Conflicts of Interest Ethics: Silencing Expertise in the Development of International Clinical Practice Guidelines

Derek J. Jones, JD; Alan N. Barkun, MDCM, MSc (Clinical Epidemiology); Yidan Lu, MDCM; Robert Enns, MD; Paul Sinclair, MSc; Myriam Martel, BSc; Ian Gralnek, MD; Marc Bardou, MD, PhD; Ernst J. Kuipers, MD; and Joseph Sung, MD, PhD, for the International Consensus Upper Gastrointestinal Bleeding Conference Group*

Background: It is unclear whether global experts with financial conflicts of interest (FCOIs) should be included in, be excluded from, or have a limited role in developing international clinical practice guidelines (CPGs). Optimal management of FCOIs to ensure independent, expert CPGs remains ethically contested.

Objective: To manage FCOIs and examine whether an ethics framework with discussion recusal by experts with FCOIs affects deliberations and voting on a CPG.

Design: Development of an ethics framework grounded on transparency and proportional management of COIs, including self-recusal, evaluation of the effect on COIs and CPG process by quantification of voting on recommendations, and qualitative assessment of experts’ ethics dialogue.

Setting: International consensus meeting to formulate a CPG in gastroenterology.

Participants: 34 experts from 15 countries.

Measurements: Counting the votes of experts with and without declared FCOIs and qualitative assessment of ethics discussions.

Results: 62% of experts reported at least 1 FCOI. Eight out of 21 declared FCOIs and qualitative assessment of ethics discussions. Measurements: Counting the votes of experts with and without declared FCOIs and qualitative assessment of ethics discussions.

Results: 62% of experts reported at least 1 FCOI. Eight out of 21 recommendations presented potential FCOIs. Experts with conflicts recused themselves from discussing 6 of the 8 recommendations, leaving a majority of nonconflicted discussants (median, 22; range, 19 to 26) for the 6 recommendations. Recusals did not affect voting outcomes but may have diluted the richness of the discussions. Ethics dialogue revealed accord on transparency but underscored challenges to proportional management of COIs beyond basic disclosure. Concerns about bias, COI definitions, expertise, and integrity express important international ethics questions.

Limitation: Small participant numbers and application of the framework to only 1 meeting of 1 CPG.

Conclusion: An ethics framework may help to identify and manage COIs and catalyze both ethics dialogue and innovative COI standards that seek to balance impartiality and expertise for trusted CPGs. Optimal balancing remains contested. Recommendations include frameworks, interdisciplinary analysis, and international policy initiatives to better manage COIs in the CPG process.

Primary Funding Source: Canadian Association of Gastroenterology; European Association for Gastroenterology and Endoscopy; Asian Pacific Society of Digestive Endoscopy; and Institute of Diabetes, Metabolism, and Nutrition of the Canadian Institutes of Health Research.


For author affiliations, see end of text.

* The Appendix (available at www.annals.org) provides a full list of the members of the International Consensus Upper Gastrointestinal Bleeding Conference Group.

Clinical practice guidelines (CPGs) are adopted to guide decisions and manage conditions by linking evidence with clinical judgment. Their contribution to standards of care presumes that they represent impartial expertise for the good of physician–patient decision making. However, that ethical foundation has come under challenge, as the relationship among industry, physicians, and CPGs generates debate on the standards, effect, and management of financial conflicts of interest (FCOIs).

Over the past decade—amid disclosure rates ranging from 3.7% to 71.2% (1–4)—FCOIs have been increasingly documented, as industry affiliations of CPG authors have sometimes reached 87% to 90% (5, 6). The relationship has been deemed a “pervasive” (7) and “profound and extensive problem” (8). It has attracted the scrutiny of a burgeoning interdisciplinary literature on bias (9, 10), which has questioned CPGs on cardiovascular conditions (11–13), sepsis (14, 15), anemia (16), and psychiatric disorders (6) for undisclosed, undocumented, or preponderant FCOIs.

In 2011, a French court annulled a government CPG on diabetes for apparent failure to adhere to COI law (17). Similar questions dog global public health guidance (18, 19); international organizations are thus refining COI procedures for their scientific panels (20). Professional societies (21–23); the Association of American Medical Colleges (24); industry (25); the Institute of Medicine (26, 27); and U.S. (28), pan-European (29), British (30), and French (31) government health authorities have recently revised COI policies or adopted reports.

Such reforms may soon inspire uniform, coherent, and detailed standards. Meanwhile, physicians’ codes of ethics (32, 33) compound ethical uncertainty by silence on the issue. Should experts with COIs be included in or excluded or limited from deliberating, drafting, or voting on guidelines?

We confronted this question for the discussion and voting of an international CPG (34). To address it, we...
developed a COI ethics framework under which experts recusing themselves from scientific discussions could nevertheless vote on CPG recommendations. We report on the COI ethics exercise by examining the content and implementation of the framework; recusals, outcomes, and expert perceptions; and critical ethics questions and policy recommendations for managing COIs in the CPG process.

**METHODS**

An international CPG on management of upper gastrointestinal bleeding (34) was developed by a multidisciplinary group of 34 experts from 15 countries. The CPG process followed national CPG standards (35), which adopted the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument (36).

**CPG Meeting Process**

In preparation for the meeting, a 4-member steering committee—all of whom had previously declared FCOIs—reviewed published guidelines on the topic and identified 20 previously published and 44 new potential recommendations that warranted updates or guidance. The selection was reduced to 21 draft recommendations (including 19 updates) through online voting by all participants.

The steering committee developed and approved search strategies for related evidence. Two participants sorted through literature by using predefined inclusion or exclusion criteria to identify pertinent evidence; a third party without conflicts validated the findings and extracted data from selected studies by using standardized forms. They then synthesized these data into systematic reviews (37–43) that were circulated to all CPG members. Final formulation of each resulting recommendation and grading of its evidence through use of the Grading of Recommendations Assessment, Development and Evaluation approach (44) by all participants followed a validated, modified Delphi process. Each recommendation was subsequently subject to a 6-point Likert scale to quantify agreement; 75% group approval was required for adoption.

**An Ethics Framework for COIs**

The process conformed to the ethics norms of the Canadian Association of Gastroenterology (45), the Canadian Medical Association (46), and the Accreditation Council for Continuing Medical Education (47). Such national norms afforded little detailed guidance on managing potential COIs with global experts.

An independent consultant advised the development of an ethics framework of integrated COI standards, process, and structures. It draws on evolving standards (24, 25, 28, 32, 46–51) and includes creation of a COI advisory committee and a COI “toolbox” (Table 1). The toolbox consists of transparency in financing and decisions, disclosure of COIs, firewalling information, restricted roles or recusals of individuals with COIs, proportionality between COI risks and COI management strategies, and documenting COI process.

The COI advisory committee identified 4 likely loci of FCOIs: meeting funding by industry sponsors, industry relations with experts, discussion and voting process, and dissemination and publication of results. To evaluate FCOIs, each expert completed a mandatory premeeting financial disclosure form. The COI advisory committee defined “FCOI” as any financial relationship—encompassing actual, potential, and perceived FCOIs—that a professional shared in the past 2 years with commercial entities having economic, commercial, or competing scientific interests in decisions about the CPG (Table 2).

Financial declarations were reviewed by the Canadian Association of Gastroenterology office and COI advisory committee and distributed to participants before face-to-face deliberations. To maximize the integrity of the process and manage FCOI risks in the absence of uniform international definitional thresholds, the committee considered any FCOI “significant.” Significant FCOIs were presumed to invoke limitations on participatory roles in the meeting.

To frame the discussion, content experts (persons other than those who researched the literature to prepare systematic reviews) reviewed the prepared evidence for each recommendation before the face-to-face meeting. The content experts prepared slides based on the evidence reports; the slides were reviewed for bias by the COI advisory committee. Selected content experts were assigned to present slides for the different recommendations. However, draft CPG recommendations likely to implicate economic interests of medical device or drug manufacturers were identified as being at risk for FCOIs by the COI advisory committee and were managed differently.

Under the ethics framework, content experts presenting evidence for these recommendations identified as “at risk” were to be free from bias unless their expertise was deemed necessary to afford essential (that is, unique or otherwise unavailable) input (Table 1). For all recommendations at risk, experts with conflicts were invited to recuse themselves from discussions at the meeting but thereafter joined experts without conflicts in voting (Table 1).

Voting was done by private electronic touchpad, so no one knew how another person voted. All experts voted, because votes would be tracked and those of recused experts could be discounted if “conflicted” votes would determine the outcome of a recommendation. The meeting concluded with a group discussion about ethics that everyone attended and a postmeeting online COI dialogue.

**Framework Evaluation: Quantitative and Qualitative Analyses**

Participants were briefed on the COI ethics framework at the start of the meeting. However, to avoid affecting voting results, they were not informed beforehand that voting results could be discounted. They were so advised after voting had been completed. Written consent to use ano-
nymized data was obtained. Because the purpose of the exercise was policy formulation and evaluation, review of research ethics was not sought.

Elements of the applied ethics framework were examined, including the COI process, voting outcomes, and effect of recusals. Quantitative voting data were collected for each statement. Qualitative analysis of the ethics commentary was performed after coding and thematic grouping by using modified grounded theory (52).

**Role of the Funding Source**

Conference funding was provided by the Canadian Association of Gastroenterology; European Association for Gastroenterology and Endoscopy; Asian Pacific Society of Digestive Endoscopy; and Institute of Diabetes, Metabolism, and Nutrition of the Canadian Institutes of Health Research and by arms-length contributions from AstraZeneca Mölndal (Sweden), Abbott Canada, and Olympus Canada to the Canadian Association of Gastroenterology. The Canadian Association of Gastroenterology administered all aspects of the meeting and provided additional in-kind support. The funding sources had no role in developing recommendations, abstracting data, synthesizing results, grading evidence, or preparing or submitting the manuscript.

**RESULTS**

**Types of COIs**

Sixty-two percent of our CPG experts (21 out of 34) reported at least 1 FCOI in the following categories: speakers’ bureau (53%), research support (35%), consultant (26%), advisory board (18%), employee (0%), and stock or equity (0%) (Table 2). Experts with conflicts reported a median of 6 FCOIs (range, 1 to 15) and a median of 2 categories of FCOI (range, 1 to 4).

**CPG Recommendations at Risk for FCOIs and Voting Outcomes**

Eight of 21 recommendations were designated as being “at risk” for FCOI (34). Experts with potential FCOIs recused themselves from discussions for 6 recommendations; 2 recommendations prompted no self-recusals because no expert perceived a relevant FCOI. We required recourse to conflicted experts with unique expertise to discuss and give a presentation on evidence for 2 recommendations. The median number of recusals per recommendation was 12 (range, 8 to 15), leaving an average of 22 nonconflicted discussants (range, 19 to 26) per recommendation.

Fifteen recommendations were discussed and voted on by all 34 experts; 6 recommendations were voted on by all 34 on the basis of discussion by an average of 22 experts (Figure). The overall voting outcomes (agree vs. disagree) did not change when votes of recused members were included (Figure). No “conflicted” votes were discounted because none affected the outcome of a recommendation.

**Qualitative Analysis: Ethics Concerns**

All experts attended a postvoting ethics session; 14 of 34 joined a subsequent online ethics conversation. All acknowledged the importance of addressing FCOIs while air-

<table>
<thead>
<tr>
<th>Table 1. Excerpts of Ethics Framework</th>
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<tbody>
<tr>
<td><strong>COI Management Toolbox</strong></td>
</tr>
<tr>
<td>Transparency: In financing and decisions</td>
</tr>
<tr>
<td>Disclosure: Mandatory declaration of FCOIs for conference and public disclosure</td>
</tr>
<tr>
<td>Firewalling: Structure or delineate access, roles, duties (e.g., financing, information)</td>
</tr>
<tr>
<td>Role restrictions: Recusals and key role restrictions (e.g., voting, discussion, authorship) for FCOIs</td>
</tr>
<tr>
<td>Proportionality: Calibrate FCOI risks to FCOI management options and strategy</td>
</tr>
<tr>
<td>Evidence-based: Calibrate FCOI risks to FCOI management options and strategy</td>
</tr>
<tr>
<td><strong>Implementation: Premeeting</strong></td>
</tr>
<tr>
<td><strong>Funding</strong></td>
</tr>
<tr>
<td>No direct industry funding of participants</td>
</tr>
<tr>
<td>Conference funded by pooled unrestricted grants from international medical societies, government, and industry</td>
</tr>
<tr>
<td>Funders have no role in identifying statements, abstracting data, synthesizing results, grading evidence, or authoring recommendations or manuscript</td>
</tr>
<tr>
<td><strong>Creation of ad hoc COI advisory committee</strong> to:</td>
</tr>
<tr>
<td>Implement ethics framework for the management of FCOI</td>
</tr>
<tr>
<td>Review and advise on results of FCOI disclosure forms and FCOI questions</td>
</tr>
<tr>
<td>Identify and address other likely FCOIs</td>
</tr>
<tr>
<td>Identification of likely loci of FCOI</td>
</tr>
<tr>
<td>Funding by industry sponsors</td>
</tr>
<tr>
<td>Industry relations with experts</td>
</tr>
<tr>
<td>Discussion and voting process</td>
</tr>
<tr>
<td>Dissemination and publication of results</td>
</tr>
<tr>
<td><strong>Identification of recommendations “at risk” for FCOI</strong></td>
</tr>
<tr>
<td>Those likely to implicate economic interests of medical device or drug manufacturers</td>
</tr>
<tr>
<td><strong>Identification and management of experts’ FCOIs</strong></td>
</tr>
<tr>
<td>Disclosure: Mandatory declaration of experts’ financial relationships, for disclosure in conference slides, documentation, discussion, and publications</td>
</tr>
<tr>
<td>Definition: To maximize integrity in the absence of uniform international definitions, “significant” COIs include any FCOI</td>
</tr>
<tr>
<td>Management: Proportionally limit participation of experts with significant FCOIs, per COI toolbox</td>
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<tr>
<td><strong>Implementation: CPG Meeting Process and Procedures</strong></td>
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<tr>
<td><strong>Ethics norms conforming to:</strong></td>
</tr>
<tr>
<td>Recognized and emerging (24, 32, 47), national (46), institutional, and professional (45) standards (25, 28, 48–50)</td>
</tr>
<tr>
<td><strong>Discussion recusals and voting</strong></td>
</tr>
<tr>
<td>For recommendations implicating FCOI issues, conflicted experts recuse themselves from discussion of recommendations, unless their input is necessary to afford essential expertise (e.g., unique or otherwise unavailable input)</td>
</tr>
<tr>
<td>All experts vote privately on all recommendations</td>
</tr>
<tr>
<td>Track votes and discount those of recused experts if they determine adoption/rejection of a recommendation</td>
</tr>
<tr>
<td><strong>Implementation Postmeeting: Writing and Publication</strong></td>
</tr>
<tr>
<td>Adhere to standard peer review process and to International Committee of Medical Journal Editors Uniform Requirements for Manuscripts</td>
</tr>
<tr>
<td>Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication, Part D: Conflicts of Interest (51)</td>
</tr>
</tbody>
</table>

COI = conflict of interest; CPG = clinical practice guideline; FCOI = financial conflict of interest.

* COI advisory committee comprised an independent ethics consultant, the guideline’s principal organizer, and a representative of the Canadian Association of Gastroenterology.
The exercise enabled us to document, evaluate, manage, and debate COIs in CPG development. An evaluation revealed no effect on CPG voting outcomes by experts with FCOIs, but an apparent effect on the richness of scientific discussion by the recusals was found. The exercise also identified key COI ethics issues. We elaborate the outcomes and policy issues through 10 critical questions that survive the exercise.

**How Frequent Are COIs Among Authors of CPGs?**

Our exercise suggests that the high incidence of financial relations between international clinician-investigators and industry presents serious challenges to developing guidelines with experts free of potential FCOIs. Paralleling previous reports of a 35% to 87% frequency of FCOIs among authors of CPGs (3, 5), 62% of our experts declared some financial relationship with industry. The most prevalent categories of FCOIs were speakers’ bureaus, research grants, and consultancies, even if not all of the declared interests presented FCOIs, because some were irrelevant or remote. However, without uniformity of COI definitions, declaration standards, and screening procedures, comparing such figures warrants caution.

**What Is a “Significant COI”?**

Conflicts of interest may divide loyalties and impair independent professional judgment. The concept has yet to yield a uniform global definition of “significant COI,” with “primary,” “direct,” qualitative, and quantitative thresholds (26, 29, 53). As a result, international CPGs rely on national or institutional norms.

**Discussion**

Absent uniform and comprehensive standards, we developed and implemented an ethics COI framework grounded on the proposition that, for the integrity and credibility of an international CPG, it may be ethical in some circumstances to exclude global experts with significant FCOIs who are involved in the process. We premised the framework on a proportionality principle that CPG participatory standards should be commensurate with COI risks. Applying this principle yielded a process by which experts with conflicts who recused themselves from scientific discussions at the CPG meeting nevertheless voted on recommendations.

**Table 2. Distribution of Declared FCOIs**

<table>
<thead>
<tr>
<th>Category of COI</th>
<th>Participants with COIs, n (%)</th>
<th>Total COIs, n</th>
<th>Median COIs (Range), n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speakers’ bureau</td>
<td>18 (53)</td>
<td>44</td>
<td>2 (1–8)</td>
</tr>
<tr>
<td>Research support</td>
<td>12 (35)</td>
<td>35</td>
<td>3 (1–7)</td>
</tr>
<tr>
<td>Consultant</td>
<td>9 (26)</td>
<td>24</td>
<td>2 (1–6)</td>
</tr>
<tr>
<td>Advisory board</td>
<td>6 (18)</td>
<td>14</td>
<td>1 (1–8)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (9)</td>
<td>3</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Employee</td>
<td>0 (0)</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>Stock/equity</td>
<td>0 (0)</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>Participants and COIs</td>
<td>21 (62)</td>
<td>120</td>
<td>–</td>
</tr>
</tbody>
</table>

COI = conflict of interest; FCOI = financial conflict of interest.
* Significant FCOI is defined as any financial relationship in the past 2 years—encompassing actual, potential, and perceived COIs—that a professional shared with commercial entities having an economic, commercial, or competing scientific interest in decisions of the conference.
† Total number of participants is 34, 21 of whom have declared COIs.
‡ Participants could declare more than 1 COI per category.
§ The Canadian Association of Gastroenterology’s 2007 disclosure form grouped financial declarations into these categories. The form was based on analogous policies of the Canadian Medical Association and the 2004 policy of the Accreditation Council for Continuing Medical Education (46, 47).
¶ Participation in educational activities, as reported by 3 participants.
¶ A maximum of 1 COI per category, even if many COIs were reported for that category.
On the spectrum of 1 to 5 years (20, 29, 54), we used a 2-year period for declarations (Table 2). Broadening definitions reflect a belief that most conflicts warrant identification (30, 55); thus, 2011 U.S. law decreased the threshold for a “significant financial interest” from $10,000 to $5,000 (56). We found that a focus on FCOIs does not address bias from intellectual or nonfinancial interests, although policies increasingly address them (30, 57).

**Do COIs Affect CPG Voting and Discussion?**

Our exercise paralleled findings that COIs may not affect voted recommendations (58) and revealed no substantial differences in the adoption of recommendations that include conflicted experts. All recommendations were voted on by a majority of nonconflicted experts. The outcome suggests that CPGs voted by a minority of experts with conflicts are generally unlikely to have recommendations altered by COIs. This parallels reforms to limit experts with conflicts on committees to a “distinct minority” (26).

Our COI standards more likely affected discussion. Experts with conflicts recused themselves from discussing 6 out of 21 recommendations, leaving a majority of nonconflicted experts. Although the statistics suggest a modest effect, colleagues raised concerns about diluted scientific discussion. Future analyses of how recusals affect discussion may benefit from quality assessment measures beyond the scope of our exercise.

**Does Disclosure Sufﬁce?**

Conflict of interest disclosure practices may be inaccurate (4), inconsistent, and incomplete (59) and may increase biased advice (60). Still, standard use of financial declarations in international CPG process underscores disclosure as a basic COI management tool for transparency (61). In our exercise, some persons argued that disclosure sufﬁces, which echoes the practice of declaring COIs before participating fully in decisional meetings. Yet, our ethics framework and others consider disclosure insufﬁcient (28, 49, 62).

**Unconscious Bias: A Role?**

Competing theories may explain divergent views. Does “disclosure sufﬁces” reﬂect “unconscious bias”? It arises in dual-role professionals “seduced” (63) into moral complacency and bias by ethically gray practices that become community norms (64), for example, FCOIs from systemic industry–physician relations (65).

Believing in one’s objectivity, minimizing COIs, and “biased information processing” are consistent with unconscious bias (10, 64). Or, does “disclosure sufﬁces” reﬂect conscious choice? Sometimes, tangible expertise bests perceived impartiality. Answers should build on ethics codes, fiduciary duties, and increasing insights from the behavioral sciences (66) and enable interdisciplinary knowledge.

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**Table 3. Ethics Concerns Identified by Qualitative Analysis**

| Criteria for self-recusal by experts with an FCOI seem subjective, and bias seems impossible to eliminate. Although FCOIs are emphasized, nonfinancial interests also present COIs. Screening for COIs may weaken the scientiﬁc process by excluding participants with important expertise. Some argue that once potential biases are made explicit, experts with FCOIs should participate in the discussion or vote. Others argue that there is no effect on the process if members with FCOIs vote. Some think that disclosure is insufﬁcient to manage FCOIs. Although professional conduct affects public conﬁdence, few believed that experts with FCOIs should recuse themselves to further public trust. Recusal decisions should come from an ethics committee rather than the participant. |

COI = conﬂict of interest; FCOI = ﬁnancial conﬂict of interest.

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**How High the COI Standard?: Proportionality**

Disagreement over which COI management tool sufﬁces also ﬂows from differing answers to a question: To what standard should CPGs be held? Proportionality calibrates COI processes to risks. Low risks demand disclosure; high risks demand limitations or exclusion. We reasoned that commercial inﬂuence creates substantial risks, because CPGs inﬂuence clinical thought, standards, and patients (67). Thus, some call for CPGs to be held “to the most stringent of COI standards” (68).

Does doing so mean that we ban or manage COIs? We found that if blunt prohibitions silence expertise essential for informed discussion and decisions (69), they poorly serve scientiﬁc integrity. Then, the optimal option is to manage COI risks with proportionality.

**How to Manage COIs Beyond Disclosure?**

After disclosure, should experts with conﬂicts participate in CPGs? Responses range from case-by-case analysis to inclusion or presumptions against inclusion (24) to exclusion from leadership roles (70), unless exceptions apply (26). The spectrum bespeaks an ethical pluralism of no “absolute rules” (71). However, each option asks whether or where to strike a balance.

Our exercise echoes international uncertainty (62, 72) in that we identiﬁed no simple response or universal solution. Absent detailed global norms, we developed an ethics framework (73) of integrated standards, process, and structures (Table 1). The framework helped to identify and manage FCOIs, catalyze ethics dialogue, and innovate procedures and pilot COI recusals.

**Conﬂicted Experts: Voting or Discussion Roles?**

Our exercise indicates that comparative risk analysis of COIs may reﬁne CPG participatory roles. We applied it to modify one standard approach under which conﬂicted experts participate in discussion but recuse themselves from voting. The logic of the standard approach is that colleagues advised of COIs beneﬁt from and weigh conﬂicted expertise in discussions but are not bound by COIs in decisions because conﬂicted experts do not vote.
Table 4. Policy Recommendations for COI Management

<table>
<thead>
<tr>
<th>COI policy reform</th>
<th>Rigorous, detailed, and effective guidance on COIs in the CPG process should be developed by international organizations, professional groups, universities, and industry.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethics frameworks</td>
<td>CPGs should be guided by coherent ethics frameworks that identify and manage COIs with robust standards, effective procedures, and accountable structures. Standards should reflect proportionality between COI risks and management procedures, such as recusals and exclusion. As a part of frameworks, independent COI or ethics committees enable interdisciplinary COI review, advice, and education.</td>
</tr>
<tr>
<td>Model policies and best practices</td>
<td>Opinion leaders with particular expertise (e.g., Council for International Organizations of Medical Sciences, professional and medical associations, interdisciplinary ethics groups) should translate their expertise into model policies and revised practices that make reasonably uniform COI definitions, procedures, standards, and norms to balance CPG independence and expertise when they conflict.</td>
</tr>
<tr>
<td>Interdisciplinary research and analysis</td>
<td>The conceptual, definitional, ethical, legal, empirical, theoretical, and policy facets of COI in the CPG process demand more interdisciplinary research and analysis. A research agenda (26) that targets knowledge and policy gaps warrants priority development.</td>
</tr>
<tr>
<td>CPG funding</td>
<td>Experiences with pooled monies should inspire creative consideration of independent funding options; for example, medical specialty organizations, government, foundations, and industry might partner to fund independent CPGs by creating a blind CPG trust fund as a 5-year demonstration project.</td>
</tr>
<tr>
<td>Summit</td>
<td>An international conference should be convened to address harmonization of standards, major issues, and management of COIs in the CPG process.</td>
</tr>
</tbody>
</table>

COI = conflict of interest; CPG = clinical practice guideline.

How to Balance Expertise and Impartiality?

To manage COIs, we calibrated voting and discussion roles to risk–benefit. Under our modified approach, the votes of conflicted experts count, unless they determine voted recommendations; such experts recuse themselves from discussion, unless their participation is “necessary for essential expertise” (Table 1). We invoked the discussion exception for unique methodological expertise.

Like U.S. reforms (75), the exception relies on the necessity to reconcile and balance the expertise and impartiality on which trust in medicine depends (76). Nonessential, conflicted expertise is excluded. A CPG ethics standard that limits participation of global experts with significant COIs to instances of demonstrable necessity seeks optimal risk–benefit equipoise.

How to Finance Independent CPGs?

Clinical practice guidelines—which typically cost $300 000 and are often developed by specialty societies (26)—may be financed by diverse sources. If industry funding of societies raises “institutional” FCOI issues (68), routine failure to disclose sources and amounts of funding undermines data analysis. Our international meeting costs approximately $200 000, with 31% financing from industry and 69% from medical organizations and government.

Our meeting was unlikely to occur without nonindustry funds. However, expertise would have been compromised without industry underwriting. Our experience suggests that arms-length, pooled financing provides a model for funding CPGs.

What Policy Implications?: Recommendations

The revising of dated COI policies by governments and international agencies, proliferation of more stringent professional norms, and the recent reports of the Institute of Medicine (26, 27) together indicate that the international biomedical community has entered a transformative era for refining ethical COI norms for heightened integrity of modern CPGs. To address key issues, we invite attention to the foregoing questions and recommend the specific policy initiatives shown in Table 4.

Limitations

Our CPG ethics exercise had limitations. We relied on self-reporting and voluntary self-recusals for COIs, which may have affected accuracy. Our small numbers limited the sample size. Financial COI risks encountered here may differ from those in other clinical contexts. The scope of effect was limited by focusing the ethics framework on the CPG meeting phase rather than on the entire development process. Despite these limitations, the exercise evokes issues central to the ethics of COIs in CPG development.

Conclusion

Echoing the evolving international state of the art and debate, our ethics initiative expressed accord on basic principles like transparency but ethical uncertainty on how best, beyond disclosure, to manage COIs in CPG process. Some contend that it is unethical to include important, conflicted expertise in CPG development; others contend that it is ethical to do so.

A standard that, for the integrity of CPGs, limits participatory roles of experts with significant COIs to narrow circumstances of necessity seeks to balance the values of impartiality and expertise that underlie trusted scientific decision making. Optimal points of balancing remain contested. Because critical questions on COIs in the CPG process survive our exercise and reverberate through international medical practice and the literature, they demand concerted deliberation, debate, research, and ethics policy initiatives.

From McGill University, Montreal, Quebec, Canada; St. Paul’s Hospital, University of British Columbia, Vancouver, British Columbia, Canada; Canadian Association of Gastroenterology, Oakville, Ontario, Canada;
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Technion-Israel Institute of Technology, Rambam Health Care Campus, Haifa, Israel; INSERM CIC-P 803, CHU de Dijon and Bourgogne University, Dijon, France; Erasmus Medical Center, Rotterdam, the Netherlands; and The Chinese University of Hong Kong, Hong Kong, China.

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Requests for Single Reprints: Alan N. Barkun, MDCM, MSc (Clinical Epidemiology), Division of Gastroenterology, Montreal General Hospital Site, McGill University Health Centre, 1650 Cedar Avenue, Room D7-346, Montreal, Quebec H3G 1A4, Canada; e-mail, alan.barkun @muhc.mcgill.ca.

Current author addresses and author contributions are available at www.annals.org.

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Current Author Addresses: Mr. Jones: Research Group on Health and Law, McGill University Faculty of Law, 3664 Peel Street, Montreal, Quebec H3A 1W9, Canada.
Drs. Barkun and Lu: Division of Gastroenterology, Montreal General Hospital Site, McGill University Health Centre, 1650 Cedar Avenue, Room D7-346, Montreal, Quebec H3G 1A4, Canada.
Dr. Enns: St. Paul’s Hospital, 770 1190 Hornby Street, Vancouver, British Columbia V6Z 2K5, Canada.
Mr. Martel: Montreal General Hospital Site, McGill University Health Centre, 1650 Cedar Avenue, Room T8-314, Montreal, Quebec H3G 1A4, Canada.
Dr. Gralnek: University of California, Los Angeles, Center for the Study of Digestive Health Care Quality and Outcomes, 11301 Wilshire Boulevard, Building 115, Room 318, Los Angeles, CA 90073.
Dr. Bardou: INSERM CIC-P 803, CHU de Dijon, Bâtiment du Pr Marion, 14 rue Gaffarel, BP 77908, 21079 Dijon Cedex, France.
Dr. Kuipers: Erasmus University Medical Centre, Room Ba-391, Box 2040, 3000 CA Rotterdam, the Netherlands.
Dr. Sung: Department of Medicine and Therapeutics, 9/F Clinical Science Building, Prince of Wales Hospital, Chinese University of Hong Kong, Sha Tin NT, Hong Kong, China.

Author Contributions: Conception and design: D.J. Jones, A.N. Barkun, R. Enns, I. Gralnek.
Drafting of the article: D.J. Jones, A.N. Barkun, Y. Lu, R. Enns, I. Gralnek, E.J. Kuipers.
Critical revision of the article for important intellectual content: D.J. Jones, A.N. Barkun, Y. Lu, R. Enns, I. Gralnek, M. Bardou, E.J. Kuipers.
Final approval of the article: D.J. Jones, A.N. Barkun, Y. Lu, R. Enns, P. Sinclair, I. Gralnek, M. Bardou, E.J. Kuipers.
Statistical expertise: A.N. Barkun, M. Martel.
Administrative, technical, or logistic support: Y. Lu, P. Sinclair.

APPENDIX: MEMBERS OF THE INTERNATIONAL CONSENSUS UPPER GASTROINTESTINAL BLEEDING CONFERENCE GROUP

Lars Agreus, Karolinska Institutet, Sweden; David Armstrong, McMaster University, Canada; Xavier Calvet, Institut Universitari Parc Taulí, Spain; Naoki Chiba, Guelph General Hospital, Canada; Livio Cipolletta, Hospital Agostino Maresca, Italy; Henry Cohen, Hospital de Clínicas, Uruguay; Lars-Gunnar Ericsson, Uppsala University, Sweden; Richard Hunt, McMaster University, Canada; Dennis Jensen, University of California, United States; Michio Kaminishi, Showa General Hospital, Japan; Fasiha Kanwal, John Cochran Veterans Affairs Medical Center and Saint Louis University School of Medicine, United States; Loren Laine, University of Southern California, United States; Angel Lanas, University of Zaragoza School of Medicine, Spain; James Lau, Chinese University of Hong Kong, China; Grigoris Leontiadis, McMaster University, Canada; Lars Lundell, Karolinska University Hospital, Sweden; Peter Malfertheiner, Otto von Guericke University, Germany; John Marshall, McMaster University, Canada; Janet Martin, University of Western Ontario, Canada; David Metz, University of Pennsylvania School of Medicine, United States; Paul Moayyedi, McMaster University, Canada; Jean-Pierre Quenot, University Hospital Dijon, France; Erik Rauws, Academic Medical Centre University of Amsterdam, the Netherlands; Joseph Romagnuolo, Medical University of South Carolina, United States; Alaa Rostom, University of Calgary, Canada; Brennan Spiegel, Veterans Affairs Greater Los Angeles Healthcare System and University of California, United States; Frances Tse, McMaster University, Canada; Monique Van Leerdam, Erasmus University Medical Centre, the Netherlands; Christo Van Rensburg, University of Stellenbosch, South Africa.