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2 **The reporting of declarations and conflicts of interest in WHO**

3 **guidelines can be further improved**

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26

27 **Abstract**

28

29 **Objectives:** We aimed to examine the declaration of interests (DOI), management of conflict of interest (COI), and  
30 the funders for World Health Organization (WHO) guidelines.

31 **Study Design and Setting:** We examined all Guidelines Review Committee (GRC)-approved WHO guidelines  
32 published in English from January 2007 (inception of the GRC) to November 2016. We obtained a list of all such  
33 guidelines from the GRC Secretariat. Characteristics of guidelines including funders and individual contributors'  
34 DOI were independently extracted by two researchers. Binary logistic regression was used to assess the association  
35 between declarations and the number of organizations involved in development.

36

37 **Results:** 176 guidelines fulfilled inclusion criteria, encompassing 14 clinical or public health fields. Funders were  
38 reported in 128 (73%) of the guidelines: the most common were governments. DOI for external contributors were  
39 reported in 157 (89%) of the guidelines: 75 (48%) indicated no contributors with COI, 57 (36%) reported  
40 contributors with COI, and 25 (16%) reported collecting DOI but not whether COI existed. Financial COI were  
41 reported more frequently than nonfinancial COI. Of 57 guidelines that reported COI, 45 (79%) indicated how the  
42 COI were managed.

43 **Conclusion:** The majority of WHO guidelines reported their funding sources, and the DOI and COI of external  
44 contributors in their guideline documents. However, there is a need for improvement, in particular for reporting of  
45 funders and their role, declaration processes, and management of COI.

46 **Key words:** practice guideline; WHO; declaration of interest (DOI); conflicts of interest (COI); reporting quality

47

48 **Background**

49

50 Conflicts of interest (COI) - personal, organizational and financial factors which may affect the objectivity and  
51 independence of guideline contributors – are a potential source of bias in the development of clinical practice  
52 guidelines (CPGs) [1,2]. COI occur when professional judgment concerning a primary interest (such as the validity  
53 of research) tends to be unduly influenced by a secondary interest (such as financial gain) [3]. Secondary interests  
54 can be classified as financial and nonfinancial, and include interests directly or indirectly (e.g., through relatives  
55 and close friends) related to the guideline contributor. Financial interests include shares or bonds in a commercial  
56 entity, personal financial gain (payment for work or research, consulting income or honoraria), gifts, proprietary  
57 interests and patents related to the topic, and grants or fellowships from a commercial entity that has an interest in  
58 the subject-matter of the guideline. In addition to the financial interests of individual contributors, funding for the  
59 guideline itself may also be a source of COI[4]. Non-financial interests of guideline contributors are also important  
60 and include previously published research related to the potential recommendations in guidelines, and personal  
61 political, religious or ideological beliefs that might influence evidence assessment and recommendation  
62 development [5-8]. There is no universally agreed upon taxonomy and management strategy for non-financial  
63 interests, which thus can be particularly challenging to manage [9].

64

65 Research findings are associated with the COI of authors and funders [10-17], thus management of COI of  
66 guideline contributors is critical to ensure the validity of recommendations in guidelines. Financial relationships  
67 between guideline organizations and biomedical companies are common but declarations of interest (DOI; the  
68 declaration of all potentially relevant secondary interests) are infrequently reported in guidelines [18-21]. Even  
69 when financial sponsorships are disclosed, few studies described the role of sponsors [10, 22,23].

70

71 The World Health Organization (WHO) produces guidelines to inform various stakeholders in the 194  
72 Member States of the United Nations. These guidelines provide information about what policy-makers, healthcare  
73 providers or patients should do, assist in making choices between different interventions that have an impact on  
74 public health and resources, and help health care providers and recipients and other stakeholders to make informed  
75 decisions [6]. WHO has clear requirements for DOI and assessment of COI of contributors to its information  
76 products including guidelines, taking into account both financial and nonfinancial interests [6,24]. The WHO  
77 Guidelines Review Committee (GRC) was established in 2007 to ensure the use of internationally accepted best  
78 practice in WHO guidelines. The GRC critically reviews planning protocols and final versions of guidelines, and  
79 ultimately approves documents that meet the Organization’s standards, including those related to COI [25].

80

81 The objective of this study was to examine DOI, COI, and funders reported in WHO guidelines, and the  
82 potential association between the reporting of DOI and whether WHO was the sole developer of a guideline.

83

84

85 **Methods**

86 **Eligibility criteria and study selection**

87 We included all GRC-approved, WHO guidelines published in English from January 2007 to November 2016,  
88 including those developed in collaboration with other organizations. We obtained a list of all such guidelines from  
89 the GRC Secretariat, and downloaded documents from the WHO website  
90 (<http://www.who.int/publications/guidelines/en/>). We included only the latest English-language version of each  
91 guideline. The full text of each guideline was independently screened by two researchers (XQW and QFW);

92 disagreements regarding inclusion were resolved by discussion or consultation with a third researcher (YLC).

93

#### 94 **Data Extraction and analysis**

95 Data were independently extracted by two researchers (HXZ and RL) and disagreements were resolved by  
96 discussion or consultation with a third researcher (YLC). Referring to the requirements of WHO [5], the following  
97 data were extracted: 1) title, developers, year, topic(s); 2) funders, including their role in the development process;  
98 3) DOI, including information on who declared their interests, and the methods and processes that were used to  
99 collect, evaluate, and report them; and 4) COI, including information on who declared them, their type (financial or  
100 nonfinancial), who assessed them, and how they were managed.

101

102 WHO, together with the other organizations involved in the development of a guideline, generally need to  
103 form four groups of contributors to complete the work: the steering group, the guideline development group, the  
104 external reviewer group, and the systematic review team. We investigated whether WHO guidelines reported DOI  
105 for all of these groups. DOI refers to declaration of all potentially relevant secondary interests, for example patent  
106 or stock ownership or prior authorship of a technical report on the same topic for the another group [24]. COI refers  
107 to the judgement that a declared secondary interest could potentially influence the guideline development process  
108 or outcomes, or the credibility of the final product. For example, if a guideline contributor declared owning stock in  
109 a drug manufacturer and that drug is being examined in a guideline, that is a COI. On the other hand, if the declared  
110 stock has no relevance whatsoever to the guideline at hand, that DOI is not a COI.

111

112 After extracting DOI from each guideline, we report if and how declared interests were assessed, and how  
113 conflicts, if any, were managed. If the guideline only reported DOI but did not indicate that the declared interests  
114 were assessed, we considered the situation to be “unclear”. We then examined DOI and the assessment process  
115 across publication years.

116

117 We used binary logistic regression to assess the potential association between WHO as the sole developer of  
118 guidelines (versus having multiple contributors) (independent variable) and reporting of DOI in guideline  
119 documents or their annexes (dependent variable). We hypothesized that guidelines that were developed  
120 collaboratively by several organizations may have lower rates of reporting DOI and COI management than  
121 guidelines developed by WHO because the other organizations may have less robust COI policies and practices.  
122 The regression analysis was conducted in SPSS Statistics 22 (SPSS Inc., Chicago, IL, USA).

123

#### 124 **Results**

125 We identified 208 guidelines approved by the GRC since its inception. Of these, 32 guidelines were excluded  
126 because they had been superseded by newer versions or were not published in English. Thus 176 guidelines  
127 fulfilled eligibility criteria (Fig. 1).

128

129 The characteristics of included guidelines are shown in Table 1. The number of guidelines published annually  
130 ranged between 6 and 29. Of the guidelines, 143 (81%) were developed solely by WHO, including its regional  
131 offices; the remainder were developed in partnership with external organizations.

132

**Table 1. Characteristics of the included guidelines (n=176)**

Characteristic		Number (%)
Publication year	2008	22 (13)
	2009	29 (16)

	2010	21 (12)
	2011	29 (16)
	2012	20 (11)
	2013	17 (10)
	2014	16 (9)
	2015	16 (9)
	2016	6 (3)
Developers	Developed by WHO	143 (81)
	Developed by WHO in partnership with other organizations	33 (19)
Type of funder*	No information on funding sources	48 (27)
	Governments	105 (60)
	WHO and its programs	25 (14)
	International non-profit organizations	24 (14)
	Foundations	21 (12)
	Institutes or societies	15 (9)
	Other (universities or hospitals)	3 (2)
Number of funders	No information on funding resources	48 (27)
	1	55 (32)
	≥2	73 (41)
Role of funders*	No information	120 (68)
	None	7 (4)
	Unspecified support for guideline development	26 (15)
	Meeting support	12 (7)
	Support the evidence review(s)	7 (4)
	Support publication and printing	7 (4)
	Provide technical support and consultation	3 (2)
	Appoint observers	1 (1)
	Supply products	1 (1)
	Edit	1 (1)
	Topic	Infectious diseases**
Maternal and child health		36 (20)
Nutrition, chronic disease prevention		21 (12)
Cancer		6 (3)
Mental health and neurologic disorders		6 (3)
Environment and health		6 (3)
Smoking and substance abuse		5 (3)
Health policy		5 (3)
Public health emergencies including pandemics		4 (2)
Food and health		3 (2)
Non-communicable diseases		3 (2)
Medical devices		3 (2)
Disability		1 (1)
Violence		1 (1)

133 \* One guideline could be included in multiple categories.

134 \*\* 63 focused on TB or HIV.

135

136 Funding sources for guideline development were reported in 128 (73%) of the guidelines. Of guidelines  
137 reporting funding sources, 55 (43%) were supported by one source and 73 (57%) received funding from two or  
138 more sources. The funders contributing to the greatest number of guidelines were governments (105, 82%),  
139 followed by non-profit organizations (24, 19%) and the WHO itself (25, 19%). Only 51 (40%) of the 128  
140 guidelines reporting funding sources described the role of the funders. None of the included guidelines reported  
141 receiving funding from commercial entities.

142

143 A total of 157 (89%) guidelines reported the declared interests of external contributors (contributors who are  
144 external to WHO and participate in the guideline development process) (Fig. 1). Of the 157 guidelines, 97 (62%)  
145 reported the methods used to collect DOI (56 used a declaration form and 41 used a form plus verbal declaration),  
146 and 90 (57%) presented the process for assessing DOI (reported who assessed the DOI and by what criteria).  
147 Seventy-five (48%) of the 157 guidelines that reported DOI clearly indicated that no COI existed, and 57 (36%)  
148 reported one or more COI. The remaining 16% of guidelines provided the DOI without reporting if COI existed. Of  
149 the 57 guidelines that reported COI, 45 (79%) presented the management decisions that were made to deal with the  
150 COI (Table 2).

151

152

**Table 2. The management decisions for conflicts of interest**

Decision	Number (%)
The contributor should not contribute to deliberations on or formulation of the recommendations	34 (75)
Requires no action beyond declaration at the meeting and reporting in the final guideline	14 (31)
The contributor should not participate in evidence evaluation	8 (18)
The contributor should not provide comments on the final document	4 (9)
The contributor should not participate in relevant discussions and meetings	5 (11)
The contributor should not chair the screening discussion or identify the main sources of data	2 (4)
The contributor should not participate in developing provisional framework	1 (2)

153 Note: The total number is the 45 guidelines that reported this information.

154

155 Of the 57 guidelines reporting COI, 37 (65%) reported both financial and nonfinancial interests among the  
156 external contributors. The three most commonly reported types of COI were personal financial gain, personal  
157 research support, and participation in related research projects or presentations on related topics (Table 3).

158

159

**Table 3. Types of conflicts of interest**

Item (n, %)	Types of conflicts of interest	Number (%)
<b>Financial</b> (48, 86%)	Personal financial gain <sup>a</sup>	33 (58)
	Personal research support <sup>b</sup>	40 (70)
	Personal or organizational financial aid or scholarship	7 (12)
	Proprietary interests and patents	2 (4)
	Stock, shares or bonds	9 (16)
<b>Nonfinancial</b> (44, 79%)	Occupation or position, such as acting as chair or unpaid consultant for relevant organizations	29 (51)

Participation in related research projects or presentations on related topics	35 (61)
Personal political, religious or ideological beliefs	0 (0)

160 <sup>a</sup> Personal financial gain includes compensation, remuneration, travel allowance and other financial gain.

161 <sup>b</sup> Research support includes direct investment, device or product donation and other forms of support.

162 Note: The total number (n) is the 57 guidelines that reported this information. Different types of conflict of interest can exist in the  
163 same guideline.

164

165 A total of 145 guidelines (82%) reported the specific individuals or groups who declared their interests (Table  
166 4). Members of the guideline development group (54, 31%), external or peer reviewers (48, 27%), and experts  
167 participating in meetings where recommendations were formulated (32, 18%) were the most frequent groups to  
168 provide DOI. DOI from the systematic review teams and from the guideline methodologists were rarely reported.

169

170

**Table 4. Contributors declaring interests**

Options	n (%)
Guideline development group	54 (31)
External reviewers or peer reviewers	48 (27)
Experts participating in meetings	32 (18)
Expert groups	31 (18)
Counselors/technical experts	24 (14)
Contributors/participants	11 (6)
Working groups	7 (4)
Core groups/members	4 (2)
Authors	4 (2)
Systematic review/ evidence groups	3 (2)
Methodologists	3 (2)
Steering groups	3 (2)
Observer, writing group, editor, external expert	8 (4)

171 Note: Because the labels for contributors varied across guidelines, some of these groups likely have similar roles to each other (e .g.,  
172 guideline development group members and experts participating in meetings). The total number (n) is the 145 guidelines that reported  
173 this information.

174

175 Reporting of how DOI were collected and the process to assess DOI improved substantially between 2009 and  
176 2011, and stayed relatively stable thereafter. Reporting of the judgements about whether COI existed changed little  
177 over time (Fig. 2). When WHO was the sole author of a guideline, DOI was reported more frequently (131/143,  
178 92%) than for guidelines that were co-developed with other organizations (26/33, 79%) (odds ratio [OR]= 2.9, 95%  
179 confidence interval [CI] 1.1-8.2). The rates of DOI remained stable around 90% over time, except in 2010 when  
180 only 67% reported DOI.

181

## 182 Discussion

183 The majority of WHO guidelines reported their funding sources, however less than half presented the role of  
184 funders. Nearly 90% of the guidelines reported DOI, however of guidelines collecting DOI 38% did not provide  
185 details on how DOI were collected and nearly half did not report how DOI were assessed. In addition, 21% of  
186 guidelines that reported one or more COI gave no information on how COI were managed. Seventeen percent of

187 guidelines providing DOI did not report if COI existed. The most commonly reported type of COI was personal  
188 financial gain, and guidelines developed solely by WHO tended to report DOI more frequently than those  
189 co-developed with other organizations, although the difference was small.

190

191 Guideline development usually requires significant financial resources, and WHO staff may have to seek  
192 external funding in addition to mobilizing internal resources. External funding can, however, lead to biased  
193 recommendations [4,12,26] and thus many guideline developers and organizations producing systematic reviews  
194 set restrictions on the sources of funding. For example, the American Thoracic Society refuses any outright  
195 sponsorship [27] and the Cochrane Collaboration does not accept support for reviews from commercial sponsors  
196 that have a financial interest in the outcome [28]. Similarly, WHO does not permit guidelines funded by commercial  
197 entities [6]. Trustworthy guidelines must be transparent, including reporting of all funders [29, 30]. However,  
198 almost one-third of WHO guidelines did not provide this information, and less than half of those reporting funding  
199 sources described the exact role of funders.

200

201 Organizations including the Guidelines International Network [31], the New Zealand Guidelines Group [32],  
202 the British HIV Association [33], the U.K. National Institute for Health and Clinical Excellence [34], and WHO [6]  
203 all explicitly require DOI and the assessment of all disclosures for potential COI, followed by appropriate  
204 management of any conflicts. Standardized and complete reporting of DOI, COI and their management should be  
205 further improved at WHO. WHO requires the guideline development group, external reviewers, systematic review  
206 team and methodologists to declare their interests [6], but the results showed that the actual DOI varied greatly  
207 across contributors and guidelines. The labelling of guideline contributors varies across guidelines, which makes  
208 it difficult for end-users to understand the types of contributors and to compare rates of DOI and COI management  
209 across guidelines. In addition, there is no specific place for DOI reporting in WHO guidelines – the reader may  
210 have to look through the entire document and its appendices to find this information.

211

212 As this topic now receives more attention, DOI and COI are increasingly being reported in guidelines. George  
213 and colleagues reported in 2001 that only 3.7% of the included guidelines reported DOI information [35]. A 2012  
214 study showed that only 60% of guidelines included in the US National Guidelines Clearinghouse (NGC) reported  
215 DOI and reporting of the management of COI was poor [20]. A more recent (2016) study of NGC guidelines  
216 showed that 65% of the guidelines reported DOI [21]. The results of our study suggest that reporting of DOI and  
217 COI management at WHO is better than that for other guideline developers: this may reflect rigorous  
218 implementation of the WHO COI policy and oversight by the GRC.

219

220 Financial COI can substantially affect research findings, usually in favor of commercial entities  
221 [11-13,16,36,37]. The effects of nonfinancial interests on research and decision-making are less clear-cut and  
222 there is debate about whether or not such interests are an important source of bias [9]. Many researchers do feel  
223 that nonfinancial COI can influence primary research, synthesis, and recommendations in guidelines [38-40]. One  
224 study in fact suggests that nonfinancial COI might have an even greater impact on patients or volunteers [41], and a  
225 survey reported that grant reviewers were more concerned about non-financial COI than financial interests [42].  
226 The management of nonfinancial COI is particularly challenging, as all individuals, including content experts, have  
227 such interests [43,44]. The only approaches to minimize the risk of bias from such interests are to try and balance  
228 the perspectives, experiences, values and viewpoints across individuals contributing to the recommendations [5].  
229 Both financial and nonfinancial COI were frequently reported in WHO guidelines, suggesting that WHO staff are  
230 aware of the importance of both types of interests, and complete reporting enables end-users to appropriately



231 interpret the guidelines.

232

233 The number of organizations involved in guideline development may influence DOI reporting [20]. We found  
234 that guidelines developed solely by WHO reported DOI more often than those co-developed with other  
235 organizations. However, the difference was small and the statistical analysis was not able to provide strong  
236 evidence of a true association. The small difference may be related to WHO's uniform requirements, regardless of  
237 the number of collaborators. We also explored changes in reporting over the 9-year period of guideline  
238 development since inception of the GRC. Although the rates of reporting DOI remained stable across the years, and  
239 details of DOI collection and management were reported more frequently in recent years. This may be partly  
240 attributed to continuous advances in the requirements for guideline development both internationally and at WHO  
241 [6,45-47].

242

### 243 **Strengths and limitations**

244 To our knowledge, this is the first study to evaluate the reporting of DOI and COI of guidelines related to both  
245 clinical practice and public health or health policy. Although the same principles for developing trustworthy  
246 guidelines apply to WHO guidelines as to clinical practice guidelines, WHO guidelines (which are usually  
247 developed for a global audience) may differ with respect to funding sources, diversity of end-users, the population  
248 focus, financial constraints, and the need to address issues of equity and human rights and incorporate issues related  
249 to social determinants of health. Thus the results of examination of other clinical practice guidelines may not  
250 necessarily be applicable to WHO guidelines. We obtained guidelines from the WHO website and the GRC  
251 Secretariat in order to ensure a comprehensive list. We assessed the reporting of DOI and COI of WHO guidelines  
252 according to WHO's own requirements, which are consistent with those of the US Institute of Medicine [29].

253

254 Our study results are based only on information reported in the guidelines. The completed DOI forms are not  
255 publicly available (only a summary of DOI and COI is published in WHO guidelines), and we did not contact  
256 guideline authors for further information, and there are data to suggest that self-report of interests is frequently  
257 inaccurate [48,49]. In addition, we did not examine differences in reporting across topics because for most topics  
258 only a small number of guidelines were published. There may be variation across the technical units at WHO, as  
259 experience and training levels may differ. These questions should be further investigated in the future.

260

261

### 262 **Conclusion**

263 The identification and management of COI, particularly nonfinancial interests, are challenging for all  
264 guideline developers; nonetheless the collection and assessment of DOI and the management plan for any COI  
265 should be consistently reported in all guidelines. The majority of WHO guidelines performed relatively well with  
266 respect to reporting of funders, DOI and COI of external contributors in their guideline documents. This may be  
267 related to the quality assurance process at WHO implemented by the GRC, and the careful attention paid to this  
268 issue by WHO staff. However, there is a need for improvement, in particular for reporting the role of funders,  
269 declaration processes, and management of COI. WHO and the guideline community need to continue to seek more  
270 efficient and effective approaches for identifying, quantifying and minimizing potential sources of bias in guideline  
271 development.

272

273

274 **Declarations**

275

276 **Ethics approval and consent to participate** Not applicable.

277

278 **Consent for publication** All authors read and approved the final manuscript.

279

280 **Availability of data and material** All the data are presented in the manuscript.

281

282 **Competing interests** Dr SL Norris is an employee of the World Health Organization where one of her  
283 responsibilities is to help oversee the quality of WHO guidelines, including the implementation of WHO's conflict  
284 of interest policy.

285

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288

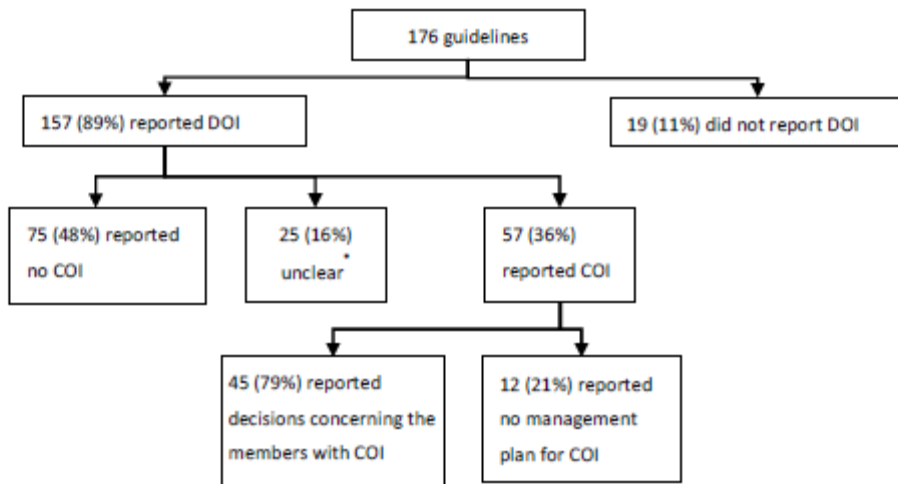
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297

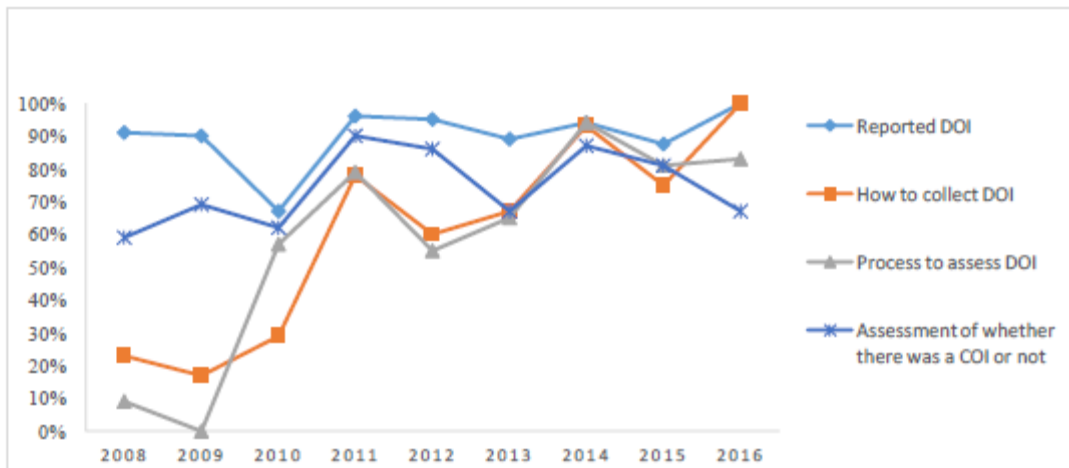
298



**Figure 1. Information on declarations and conflicts of interest in WHO guidelines**

\* These guidelines provide only DOI information without reporting whether COI existed or not.

COI, conflicts of interests; DOI, declarations of interest



**Figure 2. Reporting of declaration and conflicts of interests by year of publication**

300 **References**

- 301 [1] Richard MR, Richard NS, Robertson P. Clinical Practice Guideline Development Manual, Third Edition: A  
302 Quality-Driven Approach for Translating Evidence into Action. *Otolaryngol Head Neck Surg* 2013; 148(1  
303 Suppl): S1-55.
- 304 [2] Guidelines for declaration of interests (WHO experts). Geneva, World Health Organization, 2010.
- 305 [3] Thompson DF. Understanding financial conflicts of interest. *N Engl J Med* 1993; 329: 573–576.
- 306 [4] Boyd EA, Akl EA, Baumann M, Curtis JR, Field MJ, Jaeschke R, et al. Guideline Funding and Conflicts of  
307 Interest. *Proc Am Thorac Soc.* 2012; 19(5): 234–242.
- 308 [5] Guyatt G, Akl EA, Hirsh J, Kearon C, Crowther M, et al. The vexing problem of guidelines and conflict of  
309 interest: a potential solution. *Ann Intern Med* 2010; 152: 738–741.
- 310 [6] WHO handbook for guideline development-2<sup>nd</sup> edition. Geneva, World Health Organization, 2014.
- 311 [7] Qaseem A, Forland F, Macbeth F, Ollenschläger G, Phillips S, van der Wees P, et al. Guidelines International  
312 Network: Toward International Standards for Clinical Practice Guidelines. *Ann Intern Med* 2012; 3, 156 (7):  
313 525-31.
- 314 [8] Qaseem A, Snow V, Owens DK, Shekelle P; Clinical Guidelines Committee of the American College of  
315 Physicians. The Development of Clinical Practice Guidelines and Guidance Statements of the American  
316 College of Physicians: Summary of Methods. *Ann Intern Med* 2010; 3; 153(3): 194-9.
- 317 [9] Bero L and Grundy Q. Why having a (non-financial) interest is not a conflict of interest (Perspective) . *PLoS*  
318 *Biol* 2017; 14(12): e2001221.
- 319 [10] Boyd EA, and Bero LA. Improving the use of research evidence in guideline development: 4. Managing  
320 conflicts of interests. *Health Research Policy and Systems*, 2006; 4: 16
- 321 [11] Bekelman JE, Li Y, Gross CP. Scope and impact of financial conflicts of interest in biomedical research: a  
322 systematic review. *JAMA* 2003; 289: 454-465.
- 323 [12] Lundh A, Lexchin J, Mintzes B, Schroll JB, Bero L. Industry sponsorship and research outcome. *Cochrane*  
324 *Database of Systematic Reviews* 2017, Issue 2. Art. No.: MR000033.
- 325 [13] Als-Nielsen B, Chen W, Gluud C, Kjaergard LL. Association of funding and conclusions in randomized drug  
326 trials: a reflection of treatment effect or adverse events? *JAMA* 2003; 290: 921-928.
- 327 [14] Chren MM, Landefeld CS. Physicians' behavior and their interactions with drug companies. A controlled  
328 study of physicians who requested additions to a hospital drug formulary. *JAMA* 1994; 271: 684-689.
- 329 [15] Bes-Rastrollo M, Schulze MB, Ruiz-Canela M, Martinez-Gonzalez MA. Financial Conflicts of Interest and  
330 Reporting Bias Regarding the Association between Sugar-Sweetened Beverages and Weight Gain: A  
331 Systematic Review of Systematic Reviews. *PLoS Med* 2013; 10(12): e1001578.
- 332 [16] Dunn AG, Arachi D, Hudgins J, Malachowski C, Ioannidis JP. Financial conflicts of interest and conclusions  
333 about neuraminidase inhibitors for influenza: an analysis of systematic reviews. *Ann Intern Med* 2014; 161(7):  
334 513-518.
- 335 [17] Austvoll-Dahlgren A, Oxman AD, Chalmers I, Nsangi A, Glenton C, Lewin S, et al. Key concepts that people  
336 need to understand to assess claims about treatment effects. *J Evid Based Med* 2015;8(3):112-25.
- 337 [18] Neuman J, Korenstein D, Ross J S, Keyhani S. Prevalence of financial conflicts of interest among panel  
338 members producing clinical practice guidelines in Canada and United States: cross sectional study. *BMJ* 2011;  
339 343: d5621.
- 340 [19] Norris SL, Holmer HK, Ogden LA, Burda BU. Conflict of Interest in Clinical Practice Guideline  
341 Development: A Systematic Review. *PLoS ONE* 2011; 6(10): e25153.
- 342 [20] Norris SL, Holmer HK, Ogden LA, Selph SS, Fu R. Conflict of Interest Disclosures for Clinical Practice  
343 Guidelines in the National Guideline Clearinghouse. *PLoS ONE* 2012; 7(11): e47343.

- 344 [21] Campsall P, Colizza K, Straus S, Stelfox HT. Financial relationships between organizations that produce  
345 clinical practice guidelines and the biomedical industry: a cross-sectional study. *PLoS Med* 2016, 13(5):  
346 e1002029.
- 347 [22] Gross CP, Gupta AR, Krumholz HM: Disclosure of financial competing interests in randomised controlled  
348 trials: cross sectional review. *BMJ* 2003, 326:526-527.
- 349 [23] Choudhry NK, Stelfox HT, Detsky AS: Relationships between authors of clinical practice guidelines and the  
350 pharmaceutical industry. *JAMA* 2002, 287(5):612-617.
- 351 [24] <http://www.who.int/about/ethics/doi-form-EN.pdf?ua=1>. Accessed 6 March, 2017.
- 352 [25] [http://www.who.int/kms/guidelines\\_review\\_committee/en/](http://www.who.int/kms/guidelines_review_committee/en/). Accessed 9 July, 2016.
- 353 [26] Taylor R, Giles J. Cash interests taint drug advice. *Nature* 2005; 437(7062): 1070-1071.
- 354 [27] American Thoracic Society. Guidelines for developing documents. 2007. Available  
355 from:<http://www.thoracic.org/sections/about-ats/assemblies/guidelines-for-developingdocuments.pdf>.
- 356 [28] Conflict of interest and commercial sponsorship. Available from:  
357 <http://www.cochrane.org/handbook/26-declaration-interest-and-commercial-sponsorship>. Accessed 9 July,  
358 2016.
- 359 [29] Institute of Medicine. Clinical Practice Guidelines We Can Trust; Graham R, Mancher M, Wolman DM,  
360 Greenfield S, Steinberg E, editors. Washington, D.C.: The National Academies Press. 2011, 197 p.
- 361 [30] Graf C, Wager E, Bowman A, Fiack S, Scott-Lichter D, Robinson A. Best practice guidelines on publication  
362 ethics: a publisher's perspective. *Int J Clin Pract*. 2007; 61(s152): 1-26.
- 363 [31] Schünemann HJ, Al-Ansary LA, Forland F, Kersten S, Komulainen J, Kopp IB, et al. Guidelines International  
364 Network: principles for disclosure of interests and management of conflicts in guidelines. *Ann Intern Med*  
365 2015; 163(7): 548-553.
- 366 [32] Lethaby A, Wells S, Furness S, Strid M, Arroll B, Milne R, et al. Handbook for the preparation of explicit  
367 evidence-based clinical practice guidelines. Auckland, New Zealand: New Zealand Guidelines Group,  
368 Effective Practice Institute of the University of Auckland, 2001. 2001.
- 369 [33] Williams IG, de Ruiter A, Fisher MJ, Gazzard BG, Leen C, Palfreeman AJ. British HIV Association (BHIVA)  
370 Guideline Development Manual. British HIV Association (BHIVA). 2011.
- 371 [34] National Institute for Health and Clinical Excellence. Process and methods guides: The guidelines manual.  
372 NICE, 2012.
- 373 [35] Papanikolaou GN, Baltogianni MS, Contopoulos-Ioannidis DG, Haidich AB, Giannakakis IA, Ioannidis JP.  
374 Reporting of conflicts of interest in guidelines of preventive and therapeutic interventions. *BMC Med Res*  
375 *Methodol* 2001; 1: 3.
- 376 [36] Stelfox HT, Chua G, O'Rourke K, Detsky AS. Conflict of interest in the debate over calcium-channel  
377 antagonists. *N Engl J Med* 1998; 338: 101-106.
- 378 [37] Ebrahim S, Bance S, Athale A, Malachowski C, Ioannidis JP. Meta-analyses with industry involvement are  
379 massively published and report no caveats for antidepressants. *J Clin Epidemiol* 2016; 70: 155-163.
- 380 [38] Donovan JL, de Salis I, Toerien M, Paramasivan S, Hamdy FC, Blazeby JM. The intellectual challenges and  
381 emotional consequences of equipoise contributed to the fragility of recruitment in six randomized controlled  
382 trials. *J Clin Epidemiol* 2014; 67(8):912-20.
- 383 [39] Viswanathan M, Carey TS, Belinson SE, Berliner E, Chang SM, Graham E, et al. A proposed approach may  
384 help systematic reviews retain needed expertise while minimizing bias from nonfinancial conflicts of interest.  
385 *J Clin Epidemiol* 2014; 67(11): 1229-1238.
- 386 [40] Akl EA, El-Hachem P, Abou-Haidar H, Neumann I, Schünemann HJ, Guyatt GH. Considering intellectual, in  
387 addition to financial, conflicts of interest proved important in a practice guideline: a descriptive study. *J Clin*

388 Epidemiol 2014; 67(11): 1222-8.

389 [41] Board S. Nonfinancial conflicts of interest in research. *N Engl J Med* 2002; 347(10).

390 [42] Abdoul H, Perrey C, Tubach F, Amiel P, Durand-Zaleski I, Alberti C. Non-financial conflicts of interest in  
391 academic grant evaluation: a qualitative study of multiple stakeholders in France. *PloS one* 2012; 7(4):  
392 e35247.

393 [43] Biswas T. Understanding Non-financial Conflicts of Interest. *Indian Pediatr* 2013; 50: 347-348.

394 [44] Neumann I, Karl R, Rajpal A, Akl EA, Guyatt GH. Experiences with a novel policy for managing conflicts of  
395 interest of guideline developers: a descriptive qualitative study. *CHEST* 2013; 144(2): 398-404.

396 [45] WHO Handbook for guideline development. Geneva, World Health Organization; 2008.

397 [46] WHO Handbook for guideline development. Geneva, World Health Organization; 2010.

398 [47] WHO handbook for guideline development. Geneva, World Health Organization; 2012.

399 [48] Okike K, Kocher MS, Wei EX, Mehlman CT, Bhandari M. Accuracy of conflict-of-interest disclosures  
400 reported by physicians. *N Engl J Med* 2009; 361(15): 1466-1474.

401 [49] Andreatos N, Zacharioudakis IM, Zervou FN, Muhammed M, Mylonakis E. Discrepancy between financial  
402 disclosures of authors of clinical practice guidelines and reports by industry. *Medicine (Baltimore)* 2017; 96(2)  
403 :e5711.

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