Reporting of conflicts of interest in guidelines of preventive and therapeutic interventions

George N. Papanikolaou, MD*
Maria S. Baltogianni, MD*
Despina G. Contopoulos-Ioannidis, MD*
Anna-Bettina Haidich, MSc*
Ioannis A. Giannakakis, MD*
John P.A. Ioannidis, MD*‡

* Clinical Trials and Evidence-Based Medicine Unit, and Social Medicine and Public Health Unit, Department of Hygiene and Epidemiology, University of Ioannina School of Medicine, Ioannina 45110, Greece;
‡ Department of Pediatrics, George Washington University School of Medicine, Washington, D.C., USA;
‡ Department of Medicine, Tufts University School of Medicine, Boston, MA, USA.
ABSTRACT

Background. Guidelines published in major medical journals are very influential in determining clinical practice. It would be essential to evaluate whether conflicts of interests are disclosed in these publications. We evaluated the reporting of conflicts of interest and the factors that may affect such disclosure in a sample of 191 guidelines on therapeutic and/or preventive measures published in 6 major clinical journals (Annals of Internal Medicine, BMJ, JAMA, Lancet, New England Journal of Medicine, Pediatrics) in 1979, 1984, 1989, 1994 and 1999.

Results. Only 7 guidelines (3.7%) mentioned conflicts of interest and all were published in 1999 (7/40, 17.5%). Reporting of conflicts of interest differed significantly by journal (p=0.026), source of funding (p<0.001) and number of authors (p=0.004). In the entire database of 191 guidelines, a mere 18 authors disclosed a total of 24 potential conflicts of interest and most pertained to minor issues.
Conclusions. Despite some recent improvement, reporting of conflicts of interest in clinical practice guidelines published in influential journals is largely neglected.
Background

Guidelines have assumed a major role in forming practitioner and patient decisions about appropriate health care [1]. It is important that such efforts are not affected by conflicts of interest and that guidelines are transparent to such potential conflicts. This is even more significant for practice guidelines published in influential medical journals that are likely to have a major impact upon therapeutic and preventive clinical care and public health worldwide. However, there has been no study of the reporting of conflicts of interest in guidelines published in medical journals. We undertook an evaluation of this issue in a large sample of publications of practice guidelines.

Materials and Methods

Our study evaluated 6 prestigious medical journals that are likely to publish influential guidelines. We hand-searched the Annals of Internal Medicine, British Medical Journal (BMJ), Journal of American Medical Association (JAMA), Lancet, New England Journal of Medicine and Pediatrics for guidelines published during 1979, 1984, 1989, 1994 and 1999. This sampling approach allowed evaluation of trends in guidelines over a 20-year period. We preferred hand searching over computerized searches in an attempt to minimize loss of retrievals due to incomplete computerized coding. Hand searching was performed independently by two investigators and discrepancies were solved by a third investigator to reach consensus.

In order to reduce subjective interpretation of what constitutes a guideline publication we developed strict eligibility criteria. Eligible for the study were all articles that (I) contained in their titles, heading or abstracts (or introductory / summary paragraph when an abstract was missing) key words that were characteristic
of guidelines ("guidelines" or "recommendations", "consensus [panel-statement-conference]", "clinical synthesis conference", "guidance", "policy statement", "practice parameter" and "position [paper-article-statement]"; and (II) had main focus on preventive and/or therapeutic interventions including health care delivery. We excluded papers where the main focus was on descriptive epidemiology, research design, diagnosis (diagnostic performance rather than clinical impact of diagnostic methods), risk assessment, legal issues, biology and/or pathophysiology. We specifically excluded editorials, commentaries, original randomized controlled trials, as well as systematic reviews and meta-analyses unless they were part of the guideline. Both full-length and shortened versions qualified, but comments and discussion items concerning guidelines were excluded. The last search for eligible guidelines was performed in mid-October 1999.

Data extraction, including journal, year, main subject focus, main country of origin, authorship, type(s) of interventions and funding, was performed on standardized forms. We also recorded whether conflicts of interest were mentioned at all, and if so, how much space was given for such disclosures. Finally, we recorded the nature of specific disclosed conflicts. Using Fisher’s exact test we evaluated whether there were significant associations between characteristics of guidelines and the reporting of conflicts of interest. Analyses were conducted in SPSS 9.0 (SPSS Inc, Chicago, IL). P-values are two-tailed.

**Results**

We recovered 191 publications of eligible guidelines (table 1). Only 7 guidelines (3.7%) disclosed potential conflicts of interest. One additional guideline simply stated: "competing interests: none declared." All disclosures had been made in 1999, but even for this year the percentage was still only 17.5% (7/40). Reporting was also related to specific journals (p=0.026), but the rate of disclosure was very low even in the journal with the highest disclosure rate (*JAMA*, 4/35 [11.4%]). The country of origin, focus (therapy, prevention or both), group authorship and emphasis
on medication vs. other interventions were not related to reporting of conflicts of interest (p=1.00, 0.14, 1.00 and 1.00, respectively) suggesting the deficiency is universal. Guidelines funded mostly by the government or major professional organizations almost never reported on potential conflicts of interest while guidelines funded by private or mixed sources were more likely to disclose potential conflicts (p<0.001). Among guidelines where specific authors assumed primary responsibility for writing the manuscript, reporting of conflicts of interest was more common when there were more authors (p=0.004).

Further analysis revealed that all guidelines reporting conflicts of interest dedicated less than 1/20 of a page for this reason and less than 1/100 of the total length of the article - with one exception where disclosure took 13 lines to report. In the entire database of 191 guidelines, a mere 18 authors disclosed a total of 24 potential conflicts of interest (table 2). The majority of the alluded items of conflict were for relatively minor issues (such as travel fees, speaker funds and consultation) while no author disclosed possessing stock in a company.

**Discussion**

Our study revealed that reporting of conflicts of interest in practice guidelines of healthcare interventions is probably largely neglected despite some recent improvement. Even in 1999, only 1 out of 6 guidelines disclosed conflicts of interest. Reporting varied by journal. A recent study showed that 50% of US medical journals with a circulation more than 1000 (including all journals we searched in our study) have written policies regarding conflicts of interest [2,3]. Conflicts of interest may not be reported either because they are not disclosed by the authors or because they
are not published by the journals. Furthermore, cases of inconsistency between stated journal policy and practice have appeared in the recent literature [4].

Our study design could not discriminate whether guideline authors failed to disclose existing conflicts of interest or had none such conflicts. However, it is estimated that the industry in the United States spends $8000 to $13000 per year on each physician simply for marketing purposes [5,6]. Field experts are likely to receive much larger amounts of direct or indirect funding. Although these associations may not necessarily translate to conflicts of interest, the connotations are not always straightforward.

We found that conflicts of interest were rarely, if ever, reported by guidelines funded by the government, universities or professional physician organizations. Although it may be anticipated that such funders may make more stringent efforts to assure objectivity in guideline development, it is still important that potential conflicts of interest of the individuals participating in the process should be acknowledged. This holds true even if group authorship is assumed. Conflicts of interest may be more worrisome when there is individual authorship. One would expect the objectivity of the guideline to be more vulnerable when only one or two individuals are authoring it. Paradoxically, the likelihood of disclosing conflicts of interest was smaller when few authors took responsibility for a guideline than when several authors were involved.

Recent studies have focused on deficiencies in the development and reporting of guidelines and have stressed the need to standardize the process [7-9]. Conflicts of interest can harm the credibility of guidelines. Competing interests may negatively influence the quality of clinical practice [10], as well as prescribing and professional behavior [5]. Even original studies [11] and cost-effectiveness analyses [12] may
reach differing results depending on competing interests. Guidelines are likely to be even more vulnerable to these influences.

**Conclusions**

One would expect that field experts ubiquitously have strong financial and other connections to the industry in their field of expertise. Transparency, by means of disclosure of potential conflicts, could foster public trust. Such information would take minimal space to report and may help to obviate doubts regarding the integrity of guidelines. Both guideline authors and journal editors should pay more attention to this important issue.
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Table 1. Characteristics of practice guidelines: reporting of conflicts of interest.

|                      | Conflicts of interest reported | Conflicts of interest not reported | Exact p-value |
|----------------------|-------------------------------|-----------------------------------|---------------|
|                      | N=7                           | N=184                             |               |
| Journal              |                               |                                   |               |
| NEJM                 | 0                             | 7                                 | 0.026         |
| JAMA                 | 4                             | 31                                |               |
| Lancet               | 0                             | 9                                 |               |
| Annals               | 2                             | 31                                |               |
| BMJ                  | 1                             | 17                                |               |
| Pediatrics           | 0                             | 89                                |               |
| Year                 |                               |                                   | <0.001        |
| 1979                 | 0                             | 22                                |               |
| 1984                 | 0                             | 40                                |               |
| 1989                 | 0                             | 47                                |               |
| 1994                 | 0                             | 42                                |               |
| 1999                 | 7                             | 33                                |               |
| Focus                |                               |                                   | 0.14          |
| Therapy              | 1                             | 59                                |               |
| Prevention           | 3                             | 100                               |               |
| Both                 | 3                             | 25                                |               |
| Main country         |                               |                                   | 1.00          |
| Europe               | 1                             | 25                                |               |
| America              | 6                             | 159                               |               |
| Group Authorship     |                               |                                   | 1.00          |
| Yes                  | 6                             | 155                               |               |
| No                   | 1                             | 29                                |               |
| Drug Intervention*   |                               |                                   | 1.00          |
| Yes                  | 2                             | 50                                |               |
| No                   | 5                             | 134                               |               |
P-values are based on Fisher’s exact test.

* emphasis placed on medications rather than on vaccines, devices, surgical interventions, nutritional interventions, counseling, screening, rehabilitation and other non-pharmaceutical interventions

† other sources of funding include mostly professional organizations (American College of Physicians, American Academy of Pediatrics, American Medical Association); mixed source of funding is defined as a combination of two or more of the four categories of funding

‡ n=60 for this analysis; 30 guidelines did not have group authorship and another 30 guidelines specified specific individuals who were primarily responsible for writing the manuscript, even if group authorship was mentioned
**Table 2. Nature of potential conflicts disclosed**

| POTENTIAL CONFLICTS* | N    |
|----------------------|------|
| Paid travel fees     | 7 (29%) |
| Provided consultation| 5 (21%) |
| Received grants      | 3 (13%) |
| Received money as speakers | 3 (13%) |
| Attended symposia    | 2 (8%) |
| Salary support       | 1 (4%) |
| Worked for a specific company | 2 (8%) |
| Contract for a research project | 1 (4%) |

* Some authors disclosed more than one potential conflict of interest
Editors’ note: Another positive report was received from a reviewer who declined to make their comments public.

Mildred Cho

1) The authors address a very important topic that is relevant to both research and clinical practice.

2) The authors do not define what they mean by "conflict of interest". Possible options, among which it is impossible to distinguish in this paper are (a) all financial interests of guideline authors / only financial interests that are relevant to the guidelines / all conflicting or competing interests including both financial and non-financial interests. The authors should state whether they defined conflicts of interests in the way defined by the journals or by their own definition.

3) Some of the conclusions do not necessarily follow from the results or the literature. Specifically:

In this statement, "However, it is estimated that the industry in the United States spends $8000 to $13000 per year on each physician simply for marketing purposes [5,6]. Field experts are likely to receive much larger amounts of direct or indirect funding. ", it is not defined what "the industry" is and it does not necessarily follow that any one industry, however defined, would be relevant to the broad range of practice guidelines examined in this study. Furthermore, it is not clear where the evidence is that field experts would receive larger amounts than the amounts received by the average physician for marketing purposes, and even if that were the case, whether that would necessarily be a conflict of interest. For example, a researcher might receive a consulting fee from company A but participate on a consensus panel that reviewed the efficacy of a class of drugs not manufactured or marketed by company A. It is not clear where the evidence exists for the statement, "One would expect that field experts ubiquitously have strong financial and other connections to the industry in their field of expertise." The authors need to either support these unsupported statements or remove or modify them to be consistent with existing literature, and need to define "conflict of interest" clearly.
**Level of interest**

A paper of considerable general medical or scientific interest

**Advice on publication**

Accept after revision, which I do not need to see

**Quality of written English**

Acceptable

**Competing interests**

None declared