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Conflicts of Interest and Disclosure in the American Psychiatric Association's Clinical Practice Guidelines

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Key Words
Clinical practice guidelines · Conflict of interest · Financial associations

Abstract
Background: Clinical practice guidelines (CPG) are developed, endorsed, and disseminated through professional medical organizations such as the American Psychiatric Association (APA) as the standard of care for health care providers. Because of their influence, it is critical that CPG are based on objective data, unprejudiced by stakeholder groups, and that any financial associations between authors of CPG and the pharmaceutical industry are made transparent. The present study examined the degree and type of financial ties to the pharmaceutical industry held by authors of 3 major CPG. ***Methods:*** By using multimodal screening techniques, we investigated the financial relationships to the pharmaceutical companies of 20 work group members who authored the guidelines for the treatment of schizophrenia, bipolar disorder, and major depressive disorder. ***Results:*** Eighteen CPG authors (90%) had at least 1 financial tie to the pharmaceutical industry. All of the CPG authors who had industry relationships had financial relationships with companies whose products were specifically considered or included in the guideline they authored. The leading categories of financial interest held by CPG authors were research funding (77.7%), consultancies (72.2%), members of corporate boards (44.4%), and collaborators in industry-funded studies (44.4%). ***Conclusions:*** Ninety percent of the authors of 3 major CPG in psychiatry had financial ties to companies that manufacture drugs which were explicitly or implicitly identified in the guidelines as recommended therapies for the respective mental illnesses. None of the financial associations of the authors were disclosed in the CPG.

H.J.B. has served as a consultant to physicians and institutions seeking to craft COI policies and as a plaintiff- or defendant-retained expert in competency to consent to neuropsychoharmaceutical treatment as well as product liability cases. All of the authors had full access to the data in the study; L.C. takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Introduction

Clinical practice guidelines (CPG) have become increasingly influential on health care providers [1] because they are a 'primary mechanism for communicating clinical aspects of emerging therapies and "standard of care" expectations to practicing physicians' [2, p 419]. Given their significance and impact, concerns have been raised about the potential for bias when treatment recommendations are developed by industry-funded researchers [1–5]. In the USA, medical specialties are now grappling with external criticism from the media, Congress [6], journal editors, and medical writers [7]. The field of psychiatry, in particular, has been at the epicenter of extensive media coverage on conflicts of interest (COI). The reasons for the focus on psychiatry range from special considerations regarding the rights of highly vulnerable patient populations [8, 9] to ongoing public concerns regarding the conduct of academic, institutional, and organized psychiatry [5, 9–13] including that of the American Psychiatric Association (APA). For example, it was discovered in 2006 that all of the experts on two DSM-IV panels (schizophrenia and psychotic disorders and mood disorders) were pharmaceutical industry fundees [14], a finding that raises concerns because psychopharmacology is recommended in the CPG as being the standard of care for the treatment of these 2 categories of disorders. In an effort to protect clients' welfare and help restore the integrity of psychiatry, the APA pledged that there would be greater transparency of any potential COI in its diagnostic and treatment guidelines [15, 16]. This commitment is vital because the APA's published CPG influence the care given to millions of patients by both primary health care and mental health care providers. The present study provides data and recommendations that may be used to improve the process for developing CPG that are endorsed by the APA or other medical specialties.

Methods

The APA issued 11 clinical practice guidelines between 1998 and 2007 that correspond to specific disorders identified in the DSM. This study reports data on the extent and type of financial relationships that authors of the 3 major CPG (for schizophrenia, bipolar, and major depressive disorder, MDD) had with the pharmaceutical industry. The schizophrenia CPG was published in 2004, MDD in 2000, and bipolar in 2002. Updates for MDD and bipolar, referred to by the APA as 'guideline watches,' were published in 2005 and were also included in the present study. Following a similar methodology to a previous study [14], the name of each CPG author was put through a series of 'screens' to determine whether he or she has had financial relationships with 1 or more pharmaceutical companies whose business is potentially affected by decisions or recommendations made by the practice guidelines. Rather than relying solely on self-reporting (e.g. using surveys) these multiple screening techniques allowed for a more thorough assessment of industry relationships. The screening databases we applied included Medline, Lexis-Nexis Academic, and the US Patent and Trademark Office internet site on patents pending or awarded (to determine whether authors had any intellectual property in a drug or medical device whose sales could be affected by practice guideline recommendations). Internet search engines were used to access other reliable disclosures (e.g. author disclosures provided at peer-reviewed conferences). CPG authors were screened for any financial affiliations they had with the drug industry from up to 5 years before the publication of the 2008 guidelines.

The following categories were used to describe financial associations: honoraria; equity holdings in a drug company; principal in a startup company; member of a scientific advisory board or speakers bureau of a drug company; expert witness for a company in litigation; patent or copyright holder; consultancy; collaborator in an industry-funded study; gifts from drug companies including travel, grants, contracts, and research materials. Each finding of a CPG author's financial connection to a medical device manufacturer or drug company was then coded by its respective category. In addition to gathering data on the type of financial relationships, we identified the names and number of pharmaceutical companies with whom members had relationships.

Three investigators independently conducted screens on the work group members. Any questions about coding were resolved by a fourth investigator, who also conducted a random audit of the coding. No member was coded as having a financial connection unless there was unambiguous information confirming the relationship and a consensus reached by the reviewers.

Results

Out of 20 CPG authors comprising the 3 practice guidelines, 18 (90%) had at least 1 financial relationship with the pharmaceutical industry. None of the financial associations of the authors were disclosed in the CPG. One hundred percent of the work group members for both the schizophrenia and bipolar practice guidelines were found to have industry relationships, and 60% of the work group members for MDD had financial relationships.

Of the 18 work group members who had industry relationships, 77.7% received research funding, 72.2% were consultants, 44.4% were on corporate or advisory boards to companies, 38.8% received honoraria, 33.3% served on company speaker's bureaus, and 16.6% held equity in a drug company that manufactured the drugs identified in the practice guidelines. The majority of work group members who had ties had multiple ones; 88.8% had more

than 1 category and 66.6% were found to have 3 or more categories of financial interest with the pharmaceutical industry (e.g. ties such as being a consultant, sitting on a corporate board, and receiving research funding). Over half (55.5%) had 4 or more categories of financial interest.

One hundred percent of the working group members who had industry relationships had financial relationships with companies whose products were specifically considered or included in the guideline they authored. For example, 11 drugs were identified as meriting 'substantial or moderate clinical confidence' for bipolar disorder. All of the authors of the CPG for bipolar disorder had financial relationships with companies whose drugs were identified as 'first-line pharmacological treatment' (e.g. had equity in a company that made the medication, was a consultant or corporate board member, received honoraria). Nine drugs were identified as 'likely to be optimal medications' for MDD. All of the companies whose drugs were listed as 'optimal' provided funding to the authors of the CPG for MDD. Sixteen medications were identified as 'commonly used' in the CPG for schizophrenia. All of the authors of the CPG had financial relationships with companies whose drugs were identified as 'commonly used.'

Discussion

The 3 CPG examined in this study were selected because of their influence in medical practice and because of the potential revenue generated from sales of the recommended agents. Almost 23 million people are diagnosed with MDD, bipolar disorder, and schizophrenia [17, 18], and the revenue generated from sales of antidepressants and antipsychotics was approximately USD 25 billion in 2007 [19]. The influence of the 3 CPG examined in the present study makes it incumbent on the APA to insure that authors' COI are not only made transparent, but also are well managed. As Choudhry et al. [1, p 616] note: 'Financial conflicts of interest for authors of CPGs are of particular importance since they may not only influence the specific practice of these authors but also those of physicians following the recommendations contained within these guidelines.' The APA has made an important first step in advocating for greater transparency of potential COI, and has made available author financial disclosure statements in its diagnostic guidelines [16] as well as in some of its recently published CPG (e.g. obsessive-compulsive disorder, Alzheimer's dementia). However, there has been no information given about how potential COI are managed, and author disclosures of the current MDD, bipolar, and schizophrenia CPG have not been provided. Current policies do not address indirect conflicts (e.g. when a family member owns pharmaceutical company stock) or indirect sources of funding (e.g. having one's salary drawn from pooled industry funds given to a department) [20]. They also do not require that individuals specify the amount of money received, making it impossible to gather data on the extent of authors' financial relationships with industry.

The present study has several limitations. Some types of financial relationships were likely to be missed because they are difficult to detect. Our results should be considered de minimis figures. Another limitation is that our study cannot offer generalizability with respect to the incidence of industry financial relationships of authors of other CPG because the present study did not examine all of the APA's CPG. However, other researchers have shown that there is a strong association between authors' published opinions of products and their financial relationships with the manufacturers of those products and competing ones [21]. Also, the data on CPG authors' associations with the pharmaceutical industry are atemporal because existing disclosure policies do not consistently require that authors specify the timing of their financial relationships with industry. Nonetheless, there are ethical considerations that are relevant whether the work group member's involvement in the drug industry occurred prior to or after publication of the CPG. Finally, it should be noted that before their dissemination, the CPG are reviewed by both APA members and the Assembly of the APA. Although it was beyond the scope of the present study to address the entire process of guideline creation, it is recommended that future research address the usefulness of this multi-step review process with regard to how potential COI are identified and managed.

In light of the increasing evidence that financial associations between biomedical researchers and the pharmaceutical industry may result in the publication of imbalanced – and sometimes inaccurate – results and recommendations [4, 10, 22–26], and based on the results of the present study, we recommend that the APA institute a more rigorous COI policy for the practice guidelines that the Association publishes and endorses. This could be accomplished by inviting only those individuals who are free of substantial COI [5] to author CPG. An ad hoc committee, also comprised of a majority of individuals who do not have substantial COI, could review financial disclosure statements made by prospective work group

members. The ad hoc committee could provide oversight with regard to the inclusion of industry-funded research in the CPG. In keeping with Fava [5], we recommend that the criteria for what constitutes a substantial COI include: an employee of a private firm, a regular consultant or a member of the board of directors of a firm, a stockholder in a firm related to the field of research, and a holder of a patent or patent application directly related to the published work. In our study, we found that over 70% of CPG authors were consultants (although current disclosure guidelines make it impossible to discern the amount of money received from or the full extent of the consultancies), over 40% were on corporate boards, and over 30% served on speakers' bureaus of pharmaceutical companies. Moreover, in the CPG for bipolar disorder, all of the studies cited as supporting evidence for the efficacy of olanzapine and the olanzapine/fluoxetine combination were authored by an employee and stockholder of the firm that manufactures that medication. Using the 'substantial COI' criteria, individuals with these COI would not be eligible to serve on the ad hoc committee or as an author of a CPG.

Greater specificity in the language of disclosure policies is needed, such as: (1) an explicit statement listing all financial relationships (individual, family, or current research collaborators) regardless of whether or not an individual believes those relationships are relevant; this includes direct as well as indirect funding sources (e.g. industry funds given to one's department chair); (2) a disclosure of the total amount of money individuals received from each company; (3) an identification of the timing of the association; (4) no lower limit (e.g. USD 10,000) of disclosure – our recommendation not to include arbitrary thresholds on disclosing financial information is made because there is substantial evidence that even a small gift can influence behavior [27–29].

Random audits will better ensure compliance with existing COI policies [30], and recruiting some individuals with no industry ties to serve on these work groups may lead to a more balanced set of guidelines [31]. Additionally, future disclosure policies should require that authors report marketing ties as these may also represent potential COI. For example, in addition to their financial ties to companies that manufacture the medications recommended in the practice guidelines, CPG authors also had financial ties to consulting firms dedicated to marketing biopharmaceuticals.

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