit biased (even physicians). *JAMA.* 2008;299:2893–2895.
4. Cain DM, Loewenstein G, Moore DA. The dirt on coming clean: perverse effects of disclosing conflicts of interest. *Journal of Legal Studies.* 2005;34:1–25.
5. Cain DM, Loewenstein G, Moore DA. When sunlight fails to disinfect: understanding the perverse effects of disclosing conflicts of interest. *Journal of Consumer Research.* 2010;37:836–857.
6. Emerson GB, Warme WJ, Wolf FM, Heckman JD, Brand RA, Leopold SS. Testing for the presence of positive-outcome bias in peer review: a randomized controlled trial. *Arch Intern Med.* 2010;170:1934–1939.
7. Govender S, Csimma C, Genant HK, Valentin-Opran A, Amit Y, Arbel R, Aro H, Atar D, Bishay M, Börner MG, Chiron P, Choong P, Cinats J, Courtenay B, Feibel R, Geulette B, Gravel C, Haas N, Raschke M, Hammacher E, van der Velde D, Hardy P, Holt M, Josten C, Ketterl RL, Lindeque B, Lob G, Mathevon H, McCoy G, Marsh D, Miller R, Munting E, Oevre S, Nordsletten L, Patel A, Pohl A, Rennie W, Reynders P, Rommens PM, Rondia J, Rossouw WC, Daneel PJ, Ruff S, Rüter A, Santavirta S, Schildhauer TA, Gekle C, Schnettler R, Segal D, Seiler H, Snowdowne RB, Stapert J, Taglang G, Verdonk R, Vogels L, Weckbach A, Wentzensen A, Wisniewski T. BMP-2 evaluation in surgery for tibial trauma (BESTT) study group. Recombinant human bone morphogenetic protein-2 for treatment of open tibial fractures: a prospective, controlled, randomized study of four hundred and fifty patients. *J Bone Joint Surg Am.* 2002; 84A:2123–2134.
8. Loewenstein G, Sah S, Cain DM. The unintended consequences of conflict of interest disclosure. *JAMA.* 2012;307:669–670.
9. Nosek BA, Bar-Anan Y. Scientific utopia: I. opening scientific communication. *Psychological Inquiry.* 2012;23:217–243.
10. Okike K, Kocher MS, Mehlman CT, Bhandari M. Conflict of interest in orthopaedic research. An association between findings and funding in scientific presentations. *J Bone Joint Surg Am.* 2007;89:608–613.
11. Okike K, Kocher MS, Wei EX, Mehlman CT, Bhandari M. Accuracy

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- of conflict-of-interest disclosures reported by physicians. *N Engl J Med.* 2009;361:1466–1474.
12. Sah S, Loewenstein G, Cain DM. The burden of disclosure: Increased compliance with distrusted advice. *J Pers and Soc Psychol.* 2013;104:289–304.
13. Sung J, Siegel J, Tornetta P, Bhandari M. The orthopaedic trauma literature: an evaluation of statistically significant findings in orthopaedic trauma randomized trials. *BMC Musculoskelet Disord.* 2008;9:14.