Published in final edited form as:

J Nerv Ment Dis. 2013 February ; 201(2): 84–87. doi:10.1097/NMD.0b013e31827f6248.

Disclosures of Conflicts of Interest in Psychiatric Review Articles

Dr. Andrew M. Kopelman, MD¹, Dr. David A. Gorelick, MD, PhD², and Dr. Paul S. Appelbaum, MD³

¹Fellow in Forensic Psychiatry, Department of Psychiatry, College of Physicians and Surgeons, Columbia University, and New York State Psychiatric Institute. He is currently with the Forensic Psychiatry Service, Bellevue Hospital Center, New York, NY

²Intramural Research Program, National Institute on Drug Abuse, National Institutes of Health, Baltimore, MD

³Dollard Professor of Psychiatry, Medicine and Law, Department of Psychiatry, College of Physicians and Surgeons, Columbia University, and New York State Psychiatric Institute, New York, NY

Abstract

To characterize disclosures of conflicts of interest in review articles in psychiatry, we identified 285 reviews from ten high-impact journals in psychiatry and two in general medicine. Disclosures were reliably coded as biotech/pharmaceutical/other material interests, nonprofit/government, communication companies, or other. Authors in both types of journals frequently reported industry ties. However, reviews in psychiatric journals were significantly less likely to include industry-related disclosures (32% of reviews; 18% of authors) compared with general medical journals (64% of articles; 40% of authors). The most common types of industry-related disclosures were for consulting, research support, and speaking fees. Disclosures appeared to be of limited utility in helping readers assess possible biases, because the nature and extent of the relationship being disclosed was often unclear. Efforts to screen out authors with significant financial relationships pertaining to the topic under review may be more effective than disclosure in protecting the integrity of the medical literature.

Keywords

conflict of interest; disclosure; ethics

Introduction

Growing attention to the problem of conflicts of interest (COIs) in psychiatry has generated increased concern about the impact of relationships with the pharmaceutical industry on the integrity of psychiatric research (APA, 2010; Appelbaum and Gold, 2010; Maj, 2010). Troubling data have suggested the possibility that bias affects the design and reporting of industry-funded research in psychiatry. For example, randomized, placebo-controlled clinical trials funded by pharmaceutical companies are nearly five times more likely to

Address correspondence to Dr. Appelbaum at NY State Psychiatric Institute, 1051 Riverside Drive, Unit 122, New York, NY 10032; (p) 212-543-4184; (f) 212-543-6752; psa21@columbia.edu.

Conflicts of Interest and Source of Funding: Dr. Appelbaum holds an equity interest in COVR, Inc. Drs. Kopelman and Gorelick report no financial relationships with commercial interests. Dr. Gorelick work was supported by the Intramural Research Program, National Institute on Drug Abuse.

report a positive drug response than those without industry funding (Perlis et al., 2005). A study of industry-supported, head-to-head comparisons of second-generation anti-psychotic medications found that 90% of studies reported an outcome favorable to the study sponsor's drug, with contradictory conclusions across studies when the same drugs were compared under the auspices of different sponsors (Heres et al., 2006). Mechanisms for industry influence on study outcome may include differences in dosage of the study medications (e.g., higher effective dose of the sponsored medication than of comparison medications), dose escalation strategies, study entry criteria, study populations, and statistical analyses (Sinyor et al., 2007).

Much of the focus on authors' COIs has centered on the potential impact on primary data from randomized controlled studies (Bekelman et al., 2009; Cooper et al., 2006; Friedman et al., 2004), but in the era of evidence-based medicine, authors of review articles and meta-analyses play an increasingly critical role in helping clinicians and researchers stay abreast of discoveries in their fields (McAlister et al., 1999a). Review articles are often relied on by physicians trying to solve clinical problems (McAlister, 1999b), and may be over-represented among highly cited papers referenced by researchers, relative to articles presenting primary data (Aksnes, 2009). Readers may expect that authors of review articles are providing relatively unbiased and comprehensive surveys (Mulrow, 1987; Oxman et al., 1993), in part because of the implicit endorsement by journal editors in selecting these authors. Thus, review writers may assume positions of authority within their field, creating a class of "opinion leaders" with considerable power to shape scientific dialogue. (Fava, 2001). Potential biases in controlled studies, however, may be magnified by the inclusion of their findings in review articles, which often fail to note the original investigators' COIs (Boyd and Bero, 2006; Norris, et al., 2011; Roseman, et al., 2011). Moreover, review articles themselves are susceptible to the biases of their authors, who decide what information is pertinent to include, which studies to cite, and how to frame the discussions and controversies in their respective fields. The potential COIs of review authors therefore deserve closer examination.

Policies for addressing the COIs of review authors attracted attention later than policies for authors of primary research papers (Mayor, 2003), but, as in the case of the latter, have focused on self-disclosure (Blum et al., 2009; Foster, 2003; Mitchell, 2009). Authors are asked to disclose all financial (and sometimes other) relationships that may create potential conflicts of interests. However, many commentators have questioned the utility of these self-disclosures in revealing biases in a meaningful or informative way (Bion, 2009; Kofke, 2003; Loewenstein et al., 2012). For example, readers and editors are likely to be poorly situated to discern how an industry relationship affected an author's work or how to adjust the conclusions they draw from an article to discount for the impact of potential biases. Such disclosures, nonetheless, do provide an important window on the extent to which review authors have relationships with industry that could potentially bias their conclusions. If such relationships are extensive, other methods may be called for to mitigate their potential impact on the content of reviews.

Drawing on disclosure data that accompany review articles, this study has two aims: 1) to describe and quantify in a systematic manner the COI disclosures of authors of review articles in leading academic psychiatric journals; and 2) to compare the prevalence and characteristics of these disclosures to those found in review articles from similarly high-profile academic general medicine journals.

Methods

Articles were identified using a *PubMed* search for “review” articles (which included meta-analyses) in 10 psychiatric journals and 2 general medical journals from June 2010 through November 2011. For convenience, we sampled the 10 highest impact psychiatric journals from 1981 through 2008, as identified by Thomson Reuter’s Journal Citation Reports (SCIBYTES, 2009): *Archives of General Psychiatry*, *American Journal of Psychiatry*, *Schizophrenia Bulletin*, *Journal of the American Academy of Child and Adolescent Psychiatry*, *Psychological Medicine*, *British Journal of Psychiatry*, *Molecular Psychiatry*, *Psychosomatic Medicine*, *Journal of Child Psychology and Psychiatry*, and *Biological Psychiatry*. For comparison, we chose two high-impact general medical journals: *Journal of the American Medical Association* and the *New England Journal of Medicine*. Conflict of interest disclosure policies for each journal were compiled from the journal’s website or by correspondence with the editorial office.

Authors’ disclosures of relationships were identified and recorded from the acknowledgments, financial disclosures, and COI sections of each article, plus online disclosure forms, when available. Disclosures were categorized by the first author (AK) into one of four mutually exclusive categories: biotech/pharmaceutical/other material interests (the latter including ownership of intellectual property), non-profit/government, communication companies, or other/uncertain.

Disclosures categorized as “biotech/pharmaceutical/other material interests” were further subcategorized into consulting, speaking fees or participating in a speakers’ bureau, undefined honoraria, permanent employment or serving on the board of directors of a company, owning equity in a company, possession of patents, research support, expert testimony, travel stipends, and other/uncertain. “Other/uncertain” disclosures included: serving as an unpaid advisor to a company; affiliation with an endowed institute, position, or fellowship named after a corporate sponsor; spouse affiliation; or other undefined “compensation.”

Disclosures categorized as “non-profit/government” included any affiliation with or compensation from an academic institute, charitable or non-profit foundation or association, or government agency. Non-profit status was confirmed via online searches. All NIH institutes and centers (for example, NIAAA, NIDA, NIMH) were counted as a single entity. The “communication companies” category included affiliations with or royalties from publishing companies, websites, journals, or educational publications. The “other/uncertain” category included all disclosures that did not fall into the other three main categories, e.g., disclosure that the authors had also participated as subjects for a given study.

When disclosures were not linked to a specific author, they were counted as a single disclosure, but assigned to all of the article’s authors.

To evaluate the reliability of this categorization, disclosures from 10% of the sample (29 articles) were independently scored by a second rater (PSA). The authors agreed on 388 of the 390 scored variables (99.5%), indicating high reliability. The two disputed scores were resolved by consensus.

The proportion of various types of disclosures in the two categories of journals was compared with Pearson’s χ^2 test. The mean number of companies included in the articles’ disclosures was compared using the Mann-Whitney Wilcoxon test. A two-tailed alpha < 0.05 was considered statistically significant.

Results

A total of 285 review articles were identified for inclusion in this study, 166 from the 10 psychiatry journals and 119 from the 2 general medicine journals. Both of the general medical journals and 5 of the psychiatry journals followed the disclosure policy of the International Committee of Medical Journal Editors, which asks for disclosures of relevant relationships for 36 months prior to submission of the article (ICMJE, 2010). The remaining psychiatric journals asked for pertinent disclosures with “rule of thumb” type guidance (e.g., “Consider the conflict of interest test: Is there any arrangement that would embarrass you or any of your co-authors if it was to emerge after publication and you had not declared it?”), although only one specified a period of time (previous 2 years).

There were no significant differences between the two types of journals in proportion of articles including disclosures of any type ($\chi^2 = 0.189$, $df = 1$, $p = 0.66$) or proportion of authors providing disclosures ($\chi^2 = 0.771$, $df = 1$, $p = 0.38$) (Table 1). Reviews in psychiatric journals were significantly less likely than reviews in general medical journals to contain disclosures of relationships with “biotech/pharmaceutical/other material interests” (Pearson’s $\chi^2 = 28.759$, $df=1$, $p<0.01$), and individual authors of psychiatric reviews were significantly less likely to report such relationships (Pearson’s $\chi^2 = 21.568$, $df=1$, $p<0.01$) (Table 1). On average, psychiatric reviews with disclosures named more individual companies (biotech firms, pharmaceutical, or other corporations) than did general medical reviews (9 vs. 4, $U = 2499$, $p < 0.05$). There was also a significant difference in the number of companies named by individual authors of psychiatric versus general medicine reviews with such disclosures (5 vs. 3, $U = 2611$, $p < 0.01$).

There was no significant difference in the prevalence of subcategories of “biotech/pharmaceutical/other material interests” disclosures between the psychiatric and general medical reviews ($\chi^2 = 5.647$, $df=9$, $p=0.77$) (Table 2). In contrast, there was a higher prevalence of articles and of authors with a “non-profit/government” disclosure for psychiatric reviews: 77.5% vs. 50.1% for reviews ($\chi^2 = 22.42$, $df = 1$, $p < 0.01$) and 62.7% vs. 48.5% for authors ($\chi^2 = 17.11$, $df = 1$, $p < 0.01$) (Table 1).

There were no significant differences between psychiatric reviews or authors and general medical reviews or authors in the proportion disclosing a relationship with a “communication company” (6.6% and 1.9% vs. 10.0% and 3.6%, respectively) ($\chi^2 = 1.01$, $df = 1$, $p = 0.32$ for articles; $\chi^2 = 2.27$ $df = 1$, $p = 0.13$ for authors), or with “other” entities (0.6% and 0.8% vs. 0% and 0%, respectively).

Discussion

Physicians, ethicists, and the general public have expressed concern over the potential influence of pharmaceutical and biotechnology companies on research, education, and clinical care in medicine. Psychiatry has come under particular scrutiny. This study examined just one aspect of the relationship between psychiatry and industry, the ties between authors of review articles and companies and other entities that provide them with financial support. However, given the potential for review articles, especially in high-impact journals, to shape clinician behavior, these ties may be of special concern.

Approximately one-third of the psychiatry review articles included at least one author who disclosed a financial relationship with pharmaceutical or biotech companies, or revealed ownership of intellectual property. This prevalence was only about half that in the two general medical journals, suggesting that psychiatry does not have a particular problem in this regard. The majority of disclosures in both types of journals involved personal remuneration for such functions as consulting, speaking, and providing expert testimony, or

ownership of an equity interest in a company. Only a minority of disclosures were for research support, which typically does not go directly to the investigator.

The ostensible reason for requiring authors to disclose the existence of a relationship with a pharmaceutical or biotech company is to permit readers to take those relationships into account in determining the credence to give to an article. However, we believe that it would be nearly impossible for the average reader to do so. Disclosures offered no indication of whether a company with which an author had a financial relationship produced or marketed a product covered by the review, and information about the extent or recency of the relationships was often not included. The nature of a relationship with a given company was difficult to establish in many cases, because disclosures often were framed like the following actual example: “Dr. ‘B’ has been a consultant to, advisory board member of, and/or speaker for...” followed by a list of eight companies. Reader access to the actual disclosure forms submitted by the authors to the editors was limited. Only the *New England Journal of Medicine*, of the journals included in this study, provided an online link to the ICJME universal disclosure forms submitted along with the article. For the remainder of the journals, disclosures came in the form of synopsis statements describing potential COIs.

Further impeding the reader’s ability to identify genuine COIs was the frequent disclosure of relationships with government or non-profit entities—typically receipt of research funding—which are unlikely to create the risk of bias among authors. Nearly two-thirds of psychiatry review authors and almost half of general medical review authors disclosed their relationships with such entities, often including entities such as NIH institutes that had funded previous studies but not the current review. If anything, such disclosures may be counterproductive to the goal of transparency, with the increased volume of disclosures obscuring relationships more likely to bias the authors’ conclusions.

This study has several limitations. Because we relied on the disclosures made by the authors, our data reflect only the relationships they revealed; if authors failed to disclose financial relationships with pharmaceutical or biotech companies, we could not capture those data. A similar problem arises in the comparison between reviews in psychiatric and general medical journals. The higher rate of relationships disclosed in the latter set of journals could reflect actual differences in financial ties to industry or more thorough disclosure by general medical authors, perhaps stimulated by the greater specificity encouraged by the ICJME disclosure form. A study that compared psychiatric and general medical journals’ disclosure policies found that they were more alike than different, although the latter tend to provide more information about the nature of potential conflicts, define relevant funding sources more broadly, and offer more examples for guidance (Khurana et al., 2012). However, the less specific policies of many psychiatry journals are not necessarily less stringent, leaving us unable to identify with certainty the origins of the differences we found. Finally, we—and the readers of these reviews—are largely unable to link the relationships disclosed to the topics of the reviews themselves, or to detect whether actual bias resulted from the existence of these financial links. Disclosures would be more likely to achieve their stated goal if they were more specifically linked to the topic of the review.

Given that editors often solicit review articles or pre-review unsolicited proposals for reviews, we suggest that more attention be paid to selecting authors without financial conflicts. Because citation of articles in a review is often selective (e.g., when the total number of citations is limited by the journal) and authors often offer recommendations based on their synthesis of the literature, review articles offer broad scope for the effects of bias, both conscious and unconscious. The very real limits of disclosure, as currently practiced, as a means of compensating for authors’ conflicts of interest suggest that greater efforts, when possible, to screen out authors with significant financial relationships pertaining to the topic

under review may better protect the integrity of the medical literature. A reassuring finding of this work is the suggestion that a sizable pool of review article authors without such conflicts would remain for many topics, even with the most stringent exclusion criteria.

References

- Aksnes DW. Characteristics of highly cited papers. *Res Eval*. 2003; 12(3):159–170.
- American Psychiatric Association. Position Statement on Conflicts of Interest Principles and Guidelines: With Special Interest for Clinical Practice and Research. 2010. Available at: <http://www.psychiatry.org/advocacy--newsroom/position-statements>
- Appelbaum PS, Gold A. Psychiatrists' relationships with industry: the principal-agent problem. *Harv Rev Psychiatry*. 2003; 18(5):255–65. [PubMed: 20825263]
- Bekelman JE, Li Y, Gross CP. Scope and impact of financial conflicts of interest in biomedical research: a systematic review. *JAMA*. 2003; 289(4):454–65. [PubMed: 12533125]
- Bion J. Financial and intellectual conflicts of interest: confusion and clarity. *Curr Opin Crit Care*. 2009; 15(6):583–90. [PubMed: 19851102]
- Blum JA, Freeman K, Dart RC, Cooper RJ. Requirements and definitions in conflict of interest policies of medical journals. *JAMA*. 2009; 302(20):2230–4. [PubMed: 19934424]
- Boyd EA, Bero LA. Improving the use of research evidence in guideline development: 4. Managing conflicts of interests. *Health Res Policy Syst*. 2009; 4:16.10.1186/1478-4505-4-16 [PubMed: 17140441]
- Cooper RJ, Gupta M, Wilkes MS, Hoffman JR. Conflict of interest disclosure policies and practices in peer-reviewed biomedical journals. *J Gen Intern Med*. 2006; 21(12):1248–52. [PubMed: 17105524]
- Fava GA. Conflict of interest and special interest groups. The making of a counter culture. *Psychother Psychosom*. 2001; 70(1):1–5. [PubMed: 11150932]
- Foster RS. Conflicts of interest: recognition, disclosure, and management. *J Am Coll Surg*. 2003; 196(4):505–17. [PubMed: 12691923]
- Friedman LS, Richter ED. Relationship between conflicts of interest and research results. *J Gen Intern Med*. 2004; 19(1):51–6. [PubMed: 14748860]
- Heres S, Davis J, Maino K, Jetzinger E, Kissling W, Leucht S. Why olanzapine beats risperidone, risperidone beats quetiapine, and quetiapine beats olanzapine: an exploratory analysis of head-to-head comparison studies of second-generation antipsychotics. *Am J Psychiatry*. 2004; 163(2):185–94. [PubMed: 16449469]
- International Committee of Medical Journal Editors. ICMJE Form for Disclosure of Potential Conflicts of Interest. 2010. Available at: http://www.icmje.org/coi_disclosure.pdf
- Khurana G, Henderson S, Walter G, Martin A. Conflict of interest and disclosure policies in psychiatry and medicine: a comparative study of peer-reviewed journals. *Acad Psychiatry*. 2012; 36:17–22. [PubMed: 22362431]
- Kofke WA. Disclosure of industry relationships by anesthesiologists: is the conflict of interest resolved? *J Am Coll Surg*. 2003; 196(4):505–17. [PubMed: 12691923]
- Loewenstein G, Sah S, Cain DM. The unintended consequences of conflict of interest disclosure. *JAMA*. 2012; 307(7):669–70. [PubMed: 22337676]
- Maj M. Financial and non-financial conflicts of interests in psychiatry. *Eur Arch Psychiatry Clin Neurosci*. 2010; 260(Suppl 2):S147–51. [PubMed: 20936299]
- Mayor S. Nature group extends rules on disclosure to review authors. *BMJ*. 2003; 327:829. [PubMed: 14551073]
- McAlister FA, Clark HD, van Walraven C, Straus SE, Lawson FM, Moher D, Mulrow CD. The medical review article revisited: has the science improved? *Ann Intern Med*. 1999; 131(12):947–51. [PubMed: 10610646]
- McAlister FA, Graham I, Karr GW, Laupacis A. Evidence-based medicine and the practicing clinician. *J Gen Intern Med*. 1999; 14(4):236–42. [PubMed: 10203636]
- Mitchell PB. Winds of change: growing demands for transparency in the relationship between doctors and the pharmaceutical industry. *Med J Aust*. 2009; 191(5):273–5. [PubMed: 19740050]

- Mulrow CD. The medical review article: state of the science. *Ann Intern Med.* 1987; 106(3):485–8. [PubMed: 3813259]
- Norris SL, Holmer HK, Ogden LA, Burda BU. Conflict of interest in clinical practice guideline development: a systematic review. *PLoS One.* 2011; 6(10):e25153. [PubMed: 22039406]
- Oxman AD, Sackett DL, Guyatt GH. Users' guides to the medical literature. I. How to get started. The Evidence-Based Medicine Working Group. *JAMA.* 1993; 270(17):2093–5. [PubMed: 8411577]
- Perlis RH, Perlis CS, Wu Y, Hwang C, Joseph M, Nierenberg AA. Industry sponsorship and financial conflict of interest in the reporting of clinical trials in psychiatry. *Am J Psychiatry.* 2005; 162(10):1957–60. [PubMed: 16199844]
- Roseman M, Milette K, Bero LA, Coyne JC, Lexchin J, Turner EH, Thombs BD. Reporting of conflicts of interest in meta-analyses of trials of pharmacological treatments. *JAMA.* 2011; 305(10):1008–17. [PubMed: 21386079]
- SCI-BYTES. What's New in Research. 2009. Available at: http://sciencewatch.com/dr/sci/09/aug16-09_1/
- Sinyor M, Schaffer A, Smart KA, Levitt AJ, Lanctôt KL, Grysman NH. Sponsorship, antidepressant dose, and outcome in major depressive disorder: meta-analysis of randomized controlled trials. *J Clin Psychiatry.* 2012; 73(2):277–87.

Table 1

Author conflict of interest (COI) disclosures in review articles in psychiatry and general medical journals

	Number of articles	Number of authors	Articles with COI disclosures (N[%])	Authors with COI disclosures (N[%])	Articles with pharm/biotech COI disclosures (N[%])	Articles with pharm/biotech COI disclosures (N[%])	Articles with non-profit disclosures	Authors with non-profit disclosures
Psychiatry	165	566	138 (83.6%)	397 (70.1%)	53 (32.1%)	104 (18.4%)	128 (77.6%)	355 (62.3%)
Medicine	120	332	98 (81.7%)	242 (72.9%)	77 (64.2%)	134 (40.4%)	61 (50.1%)	161 (48.5%)

Table 2

Subtypes of author pharm/biotech conflict of interest (COI) disclosures in review articles in psychiatry and general medical journals

		Subtype (N[%])									
	Number of pharm/ biotech COI disclosures	Consulting	Speaking	Equity/stock	Patents/intellectual property	Employment	Research support	Expert testimony	Travel	Unspecified honorarium	Other
Psychiatry	209	63 (30.1%)	30 (14.4%)	11 (5.2%)	15 (7.2%)	7 (3.3%)	51 (24.4%)	5 (2.4%)	7 (3.3%)	10 (4.8%)	10 (4.8%)
Medicine	294	86 (29.3%)	34 (11.6%)	10 (3.4%)	24 (8.2%)	12 (4.1%)	77 (26.2%)	8 (2.7%)	20 (6.8%)	13 (4.4%)	10 (3.4%)