Financial Conflicts of Interest in Inflammatory Bowel Disease Guidelines

Alexander W. Grindal, Rishad Khan, Michael A. Scaffidi, MEd, Amir Rumman, MD, and Samir C. Grover, MD

Background: Industry payments can lead to financial conflicts of interest (FCOI) among authors of clinical practice guidelines (CPGs). Guidelines for inflammatory bowel disease (IBD) may be at particularly high risk. We determined the prevalence of FCOI in IBD CPGs produced by various gastroenterology societies.

Methods: We conducted a cross-sectional analysis of FCOI disclosure among CPGs related to the management of IBD. We ascertained the prevalence and types of FCOI for each guideline and determined adherence to National Academy of Medicine (NAM) standards. FCOI disclosures were compared between societies producing CPGs.

Results: We identified 11 relevant CPGs with 173 total authors. There were 117 (68%) authors who declared a payment. A total of 107 (62%) authors declared FCOI related to a medication recommended in the guideline. There was a significant difference ($P < 0.001$) between the proportion of authors with FCOI between countries or regions. Authors of US CPGs had a significantly lower FCOI prevalence (19%) compared with other societies. Authors of UK CPGs had a significantly lower FCOI prevalence (56%) compared with Canadian (84%) and European (94%) CPGs. Three (27%) guidelines adhered to both NAM standards.

Conclusions: A substantial portion of authors of IBD CPGs had FCOI. Our study found a significant difference in FCOI prevalence based on CPG sponsor nationality. Most CPGs for IBD did not adhere to NAM standards for FCOI disclosure.

Key Words: conflicts of interest, inflammatory bowel disease, clinical practice guidelines

INTRODUCTION

Financial conflicts of interest (FCOI) between physicians and industry can influence clinical practice.1 The presence of FCOI is especially important in clinical practice guidelines (CPG), as they are intended to influence practice and should be objectively created.2 Although prior studies suggest a substantial burden of FCOI among authors of CPGs,3, 4 the prevalence of FCOI among inflammatory bowel disease (IBD) guidelines is unclear.

The rise of biologic medications has led to important changes in IBD CPG recommendations. Although there is often high-quality evidence underlying these recommendations,5, 6 there may be undue industry influence on the guideline development process. In the United States, the National Academy of Medicine (NAM) attempts to set boundaries on such potential influences. Their recommendations include appointing committee chairs with no FCOI and limiting guideline authors with FCOI to less than 50% of the panel.7 These NAM recommendations have been used in the literature as standards by which to assess FCOI in guidelines.4, 8, 9 Moreover, the National Guideline Clearinghouse is studying the possibility of describing the extent to which included guidelines adhere to NAM standards.10 In other fields, adherence to these recommendations has been poor.8, 9

Evidence suggests that physicians with industry FCOI view clinical trial results more favorably9 and that there is an increased likelihood that they will prescribe brand name drugs. Although there is no evidence on the impact of FCOI on recommendations in CPGs, the presence of FCOI may nevertheless undermine physicians’ and the public’s confidence in the guidelines.12 As summarized by the NAM Committee on Conflicts of Interest, “Conflicts of interest threaten the integrity of scientific investigations, the objectivity of professional education, the quality of patient care, and the public’s trust in medicine.”13

Inflammatory bowel disease guidelines may be at especially high risk of having authors with FCOI, as gastroenterologists tend to receive more industry payments compared with physicians from other specialties.14 Moreover, biologic medications used for the treatment of IBD are among the

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highest-grossing medications worldwide. Pharmaceutical companies producing these biologic medications expend considerable resources marketing their products, including payments to physicians. Given these concerns, we evaluated the prevalence of FCOI among authors of IBD guidelines.

METHODS

Study Design
We performed a cross-sectional analysis of financial conflicts of interest declared by CPG authors of inflammatory bowel disease guidelines. No funding was required. Ethical approval was not required as this study relies on publicly available information, as defined in the Tri-Council Policy Statement for Ethical Conduct or Research Involving Humans.

Identification of Guidelines
We identified clinical practice guidelines from major North American and European gastroenterological societies based on a previous report evaluating IBD guidelines. These societies were the American Gastroenterological Association, the American College of Gastroenterology, the Canadian Association of Gastroenterology, the British Society of Gastroenterology, and the European Crohn’s and Colitis Organisation. We searched for all Crohn’s disease and ulcerative colitis guidelines and only included the most recent version of each guideline. We classified guidelines by the country or region of the society endorsing the guideline.

Identification of Financial Conflicts of Interest
We extracted a list of authors from each CPG. For each author, we reported sex, primary institution, whether they were a guideline committee chair, and whether they were a physician. We identified authors who declared FCOI in the guideline manuscript or any supplemental documents and categorized FCOI as the following: (1) general: consulting fees, speaker’s fees, honoraria, gifts, food and beverage, and travel and lodging; and (2) research: any direct compensation to physicians for research activities, such as funding for research study coordination and implementation, payments to study participants to cover expenses associated with the study, and/or funding for a research project where the physician is named as a principal investigator. We also recorded which companies each author declared FCOI with and identified if these companies made a biologic medication recommended in the CPG. Finally, we assessed adherence with two NAM recommendations for CPG reporting: appointing committee chairs with no FCOI and limiting guideline authors with FCOIs to less than 50% of the panel.

Statistical Analysis
We conducted statistical analyses using SPSS (v 24.0, IMB Corp., Armonk, NY, USA). We determined the frequency and distribution of the study population first using descriptive analyses. We used the chi-square and Fisher exact tests for categorical variables of large and small sample sizes, respectively. We also performed post hoc pairwise comparisons between societies with chi-square or Fisher exact tests. We used a 2-sided \( \alpha \) of 0.05 to determine statistical significance, with Bonferroni corrections for multiple pairwise comparisons.

RESULTS
We identified 11 clinical practice guidelines with 173 authors. Thirty-six (21%) authors were female, 147 (85%) had an academic affiliation, 20 (12%) were committee chairs, and 159 (92%) were physicians. The characteristics of the guidelines are summarized in Table 1. With respect to adherence to NAM standards, 8 (73%) guidelines did not appoint a chair(s) without any FCOI, and 8 (73%) guidelines did not limit authors with FCOI to a minority (ie, <50%) of the panel. Overall, 3 (23%) guidelines adhered to both NAM standards.

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<th>Guideline</th>
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<th>Country or Region</th>
<th>No. Chairs</th>
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Prevalence of Financial Conflicts of Interest

A total of 117 (68%) authors declared at least 1 FCOI in the guideline or supplementary documents, with 116 (67%) declaring general FCOI and 50 (29%) declaring research FCOI. A total of 107 (62%) authors declared FCOI related to a pharmaceutical company making a biologic medication recommended in the guideline, with 102 (59%) declaring a general FCOI and 6 (27%) declaring a research FCOI. There were 110 (64%) authors who declared FCOI from multiple companies.

Prevalence of FCOI organized by society is provided in Table 2. We found that the proportion of guideline authors with any FCOI ($X^2 (3, n = 173) = 61.2, P < 0.001$) and medication-related FCOI ($X^2 (3, n = 173) = 58.9, P < 0.001$) differed significantly by country or region.

For authors with any FCOI, post hoc comparisons showed the following: Authors from Canada were more likely to declare a conflict compared with those from the United States (84% vs 19%, $P < 0.001$) or the United Kingdom (84% vs 56%, $P = 0.003$), authors from the United Kingdom were more likely to declare a conflict compared with those from the United States (56% vs 19%, $P = 0.003$), and authors from Europe were more likely to declare a conflict compared with those from the United States (94% vs 19%, $P < 0.001$) or the United Kingdom (94% vs 56%, $P < 0.001$). All other comparisons were not significant.

For authors with FCOI related to a pharmaceutical company making a medication recommended in the guideline, post hoc comparisons showed the following: authors from Canada were more likely to declare a conflict compared with those from the United States (78% vs 19%, $P < 0.001$) or the United Kingdom (78% vs 33%, $P = 0.003$) and authors from Europe were more likely to declare a conflict compared with those from the United States (92% vs 19%, $P < 0.001$) or the United Kingdom (92% vs 33%, $P < 0.001$). All other comparisons were not significant.

DISCUSSION

Our cross-sectional analysis of 11 CPGs related to Crohn’s disease and ulcerative colitis revealed that more than two-thirds of CPG authors declared FCOI. Canadian and European CPGs were more likely to have authors with FCOIs compared with American and British CPGs. We found similar trends with respect to conflicts with pharmaceutical companies producing the biologic medications recommended in the CPGs. Finally, most CPGs failed to meet the NAM standards of having a chair(s) free of FCOI and restricting authors with FCOI to less than 50% of the panel.

One potential reason for the high prevalence of FCOI is that guidelines panels include academic clinical trialists. As pharmaceutical companies sponsor many trials, these physicians are all but bound to receive research funding from industry. This interpretation, however, is not consistent with our data, as a substantial percentage of authors declared a general FCOI and no research FCOI. Previous data have shown that general payments are associated with increased odds of prescribing a manufacturer’s drug. Second, financial relationships between CPG authors and industry may arise, as CPG authors are often experts in their field and provide education to their colleagues on new medications.

We must also consider differences between sponsoring organizations. One potential explanation is the presence of national standards, such as those created by NAM in the United States. Additionally, the UK National Institute for Health and Care Excellence (NICE) has created the NICE Policy on Conflicts of Interest. One of 2 British CPGs, which adhered to NAM standards, also adhered to the NICE Policy. No equivalent standards exist for Canadian or European societies. Two of 4 American CPGs and 1 of 2 British CPGs adhered to both NAM standards evaluated in this study. However, no Canadian or European guidelines adhered to either NAM standard. The presence of regional policies may explain why the prevalence of FCOI among panelists of American and British CPGs was lower compared with Canadian and European CPGs.

Our study has several limitations. First, the process of identifying FCOI is based on self-declarations. Previous studies have suggested that there is a high burden of undeclared FCOI in American guidelines. We did not perform similar analyses due to the lack of comprehensive databases of industry payments to physicians in Canada, the United Kingdom, and many European countries. Additionally, the guidelines included

| TABLE 2. Financial Conflicts of Interest by Professional Society |
|------------------|------------------|------------------|------------------|
| Characteristic, No. (%) | United States (n = 36) | Canada (n = 74) | United Kingdom (n = 27) | Europe (n = 36) |
| Any FCOI | 7 (19) | 62 (84) | 15 (56) | 34 (94)* |
| Medication-related FCOI | 7 (19) | 58 (78) | 9 (33) | 33 (92)* |

*Denotes a significant difference between proportion of authors with FCOI between country or region with $P < 0.001$.

*Refers to a declared financial conflict of interest with a company producing a biologic medication recommended in the clinical practice guideline.
were published over a range of 10 years. During these 10 years, the expectations for proper FCOI disclosure have changed. We were unable to control for the potential impact of time on our findings. We also did not assess the potential association between FCOI and how panel members vote on drugs, as most societies do not publish voting records. A recent study of Food and Drug Administration drug approvals, however, has suggested that voting for the approval of a drug is associated with receiving payments from the company making the drug. Finally, we were unable to investigate the relationship between FCOI and guideline recommendations. Variation in the detail of the recommendations, scope of the guidelines, and date of publication precluded a formal comparison.

CONCLUSIONS

We found that guidelines for Crohn’s disease and ulcerative colitis have a substantial burden of FCOI. These financial relationships may adversely affect patient and clinician trust in the objective and evidence-based nature of the guidelines. Given this, we recommend that subspecialty societies adopt stricter policies to enforce national standards of FCOI reporting. Additionally, sponsoring organizations should ensure that authors with FCOI recuse themselves from voting or participate as nonvoting members. Future research should be aimed at clarifying the reasons underlying differences in FCOI prevalence among the different societies, determining the impact of different types of payments (eg, general, research) on authors’ voting patterns during CPG development, and exploring the potential of undeclared FCOI among guidelines. Additionally, future research could be aimed at determining the presence of other conflicts of interest, such as conflicts due to intellectual property and academic research.

REFERENCES