

CIHR/PHAC Best Brains Exchange

*Reducing and managing conflicts of interest
in clinical practice guideline development:
Do we need Pan-Canadian standards?*

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Executive summary

On January 23, 2019, the Public Health Agency of Canada (PHAC), in collaboration with the Canadian Institutes of Health Research (CIHR), hosted a one-day Best Brains Exchange (BBE) event on the topic of reducing and managing conflicts of interest in the development of clinical practice guidelines (CPGs). The meeting participants included researchers and other stakeholders, including federal and provincial governments and key Canadian guideline-producing groups.

The objectives for the day were to address three policy questions:

1. What sources and types of conflict of interest exist in CPG development?
2. What are some of the barriers and facilitators to reducing and managing COI in CPG development?
3. Which approaches could be used to reduce and manage COI by Canadian CPG developers, and how should these be implemented and disseminated to maximize impact?

The morning featured presentations by, and panel discussions with, experts with a wide range of experiences, followed by group discussions. The afternoon featured small group discussions on barriers to and facilitators of implementation of best practices for identifying and managing COI, using the Guidelines International Network (G-I-N) principles as a guiding framework.

Overall, one clear theme emerged throughout the day's discussions: The need for national leadership, national standards, national approaches, national transparency. These might need to be adapted for different jurisdictions or different organizations, but such an approach would provide a baseline for action at these differing levels. This would bring Canada to the level of COI management found in other countries, remove many of the barriers to and facilitate the implementation of better ways to manage COI in the CPG development process.

A secondary theme was the need to be flexible, given the likelihood of experts having COIs, the increasing trend toward involving a broader range of stakeholders (including patients) in guideline production, and the need to balance appropriate management of COI against the need to constitute a guideline panel with the requisite expertise.

Another recurring suggestion was that more clarity about definitions and procedures would be helpful (e.g., an elaboration on the G-I-N principles paper). Such clarity, together with examples, case studies, or scenarios, would help some organizations implement the principles.

The day ended with a clear sense of options for action, which could include a national COI registry, a common COI declaration form, a national COI oversight or advisory body, and a community of practice and tools to facilitate uptake of the G-I-N principles.

List of Abbreviations

BBE	Best Brains Exchange
CADTH	Canadian Agency for Drugs and Technology in Health
CIHR	Canadian Institutes of Health Research
COI	Conflict of interest
CPG	Clinical practice guideline
DOI	Declaration of Interest
fCOI	Financial conflict of interest
G-I-N	Guidelines International Network
HAS	Haute Autorité de santé
ICMJE	International Committee of Medical Journal Editors
NICE	National Institute for Health and Care Excellence
PHAC	Public Health Agency of Canada
UK	United Kingdom
WHO	World Health Organization

Introduction

On January 23, 2019, the Public Health Agency of Canada (PHAC), in collaboration with the Canadian Institutes of Health Research (CIHR), hosted a one-day Best Brains Exchange (BBE) event on the topic of reducing and managing conflicts of interest in the development of clinical practice guidelines (CPGs). The meeting participants included researchers and other stakeholders, including federal and provincial governments and key Canadian guideline-producing groups. This report is intended to provide an overview of the proceedings and a record of what was said both by presenters and by other participants, as well as to provide potential areas of action to all those involved in the guideline development process across the country.

Best Brains Exchange

The BBE is a program of the CIHR's Knowledge Translation branch. A BBE is a one-day meeting that brings together policy makers and researchers to discuss a health topic of shared interest and high priority to the organizing partners.

These informal gatherings promote interaction, exchange and mutual learning between researchers and policy makers. The invitation-only events:

- provide senior policy makers with high-quality, timely and accessible research evidence and implementation experience tailored to meet their needs;
- enable open dialogue about the relevance of the evidence to the current policy context; and
- foster relationships among policy makers, researchers and implementation experts with shared interests.

Best Brains Exchange: Reducing and managing conflicts of interest in clinical practice guideline development: do we need Pan-Canadian standards?

The Public Health Agency of Canada (PHAC) brought together experts in CPG development, representatives of major Canadian CPG producers and end-users including federal and provincial policy makers, medical professionals and Canadian medical journals to:

1. Raise awareness among the CPG community (including policy makers) regarding:
 - a. the types and impact of conflict of interest (COI) in CPG development;
 - b. the importance of proper disclosure and management of COI; and
 - c. how to implement approaches to manage COI in CPG development.
2. Improve knowledge of effective approaches to managing COI in CPG development.
3. Increase commitment among the CPG community (including policy makers) to implement effective approaches.
4. Generate community-driven solutions to improve the management of COI in CPG development in Canada, including potentially adopting national standards.

Participants heard from academic experts in COI and CPG; they also heard about approaches taken in the United Kingdom (UK), France, Canada, and by the World Health Organization (WHO). Throughout, the principles developed by the Guidelines International Network (G-I-N)¹ were used as the foundation for discussion and comparison. Finally, participants discussed, in small group sessions, the barriers and facilitators to adopting the G-I-N principles as the Canadian standard and how best to implement these principles.

Background

CPGs are important tools for helping practitioners deliver high-quality and cost-effective care. When developed under transparent, rigorous and evidence-based protocols, and faithfully implemented, CPGs can directly influence patient care and, therefore, the health of Canadians. The Canadian Medical Association has a database of more than 1,200 CPGs, while outside of Canada, similar guidelines are being produced in countries around the world. The G-I-N supports a global network of 102 organizations and 120 individual members representing 46 countries from all continents that share an interest in CPG development.

To be maximally useful, CPGs should be free of real or perceived COI – situations in which the professional judgment of an individual involved in developing a CPG can be unduly influenced (or seen to be unduly influenced) by an opportunity to derive personal benefits, whether financial or non-financial. The result of COI can be CPGs that are biased, usually overestimating benefits and underestimating harm, and potentially having a negative impact on patient care. Even if not overtly biased, CPGs for which COI have not been appropriately managed may not be credible to stakeholders, which in turn may diminish their impact and/or reduce confidence in the healthcare system. On the other hand, most or all subject experts will likely have some sort of financial or non-financial COI, creating tension between the goals of eliminating COI and developing guidelines informed by the most knowledgeable experts.

The standards, principles and/or policies for mitigating the effect of COI on guideline development can vary among jurisdictions and organizations and are not always present or explicit. Managing COI in CPG development is, thus, an inconsistent patchwork of policies and protocols. Yet, given the health issues and conditions facing governments and health-care systems, reducing the negative impact of COI in CPG development is a pressing matter.

PHAC and its partners identified a need to hear evidence and experiences from a range of jurisdictions and organizations regarding the challenges and impacts of COI in CPG development. By providing access to a range of perspectives and practical solutions for

¹ Holger J. Schünemann et al. Guidelines International Network: Principles for Disclosure of Interests and Management of Conflicts in Guidelines. *Ann Intern Med.* 2015;163:548-553. doi:10.7326/M14-1885. www.annals.org.

consideration, PHAC hopes to facilitate the ultimate uptake of effective community-driven solutions for identifying and managing COI in CPG development.

This BBE was intended to build connections between stakeholders needed to address this important issue. Following the BBE, PHAC will continue to engage with participants and other organizations in the guideline community to develop and implement concrete solutions.

Objectives and overall conclusions

The objectives for the day were to address three policy questions:

1. What sources and types of conflict of interest exist in CPG development?
2. What are some of the barriers and facilitators to reducing and managing COI in CPG development?
3. Which approaches could be used to reduce and manage COI by Canadian CPG developers, and how should these be implemented and disseminated to maximize impact?

Overall, one clear theme emerged throughout the day's discussions: The need for national leadership, national standards, national approaches, national transparency. These might need to be adapted for different jurisdictions or different organizations, but such an approach would provide a baseline for action at these differing levels. This would bring Canada to the level of COI management found in other countries, remove many of the barriers to and facilitate the implementation of better ways to manage COI in the CPG development process.

A secondary theme was the need to be flexible, given the likelihood of experts having COIs, the increasing trend toward involving a broader range of stakeholders (including patients) in guideline production, and the need to balance appropriate management of COI against the need to constitute a guideline panel with the requisite expertise

Another recurring suggestion was that more clarity about definitions and procedures would be helpful (e.g., a document elaborating on the G-I-N principles paper). Such clarity, together with examples, case studies, or scenarios, would help some organizations implement the principles.

Structure of the day

The BBE discussions were structured to follow these objectives. The morning featured presentations by, and panel discussions with, experts with a wide range of experiences, followed by group discussions. The afternoon featured small group discussions on barriers to, facilitators of and implementation of best practices for identifying and managing COI, using the G-I-N principles (Box 1) as a guiding framework.

These presentations and discussions form the basis for this report. Chatham House rules were applied during the day, meaning that participants (apart from presenters) are not identified in this report, nor are their comments attributed.

Box 1: G-I-N principles for disclosure of interests and management of conflicts in guidelines*

1. Guideline developers should make all possible efforts to not include members with direct financial or relevant indirect COIs.
2. The definition of COI and its management applies to all members of a guideline development group, regardless of the discipline or stakeholders they represent and this should be determined before a panel is constituted.
3. A guideline development group should use standardized forms for disclosure of interests.
4. A guideline development group should disclose interests publicly, including all direct financial and indirect COIs and these should be easily accessible for users of the guideline.
5. All members of a guideline development group should declare and update any changes in interests at each meeting of the group and at regular intervals (for example, annually for standing guideline development groups).
6. Chairs of guideline development groups should have no direct financial or relevant indirect COIs. When direct or indirect COIs of a chair are unavoidable, a co-chair with no COIs who leads the guideline panel should be appointed.
7. Experts with relevant COIs and specific knowledge or expertise may be permitted to participate in discussion of individual topics, but there should be an appropriate balance of opinion among those sought to provide input.
8. No member of the guideline development group deciding about the direction or strength of a recommendation should have a direct financial COI.
9. An oversight committee should be responsible for developing and implementing rules related to COIs.

* Holger J. Schünemann et al. Guidelines International Network: Principles for Disclosure of Interests and Management of Conflicts in Guidelines. *Ann Intern Med.* 2015;163:548-553. doi:10.7326/M14-1885.

Setting the scene

BBE participants received a welcome from Dr. Howard Njoo, Deputy Chief Public Health Officer of Canada, who underscored the importance of CPGs for evidence-based science at the policy, program development, and clinical medicine levels. He noted Canada's record of international leadership in the field of guideline development and the importance of managing COI to further cement this role. Finally, he spoke of the importance of the federal government in guideline development and the value of the day's proceedings for its involvement.

Rachel Rodin, Scientific Director of the Global Health and Guidelines Division, Centre for Chronic Disease Prevention and Health Equity at PHAC, and Marcello Tonelli, Associate Vice-President of Research at the University of Calgary, then provided background for the day's discussion, noting that:

- guidelines directly influence patient care and the health of Canadians;
- financial and non-financial COIs threaten the transparency, credibility and, ultimately, the potential value of guidelines; and
- there is no accepted national standard in Canada for managing those COIs.

They noted that this is not an area in which there is a single right answer; rather, there are a range of options that have been used, including zero tolerance, recusal from voting on specific recommendations and non-participation in discussions for specific recommendations. They also discussed the important role of the G-I-N principles, particularly that much work has already been done that can be built upon to move forward; thus, the day would primarily focus on questions of implementation.

Finally they noted that, while the primary goal of the day was to create a foundation for action, a secondary goal was to develop a network that could go beyond and build on the day's discussions.

Presentation 1: What sources and types of conflict of interest exist in clinical practice guideline development?

Elie Akl, Professor, Department of Internal Medicine, American University of Beirut

Dr. Akl's presentation came in two parts: first, he defined COI and then he dealt with how to declare COI.

In defining COI, he highlighted the most widely used definition in medicine, that of Thompson (1993):

A set of conditions in which professional judgment concerning a primary interest (such as a patient's welfare or the validity of research) tends to be unduly influenced by a secondary interest (such as financial gain)

That being said, he also presented a content analysis of 23 different definitions of COI, in which the most commonly used terms included conflict, interest, person, influence, official, individual, relationship, duty, professional and financial, underscoring the multitude of definitions, but also the commonalities among them.

Other important points he raised were that a risk of bias was enough to cause a COI, and that the bias/harm does not necessarily need to occur. This is why there should be no distinction between real COI and possible/perceived COI.

He then explored the nature of declaring competing interests, examining the who, what, when and how.

The *who*, he said, is not limited only to members of a guideline panel, but should also include members of the oversight committee, systematic reviewers, editors and peer reviewers, people to whom less attention has traditionally been paid.

For the *what*, he referred to a COI classification framework he and his colleagues have developed that encompasses both individual and institutional COIs, and financial, intellectual, cultural and personal interests. He also explored the concept of relevance, noting that in order to determine if a relationship or attribute is a COI, one must first judge whether it is relevant to the task. In other words, not all relationships or interests are necessarily conflicts.

The *when* refers both to the timing – at the time of recruitment, and updating on a continual or regular basis – and to the timeframe – how many years prior to involvement should be included in the declaration and whether there should be any expectations moving forward after the completion of the task.

Finally the *how* can involve either a standardized form (he cited the one developed by the International Committee of Medical Journal Editors, or ICJME) or organization-specific forms. He emphasized, however, the lack of verification undertaken for these forms and the methodological challenges of conducting such verifications.

Discussion

Two main threads emerged in the discussion: how to measure and deal with intellectual and cultural COIs, and how to deal with people with strongly held views, including patients and other stakeholders. It was also clear in the discussion how closely these two threads are linked.

The question of intellectual and cultural conflicts of interests, for instance, becomes increasingly important with the trend to including patients and other stakeholders on guideline development panels. The guideline panel may seek to actively engage with and hear from those who have a specific or unique perspective on a clinical or public health issue. Dr. Akl noted, however, the importance of having people involved who do not have preconceived notions, and that the challenge is how to assess this, particularly since people with specific relationships can still be objective. A key point is that one must consider the risk of bias associated with different types of interests or conflicts, and plan their management accordingly. He also noted that COI management cannot go too far, lest the process exclude all potential members of a CPG panel. On the other hand, he said, there is lots of judgment on the route from evidence to guidelines, and the process needs people with open minds, who will assess the evidence and make decisions on that basis.

With regard to the latter point, Dr. Akl noted the risk in having conflicted experts with preconceived notions participate, but also in leaving them out. There are a couple of ways to get around this, he said: one is by having two panels, one comprising experts and the other comprising unconflicted clinicians and other stakeholders; another is to have panel members vote only on the recommendations they are not conflicted on.

Panel 1: How does conflict of interest impact clinical practice guidelines and healthcare in Canada?

Conflict of Interest and the Quality of Clinical Practice Guidelines

Joel Lexchin, Associate Professor, Faculty of Medicine, University of Toronto

Dr. Lexchin primarily focused on financial COI (fCOI) in his presentation. He cited numerous studies of the deleterious effect of fCOI, including one that showed an association between poor quality of guidelines and fCOI. He also presented another study indicating that anywhere from a quarter to half of CPG authors whose guidelines were published on the Canadian Medical Association website in 2012 and 2013 had fCOIs with pharmaceutical companies/companies making the recommended drug. He also noted that the impact of fCOI is not limited to CPG development – another study he cited found a link between fCOI and a higher chance of positive outcomes in clinical trials.

In comparing fCOI with non-financial conflicts such as ideological, religious, political or career, Dr. Lexchin asserted that fCOIs are much more important than non-financial COIs. He feels that non-financial COI's distract from the real issue of fCOI.

He also pointed to the dangers in declaring and managing fCOIs versus avoiding them completely, citing one study that found that, once authors have declared fCOI, they feel free to exaggerate the evidence, while audiences tend to assume what they are being told is accurate.

In the end, Dr. Lexchin suggested adhering to the precautionary principle – if the evidence points to the possibility of harm, then avoid it completely. Managing fCOI is simply not as effective as avoiding them altogether.

Competing interests in guidelines: an editor's perspective

Diane Kelsall, Editor-in-Chief (interim), Canadian Medical Association Journal

Dr. Kelsall explained the large amount of general guidance available for journal editors to consider when it comes to publishing CPGs. Unlike Dr. Lexchin, Dr. Kelsall focused on the many competing interests that all participants in the guideline development process, including those who publish them, have, and emphasized the need for journals to avoid even the perception of COI. She also noted the impossibility of journals mitigating the impacts of COIs unless these COIs are dealt with by guideline authors all the way along the development process. She noted that it can be difficult to find potential authors, even for non-research articles, who *do not* have some type of fCOI, much less other types.

Dr. Kelsall pointed to the form used by the International Committee of Medical Journal Editors (ICMJE) for disclosure of potential conflicts of interest, noting that the most recent change has been the addition of patents and intellectual property to the list of relevant disclosures. She

also pointed to the publication of disclosures over the past decade, noting the importance of not just collecting the information on potential COIs but making it public. However, she noted, disclosure alone may not be enough to prevent the negative impacts of COI.

Dr. Kelsall also addressed who needs to declare interests, including editors and peer reviewers, as well as strategies to mitigate COI, including excluding those with COI from the process, abstaining from decisions where COI might arise and investigating potential COI by impartial observers.

Finally, she addressed the need for the entire system to rest on trust, pointing out that journals cannot be the COI police. However, trust needs to be backed up and she pointed to recent changes in ICMJE guidance that make deliberate failure to disclose a matter of academic misconduct, with all that implies, including a major career impact.

Dr. Kelsall concluded by saying that there's a long way to go to reach the standards she described, but that journals must play a role in COI disclosure and management.

Discussion

While the presentations left little time for discussion, that which there was focused on several issues, including that of evidence, with Dr. Lexchin noting that, while there is good evidence that fCOI leads to bias, there is no similar evidence that other forms of COI lead to bias, thus the reason for his focus on fCOI (although one participant did point out that all Dr. Lexchin's work has focused on fCOI, thus his belief that it is the priority is itself a form of intellectual COI!) One participant challenged the idea that the biases relevant to non-financial COI are uncertain, saying that the direction of potential bias can be predicted.

Another participant mentioned the methods used in qualitative research, where reflexivity, or one's assessment of how their personal biases may impact results and their interpretation, is built into the actual text, and noted there is both theoretical and practical evidence this works.

There was also an acknowledgement that perception of COI is important to focus on.

Panel 2: Approaches to reducing and managing conflict of interest in clinical practice guidelines – best practices and experiences

Reducing and managing conflicts of interest in guideline development: experience from NICE

Gillian Leng, Deputy Chief Executive and Director of Health and Social Care, National Institute for Health and Care Excellence

Professor Gillian Leng, Deputy Chief Executive of the UK's National Institute for Health and Care Excellence (NICE) described the agency's approach to managing COIs and highlighted issues and challenging areas arising from implementation.

NICE approved its first Code of Practice in 1999 and updated it several times up to 2014. In 2017, the policy was revised to focus on Advisory Committees only, with a separate policy for staff, to make it easier to implement. At this time, the incorporation of legal advice brought about the "reasonable person" test, which asserts that a conflict of interest exists when a reasonable person would consider that an individual's ability to apply judgment or act is, or could be perceived to be, impaired or influenced by one of their interests, as a way to judge whether interests are actually conflicts. NICE makes a clear distinction between declared interests (i.e., declarations of interest, or DOI) and actual COI. Responses following a DOI can include no action (if the interest is not considered a conflict), complete exclusion or partial inclusion. Further, requirements are stricter for chairs of committees than for members, and stricter for members than for advisors. NICE's policy is aligned with the G-I-N principles, although Professor Leng noted that it is not perfect. Some principles can be adhered to in varying degrees, and thus NICE reports 'largely' adhering to these ones.

Following nine months of experience, several challenges emerged:

- Getting a complete and accurate DOI from potential members.
- Perceived conflicts linked to private practice (i.e., medical services not funded by the government via the NHS), making it difficult to find suitable committee members.
- Appropriateness of the 12-month cut off in all circumstances.
- Capturing less formal types of conflict, such as personal enmity.

The reference panel, however, which acts as an oversight committee, is working well and has made a big difference. In addition, distinguishing clearly between declarations of interest (DOI) and COI has helped the organization obtain better declarations from Advisory Committee members.

NICE has several potential solutions to these challenges and will collect further feedback on implementation issues and, if necessary, review the policy. Professor Leng noted, however, that two main points have emerged to date: first, that openness and transparency are essential and second, that there are no black and white situations or solutions.

Conflict of Interest Prevention: Health Expertise and the Haute Autorité de santé in France

Daniel Ludet, Ethicist, Haute Autorité de Santé

Unlike many other countries, France has legislation that sets out the rules for preventing COIs in the provision of public health expertise. The legislation applies not only to the activities of government departments but also to health institutions that are independent of the department, and that have jurisdiction under the law over health-related matters. The Haute Autorité de santé (HAS) is one of those health agencies, with the status of an independent public authority. Its mandate includes recommending good clinical practices and developing public health recommendations.

The French legislation outlines principles to prevent COI. Competing interests are to be declared in public declarations of interest through a central web portal, that include both direct and indirect relationships and ties that go back five years (compared to just one year for NICE); these declarations are published on a government website. Companies in the health products industry also publish, on another government website, records of benefits and remuneration to health professionals over the past five years.

COIs are assessed at the beginning of the guideline process by a committee charged with validating declarations of interests and that meets weekly; as well, all guideline panel meetings begin with a reassessment of possible COIs, recorded in meeting minutes.

M. Ludet emphasized that ties and relationships (i.e., interests) do not necessarily imply a conflict and that factors such as how recent the relationship is, whether the ties are recurrent or one-time and the amount of money in question are important factors in determining whether there is a conflict. He also emphasized the importance of perception – even the appearance of a tie or relationship can place a person in conflict, regardless of personal integrity. Finally, he warned against the problems in applying criteria rigidly, without consideration of context, noting that the result can be dissuasion of experts from participating in the CPG process or, conversely, experts not accepting payments for things that will maintain or augment their expertise (for example, participating in an international conference funded by a company in the health product industry) for fear of being ineligible to participate in the CPG process. He also noted that provisions exist for an expert to contribute, under certain conditions (for example by attending an interview or hearing by which they provide their point of view and answer CPG panelist questions as an external expert), in the CPG development process when a COI exists.

Questions arising from the French experience include whether tasks to prevent COI are actually done, including the review of COI at the beginning of each meeting; and whether the procedures demand too much from departments whose primary task is not looking for COI.

Declaration of interest and conflict of interest management for guideline development at WHO

Susan Norris, Guidelines Review Committee Secretariat, World Health Organization

Susan Norris, of the Guidelines Review Committee Secretariat of WHO discussed the organization's COI policy and adherence to it.

WHO's Guidelines Review Committee was first established in 2007, to develop and implement procedures and standards for WHO guidelines that were consistent with internationally accepted best practices, evidence-informed and transparent. WHO's 2014 COI policy defines COI as any interest declared by an expert that may affect or reasonably be perceived to affect the expert's objectivity and independence and/or create an unfair competitive advantage for the expert or persons or institutions with whom he or she has financial business interests.

Dr. Norris emphasized the critical importance of legal expertise in drafting such policies. She further explained the different kinds of interest the policy was meant to cover, including direct (financial and otherwise) interests, interests of others (e.g., family), professional or intellectual interests, or unfair or competitive advantages as a result of participating in the guideline development process. She also went over which people involved in the guideline process must declare interests. The WHO requires disclosure of current interests and those in the past four years. In assessing DOI, they use a financial threshold of \$5,000 to define a 'significant financial interest.'

She further noted that all WHO external and internal contributors have their COI appropriately managed and that its 2014 policy includes the standard DOI plus gathering of additional information (through the Internet) on potential contributors (a form of verification). The additional online searching involves the use of search engines such as Google and databases such as PubMed to identify publications. During those searches, the focus will be on sources of funding; publications that reflect a strong opinion related to the guideline topic; controversies of any sort; commercial business interests; positions held or collaborations with entities that have an interest in the outcome of the guidelines; and biographies and other narrative descriptions of the individual. A summary of relevant DOI and the assessment and management of all COI must be reported in each guideline.

Dr. Norris concluded that DOI and appropriate management of COI are essential to WHO's ability to develop valid and credible recommendations.

The Canadian Task Force on Preventive Health Care: Managing Conflicts of Interest

Brett Thombs, Chair, Canadian Task Force on Preventive Health Care

Established in 1976, the mandate of the Canadian Task Force on Preventive Health Care is to develop and disseminate CPGs for primary and preventive care. It is an independent body of

12-15 primary care, prevention and methodology experts, each of whom serves a four-year term. Dr. Thombs is the volunteer chair of the Task Force.

The Task Force strives to ensure its recommendations are relevant, patient centred, usable and credible. A strict COI policy is a major part of its credibility. Members renew their DOI statements three times a year and they are published on the organization's website. Members, content and clinical experts and peer reviewers are all subject to the COI policy, which operates along a high threshold of public disclosure and transparency. No appointed Task Force members have industry ties.

Stakeholder groups and related organizations are recruited to ensure effective and meaningful external linkages in guideline development, although in this case there is an expectation of intellectual conflict of interest because of their advocacy roles.

Key challenges that Dr. Thombs identified are moving from subjective evaluation of DOI statements to more defined criteria to determine manageable versus unmanageable COI given Task Force values; and defining and applying standards for determining when intellectual COI is present and when it is a concern in the context of Task Force values.

Discussion

Much of the discussion focused on membership on guideline panels, in particular the inclusion of those with specific views. Speakers emphasized the importance of having stakeholders, with their disparate views, at the table, with Professor Leng noting that the NICE process requires having at least two patients or community representatives at the table, but also agreed there were challenges, including the need for these panel members to understand they are there as independents, as well as the need for some education, particularly about the often-subtle role of industry, who may fund patient groups.

Dr. Norris added that we need to do a better job at embracing diversity of opinions, rather than risk driving them underground, and that the chair plays a pivotal role in managing such opinions. She also noted that external reviewers, even with COIs, can make important points, particularly with regard to implementation of guidelines.

There were also questions about France's legislative approach and how it came to be. M. Ludet explained that, due to scandals related to public health where use of certain medications led to fatalities, France passed its law that makes statements of interest mandatory in 2011. This makes the system quite simple, and allows for the imposition of significant penalties (30,000 euro fines or jail time) for false declarations.

Small group discussions 1 and 2: Barriers and facilitators to adopting the G-I-N principles as the Canadian standard

The first two small group discussions focused on the nine G-I-N principles. Results of the discussions are presented organized by principle. Each group was asked to discuss specific principles (generally two at a time), examining barriers and facilitators to their implementation. After a 30-minute discussion, groups reported back their findings to the plenary.

In cases of principles one and two, four and five, and seven and eight, comments have been combined, as they were largely identical and groups considered the two together.

It should also be noted that it is impossible to address the degree to which points were raised by large numbers of participants, as reports back to the plenary avoided repeating what other tables had already raised.

Principle 1: Guideline developers should make all possible efforts to not include members with direct financial or relevant indirect COIs.

Principle 2: The definition of COI and its management applies to all members of a guideline development group, regardless of the discipline or stakeholders they represent and this should be determined before a panel is constituted.

Groups noted that there are already organizations doing this, and that their experience informed the identification of barriers and facilitators and could also assist other organizations undertaking such activities.

Barriers

Many of the identified barriers revolved around lack of a clear understanding of COI. Unclear language was seen as contributing to the problem, as was a lack of a clear understanding of the difference between relationships, which always exist, and COI, which is not an inevitable outcome of relationships. Some feel that wording is too vague (e.g., 'should' statements), while others feel it is not strong enough. Some feel there is a lack of clarity in how to implement, although others noted they are already doing so.

Another barrier was lack of commitment, as expressed through a lack of time and resources devoted to managing COI, as well as efforts that do not go far enough or are not strong enough.

A third barrier revolved around involving the right people, including patients and, in Canada particularly, Indigenous people. If the G-I-N principles are to be implemented, the Canadian lens should be considered.

Finally, tables identified the small pool of potential participants, particularly in Quebec, as a barrier to finding sufficient guideline panel participants without relevant COIs.

Facilitators

Facilitators focused on making management of COI more transparent and accountable. Suggestions included making disclosure of COI by participants mandatory for publication in journals or infobases, publishing declarations of interests as part of the publication of the guidelines and making such efforts part of an auditing process.

Another facilitator was simply a commitment by organizations to address COI and identification of who is responsible for implementing COI rules.

Principle 3: A guideline development group should use standardized forms for disclosure of interests.

There was general agreement with the principle of a standardized national or pan-Canadian form, with some saying that such a form would make it easier to apply the G-I-N principles, but the devil is in the details, particularly given Canada's federated structure and constitution, which places responsibility for health in provincial/territorial hands.

Barriers

Foremost among the barriers was the difficulty of settling on a standardized form, with some wondering if it would even be possible, saying that different people and organizations would need different forms, and others concerned that a standardized form could be too rigid. Others said that, even if agreement is reached on such a form, interpreting the forms would not be standardized.

Facilitators

Some suggested that reaching agreement on minimum criteria for COI disclosure could be a reasonable compromise. There also was agreement that posting forms online once completed would create peer pressure to be accurate.

One suggestion was around the idea of a pan-Canadian or national DOI form that could be used, although details of that form could be challenging. One option could be different forms for different types of stakeholders.

Some suggested that creating a "conflict vitae," similar to a curriculum vitae, would be useful. Such a document could be stored in an online database, where it could be easily monitored. A central database could serve as an incentive for using a standard form and could help researchers, clinicians and others, by having a single, central repository for their information.

It was suggested that a list of examples of forms could be shared with the guideline community, which may help people implement this principle.

Principle 4: A guideline development group should disclose interests publicly, including all direct financial and indirect COIs and these should be easily accessible for users of the guideline.

Principle 5: All members of a guideline development group should declare and update any changes in interests at each meeting of the group and at regular intervals (for example, annually for standing guideline development groups).

Barriers

While there was general agreement about the need to disclose interests publicly, there were practical barriers to doing so, some of which, like ensuring information is the same in French and English, are particular to Canada. It was also thought that smaller organizations, with their dependence on volunteers would have difficulty with this.

Facilitators

Groups such as the Registered Nurses' Association of Ontario are already meeting such a requirement; they can serve as a model for others.

For smaller organizations, getting outside experts to examine and validate COIs was seen as a way to overcome their difficulties.

An online submission mechanism may decrease workload associated with gathering and posting.

There was also an idea to make declarations of COI more accessible by publishing them beside or with each recommendation statement.

Principle 6: Chairs of guideline development groups should have no direct financial or relevant indirect COIs. When direct or indirect COIs of a chair are unavoidable, a co-chair with no COIs who leads the guideline panel should be appointed.

Barriers

The primary barrier to achieving this principle was the limited pool of candidates. Finding the right person is challenging; finding an unconflicted co-chair could further magnify the difficulty. There were mixed thoughts about this barrier.

Defining indirect conflicts was also cited as a barrier, both reaching a definition and achieving consensus on that definition across Canada. Defining indirect conflicts can become difficult in practice – more clarity is needed about how best to do this.

Facilitators

These barriers could be overcome by balancing experts (who may have conflicts) with a more diverse, wider membership, including patients. This can also be done by having voting members of the CPG panel who come from outside of the topic area (e.g., generalists or methodologists) and then having external experts to advise or consult with the panel. It was pointed out that it

is relatively easy to weight benefits and harms and patient values, etc., once you have the evidence – the example of a judge was given, where no judges are experts on every case subject, but are still able to adjudicate.

Another potential solution for groups who develop many CPGs was to swap chairs for different topics, as a chair with COI in one area would not necessarily have a conflict in another. It was also suggested that journals refuse to publish guidelines from a panel with a conflicted chair.

While not necessarily a facilitator or barrier, there was also a suggestion to establish a new standard with regard to future conflict, prohibiting chairs from accepting money for anything to do with the guidelines for up to a year (though it was acknowledged that policing this would be challenging).

Principle 7: Experts with relevant COIs and specific knowledge or expertise may be permitted to participate in discussion of individual topics, but there should be an appropriate balance of opinion among those sought to provide input

Principle 8: No member of the guideline development group deciding about the direction or strength of a recommendation should have a direct financial COI.

It was pointed out that these two principles should be seen in the context of principle 1; for many diseases, especially rare diseases, principle 1 is especially challenging, so that is where these principles may come in.

Barriers

The most significant barrier is the same as for principle one, which makes these principles necessary in the first place: the shortage of volunteers without COIs, so experts with conflicts will end up chairing or serving on committees for lack of alternatives.

Others noted that it is a risk not to involve experts because of COI – not only can the quality of the guidelines suffer without their particular expertise, but they can also end up sabotaging the process or the implementation of the final product because they do not feel part of it.

Another identified barrier is the lack of a better definition of ‘relevant’ COI.

Finally, a key barrier is the need to consider non-financial COIs, such as intellectual competing interests.

Facilitators

A key facilitator was to “normalize” the DOI process by making it transparent and applying it not only to panel members, but to all those involved the process, including peer reviewers, patient groups, etc. Flexibility in the definitions could be helpful for implementation.

Having an online portal is a good first step in ensuring transparency, but the UK experience shows the importance of incentivizing participants to keep their entries up to date.

Other suggestions included using a balanced group of generalists with less reliance on experts as voting members of the panel and including experts as advisors as opposed to voting members.

One participant noted that while this could pose barriers in finding members for CPG panels, if one cannot produce good guidelines, one should not produce guidelines at all.

Finally, it was suggested that using an open application process rather than appointing panel members can help ensure a diverse range of opinions to neutralize COIs.

Principle 9: An oversight committee should be responsible for developing and implementing rules related to COIs.

There was universal support for an oversight committee, which could help to implement G-I-N principles and help in dealing with grey areas. Some groups at the meeting (e.g., HAS, NICE) have already implemented such a committee. An oversight committee could be charged with numerous tasks, including classifying degrees of indirect conflict, setting the rules for managing COI when such conflict cannot be avoided and undertaking educational initiatives to support the implementation of the G-I-N principles.

Barriers

As with guideline panels more generally, deciding on membership criteria for such a group, finding individual members and resources, and applying COI standards were all seen as barriers.

Facilitators

Creating a federal oversight committee (perhaps through PHAC) was seen as a possible facilitator, as was using already existing bodies, such as ethics advisory boards. Either way, involving legal and ethical professionals was seen as a way of ensuring an oversight body could function as needed. It would also be a useful way to educate groups on best practices and provide advice in areas of uncertainty.

Small group discussion 3: Implementing best practices for the identification and management of conflict of interest

The focus for this session turned from barriers and facilitators to actual implementation of best practices. Each group was asked to discuss their thoughts about the availability of necessary tools to implement the G-I-N principles, desired tools or mechanisms to facilitate uptake and implementation of the G-I-N principles in their organizations, and who might provide those (e.g., potential role of government). Following 20 minutes of small group discussion the tables reported back to the plenary.

Discussion

Several common themes emerged from the discussion and several needs were identified as contributing to the implementation of best practices, whether the G-I-N principles or another similar vehicle:

- **Need for leadership:** This was seen as essential, and as something that could come from the federal level, but be separate from politics. Agencies such as PHAC or CADTH (Canadian Agency for Drugs and Technology in Health) could play a role. Funders also have a role to play, for instance by making funding conditional on meeting requirements for managing COI. Roles could include:
 - Driving pan-Canadian momentum, which would in turn help spur organizational change
 - Providing an oversight committee function
 - Providing a database or other housing of resources for implementation
 - Housing a form of 'open payment' database
- **Need for a standardized form:** Such a form is needed, but it should be seen as a starting point, with different levels (e.g., federal or provincial) or organizations being able to adapt it as required.
- **Need for education/knowledge translation:** Should include vignettes or case studies, particularly for non-financial COI. A guidance document to go with each G-I-N principle could include case studies, description of challenges, lessons learned, etc.
- **Need for resources/tools:** Need to have tools, documents, best practices gathered in one place, maybe with certification. A listserv or similar vehicle where people could post questions and get guidance would help as well. This could also include checklists or other tools, as well as guidance documents to elaborate on the G-I-N principles and provide concrete examples or case studies.
- **Need to use positive language:** e.g., maintaining integrity, preserving independence. At the same time, language must make the distinction between DOI and COI clear.
- **Need to distinguish between financial and non-financial conflict:** fCOI is in some ways easier to deal with, as it is more obvious. Guideline developers need guidance on non-financial COIs, as they can be harder to spot but just as important.

Integration of discussions

In summing up the discussions over the course of the day, facilitator Terry Sullivan noted several things: Other countries seem to be ahead of Canada on this issue; there is an enormous appetite in the room for national leadership and action, and that the momentum of the day should not be lost; that legal involvement is critical; that the reasonable person standard appears to be a good one. He said in closing that this BBE is a call for people to take the next step, to create an active network to promote the need to deal with COI in the guideline process and to call out the harms that result when COI is not dealt with.

Next steps and closing remarks

At the end of the day, the discussion came full circle back to Rachel Rodin and Marcello Tonelli, who noted that they are coming away from the day with a clear sense of options for action, which could include a national COI registry, a common COI declaration form, a national COI oversight or advisory body, and a community of practice and tools to facilitate uptake of the G-I-N principles. In order to enhance consistency in the Canadian approach to managing COI in clinical practice guideline development, potential near-term next steps could also include a declaration of intent or commitment to show leadership among CPG developers before widespread changes are implemented, as well as the sharing of tools (e.g., document to elaborate on G-I-N principles, examples of forms and algorithms, etc.) with stakeholders.