

# THE ORTHOPAEDIC FORUM

## Levels of Influence

### Habituation and the Prevalence of Declared Conflicts of Interest

Jillian R.H. Bernstein, George Maliha, AB, Jaimo Ahn, MD, PhD, and Joseph Bernstein, MD, MS

*Investigation performed at Haverford High School, Havertown, Pennsylvania, and the University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania*

**Background:** The International Committee of Medical Journal Editors has devised a system of mandatory disclosure, under which authors are required to disclose all conflicts of interest and the sources of support for the submitted research. Because payments from industry to physicians generally are common, it is likely that many authors of medical manuscripts will have information to disclose. As a result, the signal-to-noise ratio of such declarations may be low, thereby undermining the effectiveness of disclosure. To our knowledge, the comparative prevalence of such conflicts has not been reported.

**Methods:** We identified 100 consecutive scientific articles from the 2014 volumes of 3 journals with high impact factors: *Pediatrics*, *The Journal of Bone & Joint Surgery (JBJS)*, and *The New England Journal of Medicine (NEJM)*. Each study was categorized by funding source and other relationships with industry.

**Results:** In *Pediatrics*, 17 of 100 studies had a declared relationship with industry. Industry relationships were declared in 68 and 77 of the studies in JBJS and NEJM, respectively.

**Conclusions:** Industry relationships were common in studies in NEJM and JBJS, but rare in *Pediatrics*. The high prevalence of conflicts of interest may weaken the meaning of declarations and undermine any bias-reducing effect intended by the disclosure system.

**Peer Review:** This article was reviewed by the Editor-in-Chief and one Deputy Editor, and it underwent blinded review by two or more outside experts. The Deputy Editor reviewed each revision of the article, and it underwent a final review by the Editor-in-Chief prior to publication. Final corrections and clarifications occurred during one or more exchanges between the author(s) and copyeditors.

Financial relationships between scientists and industry can skew the presentation of research because researchers, consciously or not, adapt to please their patrons. Bekelman et al. have reported a “significant association between industry sponsorship and pro-industry conclusions.”<sup>1</sup> Still, it is neither feasible

nor desirable to ban financial relationships between researchers and industry. Conducting research is expensive<sup>2</sup>, and money can be an appropriate incentive<sup>3</sup> for high-quality work.

To balance the desires of authors to have financial relationships and the needs of readers to know when authors may

**Disclosure:** No external funding was received for this study. The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article.

**TABLE 1** Distribution of 100 Articles According to Level of Influence\*

Journal	Level A	Level B	Level C	Level D
<i>Pediatrics</i>	16	67	12	5
<i>The Journal of Bone &amp; Joint Surgery</i>	21	11	52	16
<i>The New England Journal of Medicine</i>	2	21	35	42

\*Level A: no external funding, and no author has a relationship with industry. Level B: funding by government or not-for-profit entity only, and no author has a relationship with industry. Level C: not funded by industry, but 1 or more authors has a relationship with industry. Level D: sponsored by industry.

be subject to biases, the International Committee of Medical Journal Editors (ICMJE) has devised a system of mandatory disclosure<sup>4</sup>, and authors are required to disclose “all financial and personal relationships that might bias or be seen to bias their work.”

There are a few reasons why the ICMJE approach may not be effective<sup>5</sup>. The information provided by authors is not audited and, therefore, may not be accurate<sup>6</sup>. Also, disclosures typically omit the magnitude of the financial relationship. Additionally, disclosure statements do not help to detect any repression of results; when researchers refrain from publishing at the behest of their sponsor, no forms are filed. More fundamentally, as Loewenstein et al. have suggested, the process of disclosure may encourage writers to adopt a “let the reader beware” attitude and liberate researchers to be even more biased in their presentations<sup>7</sup>.

Even if these concerns were not an issue, disclosure may fail to edify the readers when a high percentage of all manuscripts in a given journal report relationships. In such a setting, the disclosure of a single relationship provides a scant signal above the background noise<sup>8</sup>. As a result, readers might become habituated to the routine disclosure statement.

Habituation has been defined as “a behavioral response decrement that results from repeated stimulation.”<sup>9</sup> In less technical terms, habituation refers to the process by which something that once was interesting becomes less interesting over time as the novelty wears off. Accordingly, the research question posed here is, “What is the prevalence of financial relationships between industry and authors of articles in medical journals?”

Financial relationships between researchers and industry are likely to be common since payments to physicians from industry generally are common. Data from the Open Payments program of the Centers for Medicare and Medicaid Services (which provides information about the payments that drug and device companies make to physicians) reveal that over a 5-month period (August 1, 2013, to December 31, 2013), in-

dustry payments to physicians totaled \$475 million—a sum that extrapolates to more than \$1 billion annually<sup>10</sup>.

It is not a premise of this study that a certain prevalence of financial relationships necessarily indicates a problem. In fact, if the American Academy of Orthopaedic Surgeons (AAOS) is correct in its assertion that “cooperative relationships between orthopaedic surgeons and industry benefit patients,”<sup>11</sup> a high prevalence of financial relationships might be a good thing. Rather, the premise of this study is that if the goal of disclosure is to inform readers, then it would be important to know the rate of such disclosures: when financial relationships are highly prevalent, individual disclosures will not be particularly informative.

The Open Payments program data show that payments from industry are highest in the fields of orthopaedic surgery and internal medicine, while total payments in pediatrics are among the lowest. Therefore, these fields might reasonably define the approximate upper and lower bounds of prevalence. Thus, we measured the frequency of reported relationships between industry and authors in 3 leading journals (by impact factor) in their respective specialty areas: *Pediatrics*, *The Journal of Bone & Joint Surgery* (JBJS), and *The New England Journal of Medicine* (NEJM).

### Materials and Methods

Beginning with the first issue of calendar year 2014, 100 consecutive scientific articles were identified from each of 3 journals: *Pediatrics*, JBJS, and NEJM. Reviews, editorials, and other manuscripts that did not report original data were excluded.

Each article was reviewed by 2 observers who recorded the source of any funding for the study and any declared relationships between the authors and industry. Using those data, each study was categorized according to the following “Levels of Influence” classification (Fig. 1): (1) Level A: no external funding, and no author has a relationship with industry. (2) Level B: funding by government or not-for-profit entity only, and no author has a relationship with industry. (3) Level C: not funded by industry, but 1 or more authors has a relationship with industry. (4) Level D: sponsored by industry.

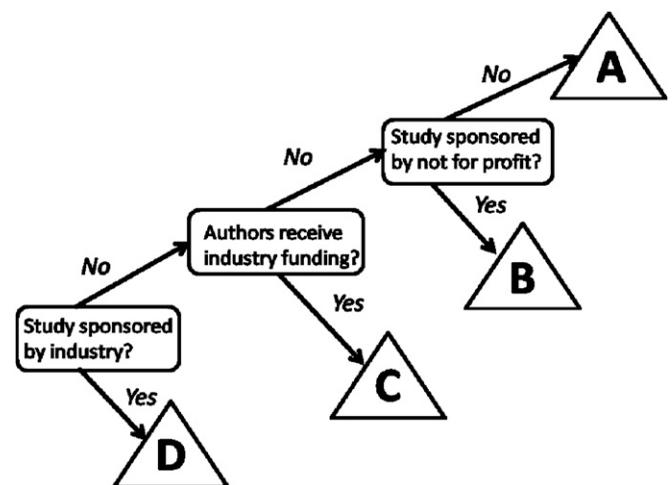


Fig. 1

A stepwise illustration showing the Levels of Influence. Studies range from level A (no funding and no relationship to industry) to level D (sponsored by industry).

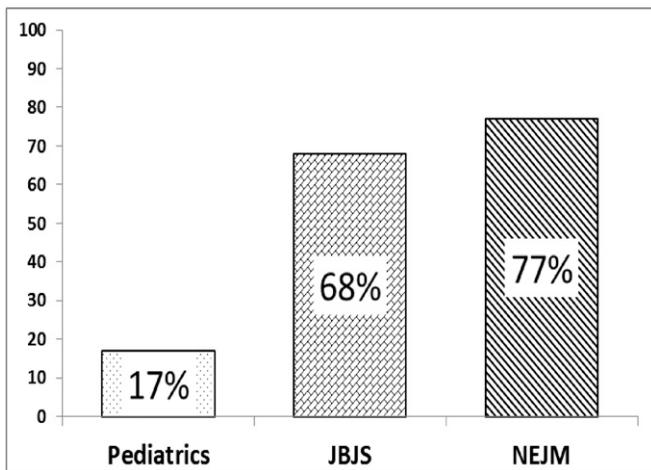


Fig. 2  
The percentage of 100 studies that disclosed a relationship between an author and industry in 3 journals with high impact factors.

The studies also were classified according to a simplified scheme in which they were designated as having no industry involvement (levels A and B combined) or having industry involvement (levels C and D combined). Studies that received only supplies or other de minimis contributions (e.g., medications) from industry were not considered to be “industry supported.” Significance for differences between journals was assessed using the chi-square test at the  $p < 0.05$  level.

### Source of Funding

None. (Level of Influence: A)

### Results

In *Pediatrics*, there were 16 studies designated as level A, 67 were level B, 12 were level C, and 5 were level D (Table I).

JBJS had 21 studies designated as level A, 11 were level B, 52 were level C, and 16 were level D.

In NEJM, there were 2 studies designated as level A, 21 were level B, 35 were level C, and 42 were level D.

As shown in Figure 2, the authors of 17 of 100 studies in *Pediatrics* had a relationship with industry; the authors of 68 of 100 studies in JBJS and 77 of 100 studies in NEJM had a relationship with industry ( $p < 0.001$ ; chi-square = 84.3, 2 degrees of freedom).

### Discussion

In an effort to increase transparency in research and thereby increase the confidence that readers can place in the works they read, the ICMJE has insisted that authors disclose all conflicts of interest and any sources of support for their research. Yet as described above, the effectiveness of this standard can be undermined by habituation. If too many authors declare conflicts, the reader will become inured to them, and the declarations may cease to be meaningful. Accordingly, we attempted to determine the frequency of declared potential conflicts of interest in 3 leading journals. We discovered that such conflicts were prevalent in NEJM (77%) and in JBJS (68%), but were seen infrequently in *Pediatrics* (17%).

There are limitations to our study. First, consolidating all authors' conflict of interest status into a single designator produces imprecision: a relationship reported by a single collaborator

rating author who exerts perhaps only a minor influence on the study is treated no differently in our analysis than numerous and pervasive conflicts held by every author. This limitation, however, also applies equally to the summary disclosure statement that often accompanies the articles. For example, a disclosure statement may report that “1 or more of the authors received payments or services from a third party in support of an aspect of this work. In addition, 1 or more of the authors has had a financial relationship with an entity in the biomedical arena that could be perceived to influence or have the potential to influence what is written in this work.”<sup>12</sup> This statement uses the same wording regardless of the number of authors to which it applies, and independent of each author's relative importance in shaping the message of the article.

Second, when making field-to-field comparisons, a difference in traditions may generate artefactual differences in disclosure. For instance, the AAOS has embraced disclosure as a requirement for its fellows<sup>13</sup>, and publicizes and maintains a web site of disclosure. Therefore, it is possible that orthopaedic surgeons are more likely to list a conflict of interest than a specialist from a field that does not promote disclosure as avidly as the AAOS. Likewise, the journal *Pediatrics* might have an artificially low rate of disclosures because of authors' perceptions of editorial attitudes toward industry-supported research. In their Instructions for Authors, the editors of *Pediatrics* express a reluctance to “accept reports of studies in which all authors are employed by a commercial entity with a financial interest in the results of the study.” This may be interpreted as also suggesting hostility toward studies in which only some of the authors are employed by a commercial entity, or hostility toward commercially supported research in general. The high rate of industry-supported studies in NEJM may be a function of its tendency to report drug trials, which historically have been sponsored by pharmaceutical firms.

Third, our investigation did not consider the intended purpose of the payment, the magnitude of the financial relationship, or whether investigators' relationships with industry necessarily overlapped with the subject matter of the study. This is not truly a limitation of our study as journal disclosure forms do not uniformly report this information either. In a related point, it has been argued that the magnitude of the relationship may be less important (since even small gifts might be influential<sup>14</sup>), although differences in the magnitude of the financial relationship might be interesting to some readers.

Fourth, we make no claim that the overall rate of disclosed industry relationships in JBJS and NEJM, 68% and 77%, respectively, is at or above a critical level. Discovering at what point a single disclosure gets lost in the background noise of other similar disclosures is left to future studies. At present, the only conclusion that can be drawn (without invoking individual beliefs and tastes) is that there is at least 1 high-impact journal that has a far lower rate of authors with industry relationships (although, as noted above, the low rate in *Pediatrics* may be artefactual).

It is reasonable to contemplate the actions that might offset habituation to the frequently seen disclosure statements with C and D Levels of Influence.

The problem of habituation to familiar statements has, to our knowledge, been addressed in the realm of public policy at least once. In 1984, the U.S. Congress passed the Comprehensive Smoking Education Act that mandated a rotation of 4 different statements to be printed on cigarette packaging. This step was taken to minimize habituation to the single phrase, “Warning: The Surgeon General Has Determined That Cigarette Smoking Is Dangerous to Your Health.” The effectiveness of the rotation of the warning statements has been questioned<sup>15,16</sup>. Rotation is even less apt to help with research disclosures since there would be no meaningful contrast between articles if nearly all authors had some industry relationship to report.

Journals could consider listing levels of influence as a footnote for each author, although it is not clear that readers would avail themselves of this information. An assessment of influence by the journal editors (after the completion of peer review and after the paper has been accepted) might be informative. Editors could possibly add a short note summarizing the nature of any financial relationships.

It is also possible that the need for policy changes to the process of disclosure may wane because of technological advances. Specifically, the advent of the Open Payments program described above, coupled with the growing popularity of online reading<sup>17</sup>, may allow for an automatic system in which each author’s name on the electronic version of a manuscript has a “hotlink” to the Open Payments database, allowing readers to examine any financial relationships the authors might have with industry.

Our findings report only the frequency of declared conflicts of interest and do not address the question of appropriateness. Undoubtedly, the financial relationships cited here are the antithesis of the alleged “money-for-nothing” kickbacks that aroused the interest of the U.S. Department of Justice<sup>18</sup>: by definition, the recipients of funding listed in these 3 journals have produced works of substance, as witnessed by their publication in the elite medical literature. Still, some may deem the frequency of declared conflicts of interest to be excessive.

The editors of *PLoS Medicine* maintain that “financial conflicts of interest impair objectivity and integrity in medicine,”<sup>5</sup> whereas others see a “convergence”<sup>19</sup> rather than a “conflict” of interests in academic/industry partnerships. Without resolving this question, it is fair to note that the data reported herein might have important ramifications regarding the perception of appropriateness. *NEJM* and *JBJS* are leading journals

in their respective fields; they are the most highly cited journals and, presumably, among the most highly read. The practices they report may define the acceptable norms for their respective fields.

The process by which prevalence translates into probity was described by Moynihan in “Defining Deviancy Down.”<sup>20</sup> Moynihan claimed that when the amount of a given bad behavior in a community increases above a critical level, society redefines its standards of deviancy “so as to exempt much conduct previously stigmatized, and also quietly raising the ‘normal’ level in categories where behavior is now abnormal by any earlier standard.” A similar course may be followed within the medical community. The high prevalence of declared conflicts of interest in the leading journals (a phenomenon perhaps reflective of the large and presumably expensive studies that are reported) might foster a tacit acceptance of such relationships, including by journals that lack a strong justification. If the editors of *PLoS Medicine* are correct in their belief that objectivity is impaired by financial relationships, then our findings might represent a problem.

In conclusion, the current ICMJE approach may be less effective than hoped. As noted by Tolo, “the impact of these disclosures remains small...few [JBJS] readers look at the conflict-of-interest forms that are attached to all JBJS articles and...most accept some conflicts of interest as being the norm among those doing and reporting research.”<sup>21</sup> Indeed, the work presented here demonstrates that declarations of industry relationships in some journals are so common that readers might tune them out. ■

Jillian R.H. Bernstein<sup>1</sup>  
George Maliha, AB<sup>2,3</sup>  
Jaimo Ahn, MD, PhD<sup>2</sup>  
Joseph Bernstein, MD, MS<sup>2</sup>

<sup>1</sup>Haverford High School, Havertown, Pennsylvania

<sup>2</sup>University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

<sup>3</sup>Harvard Law School, Cambridge, Massachusetts

E-mail address for Joseph Bernstein: Joseph.Bernstein@uphs.upenn.edu

## References

1. Bekelman JE, Li Y, Gross CP. Scope and impact of financial conflicts of interest in biomedical research: a systematic review. *JAMA*. 2003 Jan 22-29;289(4):454-65.
2. Morgan S, Grootendorst P, Lexchin J, Cunningham C, Greyson D. The cost of drug development: a systematic review. *Health Policy*. 2011 Apr;100(1):4-17. Epub 2011 Jan 21.
3. Rees M. A Longitude Prize for the twenty-first century. *Nature*. 2014 May 22;509(7501):401.
4. Internal Committee of Medical Journal Editors. Recommendations for the conduct, reporting, editing, and publication of scholarly work in medical journals. <http://www.icmje.org/recommendations/>. Accessed 2016 Aug 17.
5. EditorsPLM; PLoS Medicine Editors. Does conflict of interest disclosure worsen bias? *PLoS Med*. 2012;9(4):e1001210. Epub 2012 Apr 24.
6. Okike K, Kocher MS, Wei EX, Mehlman CT, Bhandari M. Accuracy of conflict-of-interest disclosures reported by physicians. *N Engl J Med*. 2009 Oct 8;361(15):1466-74.
7. Loewenstein G, Sah S, Cain DM. The unintended consequences of conflict of interest disclosure. *JAMA*. 2012 Feb 15;307(7):669-70.
8. Cosgrove L, Krinsky S. A comparison of DSM-IV and DSM-5 panel members’ financial associations with industry: a pernicious problem persists. *PLoS Med*. 2012;9(3):e1001190. Epub 2012 Mar 13.
9. Rankin CH, Abrams T, Barry RJ, Bhatnagar S, Clayton DF, Colombo J, Coppola G, Geyer MA, Glanzman DL, Marsland S, McSweeney FK, Wilson DA, Wu CF, Thompson RF. Habituation revisited: an updated and revised description of the behavioral characteristics of habituation. *Neurobiol Learn Mem*. 2009 Sep;92(2):135-8. Epub 2008 Nov 6.

- 10.** Marshall DC, Jackson ME, Hattangadi-Gluth JA. Disclosure of industry payments to physicians: an epidemiologic analysis of early data from the Open Payments Program. *Mayo Clin Proc.* 2016 Jan;91(1):84-96.
- 11.** American Academy of Orthopaedic Surgeons. Standards of professionalism: orthopaedic-industry conflicts of interest. 2007 Jun. <http://www.aaos.org/aaosnow/2007/jun/youraaos/youraaos6/>. Accessed 2016 May 5.
- 12.** Keener JD, Galatz LM, Stobbs-Cucchi G, Patton R, Yamaguchi K. Rehabilitation following arthroscopic rotator cuff repair. A prospective randomized trial of immobilization compared with early motion. *J Bone Joint Surg Am.* 2014 Jan 1;96(1):11-19.
- 13.** Matsen FA 3rd, Jette JL, Neradilek MB. Demographics of disclosure of conflicts of interest at the 2011 annual meeting of the American Academy of Orthopaedic Surgeons. *J Bone Joint Surg Am.* 2013 Mar 6;95(5):e29.
- 14.** Katz D, Caplan AL, Merz JF. All gifts large and small: toward an understanding of the ethics of pharmaceutical industry gift-giving. *Am J Bioeth.* 2010 Oct;10(10):11-7.
- 15.** Fischer PM, Krugman DM, Fletcher JE, Fox RJ, Rojas TH. An evaluation of health warnings in cigarette advertisements using standard market research methods: what does it mean to warn? *Tob Control.* 1993;2(4):279-85.
- 16.** Krugman DM, Fox RJ, Fischer PM. Do cigarette warnings warn? Understanding what it will take to develop more effective warnings. *J Health Commun.* 1999 Apr-Jun;4(2):95-104.
- 17.** Bernstein J, Ahn J, Veillette C. The future of orthopaedic information management. *J Bone Joint Surg Am.* 2012 Jul 3;94(13):e95.
- 18.** Healy WL, Peterson RN. Department of Justice investigation of orthopaedic industry. *J Bone Joint Surg Am.* 2009 Jul;91(7):1791-805.
- 19.** Crowninshield R. The orthopaedic profession and industry: conflict or convergence of interests. *Clin Orthop Relat Res.* 2003 Jul;412:8-13.
- 20.** Moynihan DP. Defining deviancy down. *Am Scholar.* 1993;62(1):17-30.
- 21.** Tolo VT. Are research publications original and true? *J Bone Joint Surg Am.* 2014 Jun 18;96(12):969. Epub 2014 Jun 18.