

Parsing the Guidelines on Guidelines: Balancing Sensibility and Conflict of Interest

The formulation and publishing of clinical guidelines (and guidances) by institutions and societies generally have been motivated by a desire to help enable practicing physicians to make sense of and assimilate the rapidly burgeoning, and sometimes contradictory, developments in clinical medicine. Because they sometimes rely on imperfect medical evidence and expert opinion, guidelines should not be considered foolproof nor should they substitute for sound medical judgment in an individual case. However, their exponential proliferation not only attests to their utility, but also to their potential to influence the clinical management of large populations

of patients. For this reason, legitimate concerns have been raised regarding the risk that guideline development processes could be co-opted by individuals, industries, and/or societies to promote direct financial (or intellectual) gain.⁽¹⁾ In this regard, it is notable that French Health Authority guidelines on type 2 diabetes mellitus and Alzheimer's disease were withdrawn by court order because of concerns about potential bias among the authors.⁽²⁾

To mitigate this hazard, a number of organizations, including the Institute of Medicine (IOM),⁽³⁾ the Guidelines International Network,⁽⁴⁾ and the Appraisal of Guidelines, Research and Evaluation (AGREE) Collaboration⁽⁵⁾ have issued (what else but) guidelines for the proper appraisal of medical literature, and for the appropriate management of conflicts of interest (COI) of members of the committees charged with implementing and summarizing recommendations. While these publications have focused attention and provided important guidance on this serious issue, it also has spawned a sizeable literature decrying the failure of writing groups and societies to fully comply with procedural and COI recommendations.⁽⁶⁻⁹⁾ Unfortunately, the American Association for the Study of Liver Diseases (AASLD) recently found itself ensnared by one of these investigative studies.

In a recent article in *JAMA Internal Medicine*,⁽¹⁰⁾ Jefferson and Pearson performed a retrospective document review of the American College of Cardiology and the American Heart Association cholesterol management guideline, as well as the September 2015 print version of the hepatitis C virus (HCV) management guidance jointly put forth by the AASLD and the Infectious Diseases Society of America (IDSA). After assessing the COI disclosures for the AASLD/IDSA HCV guidance panel, these authors noted that 67% of the six co-chairs and 72% of the other 23 panel members had reported potential commercial COI, which failed to comply with the recommended IOM standards of 0% and 50%, respectively. The authors added an additional admonition that COI disclosures by committee chairs did not match those identified in

Abbreviations: AASLD, American Association for the Study of Liver Diseases; COI, conflicts of interest; HCV, hepatitis C virus; IDSA, Infectious Diseases Society of America; IOM, Institute of Medicine; VA, Veterans Affairs.

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contemporaneously published articles. Given that Society integrity is considered to be of utmost importance, these findings were taken extremely seriously by the AASLD Governing Board, which thoroughly investigated the assertions. This article summarizes the conclusions of this analysis and the proposed upgrades to AASLD COI policy that resulted from the findings.

Our internal review found that the majority of the conflicts identified by Jefferson and Pearson were attributed to member participation in industry-sponsored research. Indeed, this represented the sole conflict for 33% of the chairs and 21% of the members of the HCV guidance group. In addition, most “discrepancies” in COI disclosure between the HCV guidance and coincidentally published manuscripts resulted from differences in reporting requirements for individual journals, and did not reflect true omissions. It is important to point out that Jefferson and Pearson found the AASLD/IDSA HCV guidance panel to be 100% adherent with the IOM Guideline Development and Evidence Standards, validating the careful and rigorous nature of the panel’s efforts. Still, the AASLD concluded that the number of chairs and panel members with industry conflicts did exceed IOM guidelines and also identified a lack of clarity regarding the details of COI reporting. The Governing Board subsequently tasked the Ethics Committee with the responsibility of performing a detailed review and clarification of AASLD COI policies and procedures not only for Guidelines Writing Groups, but for the society as a whole. The Ethics Committee provided the Governing Board with a series of recommendations for clarifying COI policy and simplifying COI reporting. In addition, monitoring processes, including the establishment of standard protocols for the routine vetting of all relevant leadership and committee member candidates by the Ethics Committee, have been implemented to assure ongoing compliance with AASLD policy.

It is evident that clinicians and investigators who have extensive experience in the care of patients for whom guidelines are developed are ideally positioned to synthesize a large volume of scientific knowledge, clinical trial data, and expert clinical experience into a well-reasoned, easily comprehensible, and unbiased summary that helps to inform patient evaluation and management. However, it is precisely these “content experts” whose consultation is sought by industry for advice and participation in clinical studies. Although a strict policy of zero industry interactions can minimize the prospect of the guideline development process being “hijacked” by external influences (i.e., “panel

stacking”), it comes at the nontrivial risk of weakening guideline quality. As an example, the COI-free Veterans Affairs (VA) expert committee, that produced HCV management guidelines at approximately the same time as the AASLD/IDSA, endorsed several less-expensive first-line treatments and also recommended postponing treatment in some patients. While Jefferson and Pearson have pointed to this observation as evidence of more cost-effective care in the absence of pharmaceutical company influence, we submit that the VA recommendations simply were more dated because decision making was based almost exclusively on past publications. In contrast, the AASLD/IDSA panel included a cohort of veteran investigators with knowledge and experience with the use of cutting-edge therapies, allowing for the integration and incorporation of past literature along with recent advances in diagnosis and management into the guidance document. Consequently, and not surprisingly, the AASLD/IDSA recommendations swiftly superseded those of the VA committee, and have gone on to serve as a valuable and indispensable resource for practicing clinicians, ensuring high-quality patient care and raising the status of both societies around the globe.

We submit that COI guidelines ought to be viewed in a manner similar to clinical guidelines, given that they both rely on indirect evidence and professional opinion and therefore cannot substitute for sound, objective decision making. While the need for integrity and impartiality in the guideline development process cannot be overstated (and the AASLD strives to identify and recruit qualified, nonconflicted content experts whenever possible), it is equally critical to involve individuals who possess a depth of scientific and clinical knowledge within the field. The updated AASLD policy on COI seeks to strike a reasoned balance between these potentially competing interests. Although the AASLD is not only in compliance with, but in many ways exceeds, the majority of IOM guidelines (Table 1), our consensus view is that industry-sponsored research, under circumstances where funding is provided to the institution and not the investigator, poses a relatively inconsequential conflict that should not preclude service on Guidelines/Guidance Writing Groups. Writing Group chairs will not be permitted to have corporate-related consulting and/or advisory relationships; however, these may be allowed for individual Writing Group members, as long as the majority of members do not possess such conflicts and the compensation is below established and clearly delineated limiting thresholds. The institutionalization of routine Ethics Committee review of all Writing Group

TABLE 1. Comparison of AASLD and IOM Recommended Commercial COI Policy for Chairs and Members of Practice Guidelines Writing Group

Type of COI	Writing Group Chair		Writing Group Member	
	AASLD	IOM	AASLD*	IOM*
Industry advisor or consultant	No	No	Yes	Yes
Data safety monitoring board	No	N/A	No	N/A
Speakers' bureau	No	No	No	Yes
Research grants	Yes [†]	No	Yes [†]	Yes
Stock	Yes [‡]	No	Yes [‡]	Yes
Patents/royalties	No	No	No	Yes
Consulting for equity (venture capital)	No	N/A	No	N/A

*Both the AASLD and IOM require the majority of Writing Group members to be free of all commercial COI. In addition, the AASLD sets a financial limit on compensation that can be received for those members with COI.

[†]Not considered a COI only if research funds are provided to the institution.

[‡]Not permitted for any stock that could be directly or indirectly affected by specific guideline, except if in a diversified portfolio or independently managed (blind trust).

Abbreviation: N/A, not addressed.

candidates is designed to ensure compliance with these standards as well as to preclude disproportionate representation of any single corporate entity. While some have advocated that *all* Writing Group participants with *any* conflict be relegated to nonvoting status,⁽¹¹⁾ we argue that this is a fairly impotent position given that “conflicted” individuals may continue to exert substantial influence on guideline development despite the outward appearance of a wholly “nonconflicted” panel. The AASLD is of the opinion that transparency is of higher import, and remains steadfast in its obligation to fully disclose all potential conflicts for all Writing Group members, in addition to all elected officers and members of select committees.

The AASLD affirms its unwavering commitment to integrity and transparency, and will continue to strive to achieve the highest ethical standards for our society and its representatives. Our systematic review and updating of COI policy is but one step in this ongoing process, and we believe it will help to position our society in the forefront of this issue. We encourage AASLD members to review the new COI guidelines (<https://www.aasld.org/governance-codes-site-data-policy/code-assessment-and-management-conflict-interest>), and we welcome any and all feedback. We also wish to thank the members of the Ethics Committee and the Governing Board for their resolute support, dedicated service, and thoughtful contributions to this important endeavor.

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