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Short communication

# Conflicts of interest and the (in)dependence of experts advising government on immunization policies

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ABSTRACT

There has been increasing attention to financial conflicts of interest (COI) in public health research and policy making, with concerns that some decisions are not in the public interest. One notable problematic area is expert advisory committee (EAC). While COI management has focused on disclosure, it could go further and assess experts' degree of (in)dependence with commercial interests. We analyzed COI disclosures of members of Québec's immunization EAC (in Canada) using (In)DepScale, a tool we developed for assessing experts' level of (in)dependence. We found great variability of independence with industry and that companies with the highest vaccine sales were predominantly associated with disclosed COIs. We argue that EACs can use the (In)DepScale to better assess and disclose the COIs that affect their experts. Going forward our scale could help manage risk and select members who are less conflicted to foster a culture of transparency and trust in advisors and policy-makers.



## 1. Background

Erosion of public trust in vaccination campaigns and associated public policy decisions may significantly decrease the effectiveness of these important public interventions [1,2]. Policy-makers, politicians, regulators and the public rely on the scientific advice of experts to help make decisions about controversial issues [3,4]. Conflicts of interest (COI) can undermine the public's trust in the independence of experts [5,6], be they health professionals or members of the broader scientific community [7]. A lack of confidence can have serious adverse effects on the outcomes of public health interventions (e.g., vaccination campaigns) [8]. So, in recent years there has been increased attention to the importance of identifying and managing potential COI in public health, especially for those who have a duty towards the public good [9,10].

In the production of policy and guidelines about immunization, members of expert advisory committees (EAC) can have a significant influence on public health decision-making, particularly regarding the selection of vaccines and determination of how vaccination campaigns will be deployed [11]. Policy-makers and regulators rely on EAC decision-making, so their opinions must be honest, science-based, and focused on the public good. Independence and transparency are to be expected, and COI, especially related to industry sponsorship or payments, must be mitigated to prevent EACs from being subjected to unconscious and systematic bias favoring sponsors' interests [12] and producing recommendations unduly aligning with private interests at the expense of public interests [13]. EACs should thus be supported by robust COI management mechanisms to avoid (and manage, if necessary) such influence. But while it is now largely accepted that greater transparency is needed on the part of experts and health professionals, good COI management should not be limited to disclosure [12,14]. Even if COI are disclosed, assessing the degree of independence of members of an EAC and the potential impact of various types of COI remains challenging. Quantifying the degree of closeness with commercial interests is one means of evaluating when an expert is "too close to industry"; this can then help inform COI management procedures (e.g., regarding selection or exclusion of certain experts, weighing their advice with underlying commercial interests), and foster public trust in the recommendations of EAC.

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## 2. Reviewing COI declarations of immunization experts

To gain empirical understanding of COI management practices, in 2016 we conducted a systematic documentary review of the COI declarations of members of a Canadian EAC, the *Québec Immunization Committee* [15]. This Committee advises the province of Québec's Ministry of Health on immunization objectives to be achieved, interventions to be implemented as well as the products to be used (i.e., vaccines and drugs already approved for marketing in Canada). The Committee involves four different categories of experts. *Active members* are researchers and academics recruited for their expertise in immunization; they are Committee's core members and are responsible for writing the advisory reports. *Ex-officio members* are part of the EAC due to holding another office in government organizations (e.g., health ministry, provincial public health laboratory) and *liaison members* represent organizations that can be involved in immunization-related activities (e.g., professional associations).[1] In addition, when certain expertise is required, *ad hoc experts* can be recruited for evaluating and advising the Committee on a specific intervention.

The aim of our study was to compare COI disclosed by EAC members in their expert immunization advising reports[2] with those in their scientific publications and to suggest a new way of categorizing COIs for informing COI management [15]. The sample included all publicly available reports[3]—on the EAC official website (29 Feb 2016)—for four types of vaccination-preventable diseases: invasive meningococcal and pneumococcal infections, whooping cough and human papillomavirus (HPV).[4] Very few of the reports contained a section documenting EAC member interests (and related COI), in comparison with the wide range of interests disclosed in scientific publications authored by the same EAC members.[5] In addition, very often the COI disclosed in the reports did not correspond with those described in the scientific literature. Once the extent and the nature of the COI were inventoried, it became possible to evaluate, in a secondary analysis, EAC member (in)dependence from the industry.

## 3. Assessing experts' level of (in)dependence

Newton and colleagues developed a scale to rank experts' disclosed COI in the agri-food industry [17], a means of "differentiating between levels of conflict in individuals", which ranged from "0" for complete independence, to "4" for no independence from the industry. This scale allowed Newton and colleagues to appraise the independence of experts in both government and charity boards involved with developing and assessing dietary policies in the United Kingdom. The interest in evaluating COI along a continuum is that this enables one to go beyond the moral jeopardy of a binary evaluation (i.e., good or bad, blame or appraisal), something that is detrimental to effective COI management. Furthermore, when all COI are treated as being equal in terms of severity (i.e., significant or minor), then they become difficult to manage [18]. A scale or continuum can help differentiate between sources of COI (e.g., research grants, travel funds, consulting, assets) and their risk (e.g., low, medium or high risk) for the organization (i.e., the entity involving the experts), inform the recruitment of experts and help to identify and manage potentially delicate situations.

We compared the COI classification (composed of 21 COI types) developed in our study [15] with Newton and colleagues' work. We grouped 8 broad types of COI describing different payments that experts may receive from industry. We applied these 8 COI types to Newton and colleagues' 4-rank scale to create the *(In)DepScale* (see Table 1). There was overlap between the COI declared in our study and those found by Newton and colleagues. We modified their scale in two significant ways to make it more comprehensive and relevant to the pharmaceutical sector. First, we added two types of COI that were missing in their study: "funding to experts' institutions"[6] and "honoraria for lectures and/or presentations". Second, the latter COI type required that we add a new rank (rank "3") to acknowledge that this type of activity is more restrictive than research funding (rank "2"), but entails less binding relationships with a company than acting as a consultant and board member (rank "4") Therefore, our *(In)DepScale* is a 5-rank scale, ranging from *being independent* (rank "0") to *being dependent* on industry (rank "5").

From our database of EAC member COI declarations between 2000 and 2016 (n = 918, see Fig. 1), we assessed the overall level of (in)dependence using the *(In)DepScale* (Fig. 2).[7] In our analysis, we discriminated between types of members (EAC members or *ad hoc* experts) using the declarations made in each expert report, over time and related to the four vaccination-preventable diseases.

The most common level of (in)dependence among all EAC members is "2", i.e., research funding received from a private company, and for *ad hoc* experts it is "3", i.e., honoraria received from a private company. Level "0" (100% independent of industry) represented only 4.7% of COI declarations and experts reporting that they were employed by the industry (level "5") accounted for 1.6%. Both the average and the median of COI declarations are "2" for all diseases and types of member; a notable exception were the declarations from *ad hoc* HPV experts which were notably higher than any other expert cluster (chi square test, $p \leq 0.001$) with "2.9" on average (Avg) and "4" as a median (Me). EAC members and *ad hoc* experts showed a higher COI level of independence for meningococcal (Avg:2.0, Standard Deviation (±):0.9, Me:2) and pneumococcal diseases (Avg:1.9 ± 0.6, Me:2) as compared with HPV (Avg:2.6 ± 1.3, Me:3).[8] This result is in line with numerous critiques about HPV vaccines, being the most controversial public health intervention among the four surveyed, and international concern about COI related to expert ties with the vaccine industry [4]. For all studied diseases, *ad hoc* experts (Avg:2.8 ± 1.3, Me:3) had a

[1] Contrary to other EACs, such as the U.S. Advisory Committee on Immunization Practices [16], Québec Immunization Committee does not disclose voting behavior on recommendations.

[2] There is no publicly available file listing EAC members' conflicts, the only information available is the COI disclosures within the official advisory reports aimed at the Health Ministry.

[3] These reports focus on a disease and generally include (without being limited to): an analysis of epidemiological data and characteristics of available interventions; a presentation of intervention strategies; cost-effectiveness evaluation, feasibility and acceptability; recommendations addressed to the Health Ministry on the optimal use of immunizing products.

[4] These diseases were selected because they accounted for almost half (46%) of the reports available during our data collection in 2016; these reports are representative of the Committee's mandate and recommendations. We selected all bacterial vaccination-preventable diseases (for which vaccines for certain strains were part of the routine vaccination program), and HPV (a viral vaccination-preventable disease) because it was subject to significant media coverage.

[5] The comparison stems from a literature review conducted on the COI declared in the scientific articles published by EAC members pertaining to one of the four selected diseases. 138 articles were identified and analyzed. The COI disclosures were extracted and labelled according to a taxonomy developed inductively. For additional details on the method refer to the description of our study [15].

[6] These include payments to the expert's institution for research which were not made under the expert's name. This COI type has been assigned a rank 2, equal to payments to support the expert's own research ("research funding from a private company"), considering that if the individual has declared it, the proximity of funds is close enough for the researcher to be aware and it may affect their research (e.g., this may have been used to pay for infrastructure that the expert uses, for shared staff, etc.).

[7] The actual amount linked to each COI declaration was not publicly available, therefore it could not be used in our analysis. This represents a limitation of this study, and future research on the (In)DepScale should consider to the impact of the financial amounts.

[8] When comparing meningococcal or pneumococcal diseases to HPV by expert groups (EAC members or *ad hoc*), all chi square tests showed a statistically significant difference ($p \leq 0.014$ to $p \leq 0.001$).

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**Table 1**
Ranking types of conflict of interest.

| Newton et al – "ConScale" | | "(In)DepScale" | |
|---|---|---|---|
| **Ranking** | **Disclosed COI** | **Ranking** | **Disclosed COI** |
| **0 (100% independent of industry)** | • *Zero interaction* | **0 (100% independent of industry)** | • *Zero interaction* |
| **1** | • Received hospitality | **1** | • Reimbursement of travel or registration fees for a congress from a private company |
| **2** | • Research Funding | **2** | • Research funding from a private company<br>• Research funding awarded to affiliated institution or organization |
| **3** | • Consultancy<br>• Industry Shareholder | **3** | • Honoraria for lectures or presentations |
| **4 (0% independent of industry)** | • Employed by pharmaceutical company or organisation representing industry | **4** | • Honoraria as consultant<br>• Member of the board of directors<br>• Has investment in the capital of a private enterprise |
| | | **5 (0% independent of industry)** | • Employed by pharmaceutical company or organisation representing industry |
| **Unknown** | No information available or disclosed | **Unknown** | • No information available or disclosed |

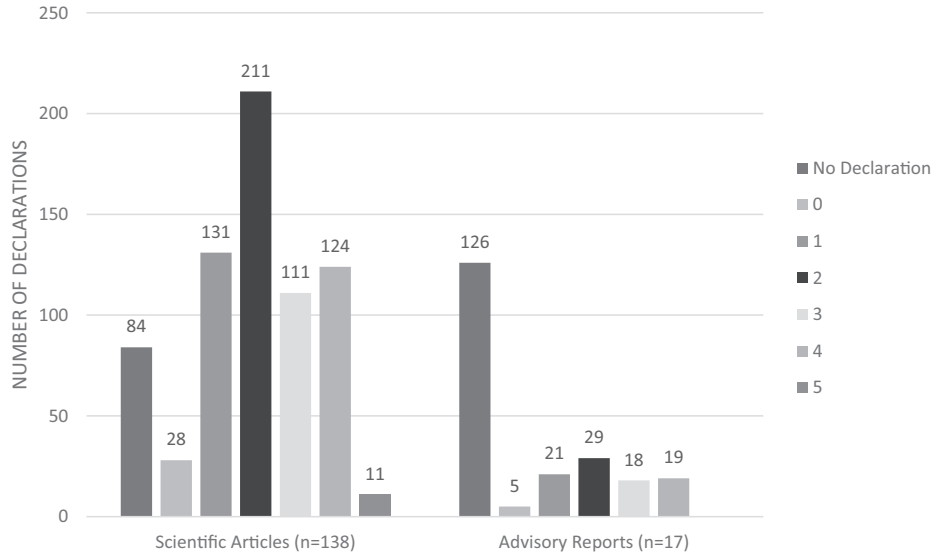


**Fig. 1.** Number of COI declarations per source (N = 918). *Note:* The number of COI declarations refers to unique statements made by surveyed EAC members and *ad hoc* experts in their scientific articles and advisory reports. The declarations come largely from scientific articles (76%). Only two of the 17 advisory reports analyzed contained COI declarations, which precludes a complete picture of members' statements. No financial amounts were disclosed in the COI declarations, therefore it is not possible to report this information.

lower level of independence with the industry than EAC members from 2001 to 2009 (Avg:2.0 ± 0.8, Me:2) and from 2010 to 2016 (Avg:1.9 ± 1.0, Me:2).[9] This indicates that scientists recruited *ad hoc* for their expertise on a specific disease or type of vaccine have, on average, stronger ties to industry. This dimension should thus be taken into account in their recruitment, in COI management, but more generally in the consideration of their opinions for policy-making.

It is also possible with our dataset to explore experts' level of (in)dependence of declared COI by pharmaceutical company. Fig. 3 shows that EAC members and *ad hoc* experts declared most COI with 5 companies: Merck (26% of declared COI), GlaxoSmithKline (22%), Pfizer (9%), Sanofi Pasteur (9%), and Novartis (8%). This is in line with the list of companies generating the most vaccines sales in 2016 [19]: Merck, Pfizer, Sanofi and GlaxoSmithKline (in 2015, Novartis divested of its vaccine division, which was sold to GlaxoSmithKline). All these companies are producing vaccines for more than one studied vaccination-preventable diseases, therefore

[9] Using a chi square, this tendency is statistically significant for HPV between EAC members (2001–2009 and 2010–2016) and *ad hoc* experts (all $p \leq 0.001$), for pneumococcal diseases between EAC members (2001–2009) and ad hoc experts ($p=0.01$).

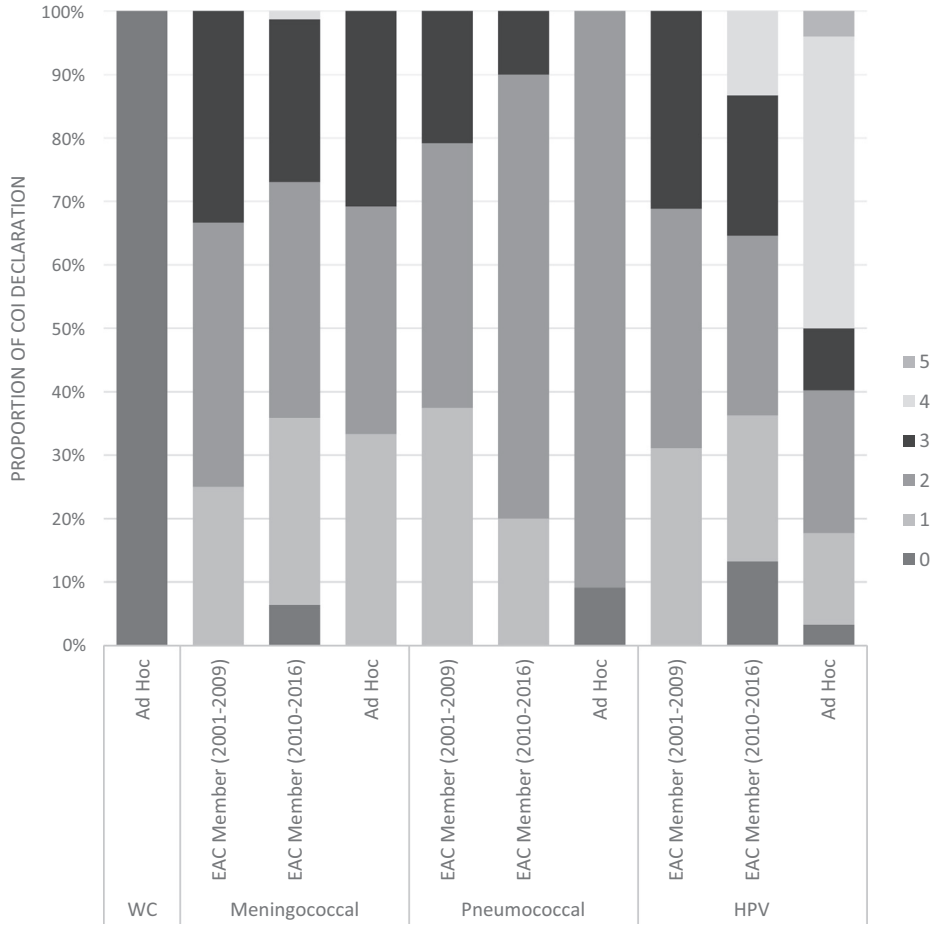


**Fig. 2.** Proportion of COI declarations by type of EAC member for 4 vaccine-preventable diseases. *Note:* Prior to 2010, the exact role of the members (active member, ex-officio, liaison) was not consistently specified in the advisory reports. Therefore, for the purpose of this analysis, all EAC members have been clustered (excluding *ad hoc* experts) and reported distinctly for these two periods. No declaration had been made by EAC members for whooping cough (WC). The 210 cases with no information available (undisclosed) are not included in this figure.

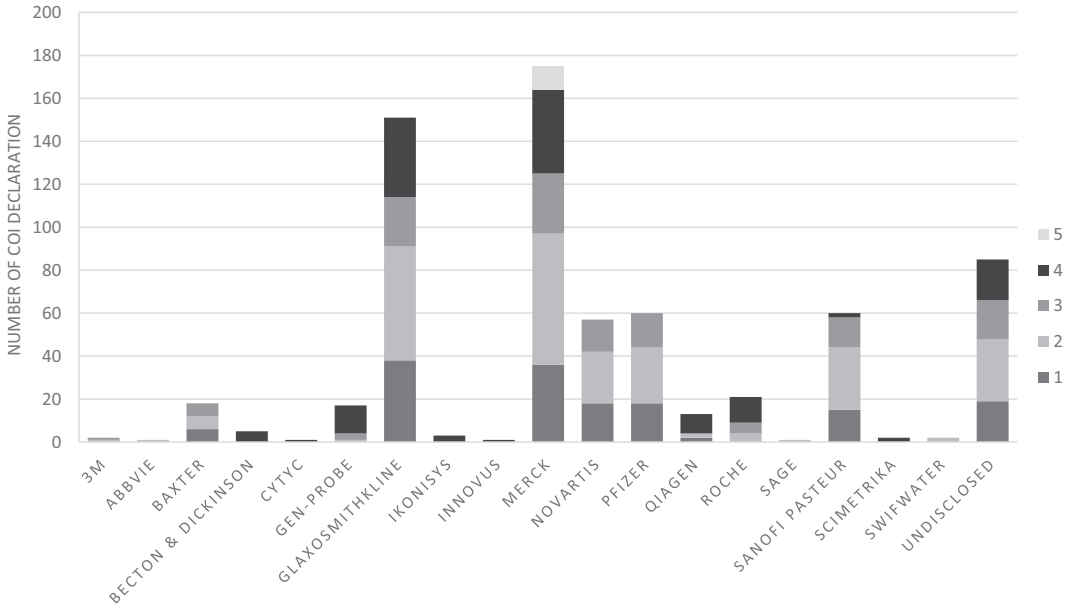


**Fig. 3.** Number of COI declarations associated with companies. *Note:* The total number of COI declarations associated with a company is 675. Were excluded the 33 declarations with a rank 0 ("No COI to declare") and the 210 times an expert omitted to provide a COI declaration in scientific publications or in advisory reports. In the figure, "Undisclosed" implies that a COI declaration has been made, but the associated company has not been disclosed by the expert.

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they all have important commercial interests. The other (and smaller) companies are mainly involved in testing and screening for diseases (combined they represent 13% of disclosures); a non-trivial proportion of disclosures did not specify the company's identity (13%). Overall, 42% of COI declared were associated with mid to high levels of dependency to the industry (level 3 to 5), involving direct payments from industry to experts. It is thus not surprising that companies that have or are developing vaccines have substantially more ties with experts, which is reflected by the number of the declared COI. However, while there tended to be fewer COIs between experts and smaller companies, these COI involved much greater dependency (higher ranks: 4 and 5; chi square $p \leq 0.001$).

## 4. Conclusion

An expert with a COI is not necessarily less objective, but studies have shown that COI are associated with a more positive attitude (consciously or unconsciously) toward companies with whom experts have secondary interests (e.g., research grants, travel funds, consulting, assets) [20,21]. Our study highlights the importance of conducting more comprehensive assessments based on the various COI types, and the need for clear and detailed COI disclosure by experts and EACs. Specifically, we suggest that a gradation of expert (in)dependence with industry may help to better categorize and characterize the relationships that experts have with the industry, which is needed to inform COI management. We strongly recommend that all EACs include an assessment of the level of (in)dependence—such as the (In)DepScale—related to COI disclosures, and a complete public list of the named companies in their expert's reports and publications. This assessment should be included in policies and procedures to ensure impartial and evidence-based decision-making.

Increased transparency on the part of immunization experts is necessary, and this includes making all COI information publicly accessible. EACs as well as journals should require more detailed COI declarations (including information about the amount of payments, the time it happens, etc.), so COI impact assessment may be conducted to support and inform COI management. For instance, financial amounts (as higher payments are linked with lower independence) as well as the timing of COI (e.g., recent financial relationships would likely be more influential than older ones) could help determining the level of dependency and give more dimensions to the (In)DepScale. If such data is disclosed, future research could explore financial and temporal thresholds for eligibility as EAC members. Also, votes should be made public to foster transparency and public as well as to help evaluate the relationship between level of (in)dependence and voting behaviors. This granular information would be instrumental in assessing the merit of decisions made by members as well as implementing more individualized COI management processes (ranging from recusing an expert from a vote or from assessing a campaign, to their exclusion from the Committee). Such information could guide the establishment of guidelines for recruitment (e.g., a specific threshold for only recruiting experts under a certain level of dependence, with special attention to *ad hoc* experts). EACs must take actions to assess and manage situations where their experts work closely with industry as there is a major concern that such relationships may unduly influence advisory (and research) outcomes [5,8,13,14]. Such COI management is essential for the public to better hold experts accountable and to foster more transparent and trustworthy advisory processes [22].

The public has the right to expect advisors and policy-makers to work towards the public good, and this means not having high levels of dependency on industry, nor being influenced by commercial interests. Tools, such as the (In)DepScale, can help assess the nature and intensity of ties between experts and commercial interests. It is also in the interest of experts to maintain public trust and credibility, if they are to be able to positively influence the public uptake of their recommendations. EAC members "must remain visibly trustworthy, which requires a careful and explicit management of [COI]" [5].

## Declaration of interest

None to declare.

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## Contribution

JCBP and LR designed the study. LR and AIC collected and validated the data. JCBP, LR and AIC analyzed the data. All authors participated in writing the manuscript and have approved the final article. All authors attest they meet the ICMJE criteria for authorship.

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