

Cochrane Conflict of Interest 2019

Selective review of organizational conflict of issue policies

Prepared by Fergus Macbeth, Angela Webster, Ruth Foxlee, Graham Smith and Kirsty Loudon, with input from the COI Project Board.

Contents

Cont	tents		2		
1	Brief report				
2	Detailed report				
2.1	Backg	round	5		
2.2	Objec	tives	5		
2.3	Metho	ods	5		
2.4	Result	S	6		
	2.4.1	Financial Conflicts of Interest	6		
	2.4.2	Non-financial Conflicts of Interest	10		
	2.4.3	Policy Governance	18		
	2.4.4	Policy Management Processes	18		
	2.4.5	Policy Presentation	20		
3	Concl	usions	21		
4	Biblio	graphy	22		
Арре	endix 1		26		
List	of orgai	nizations	26		
Арре	endix 2		28		
Glos	sary of	terms and abbreviations	28		
Арре	e <mark>ndi</mark> x 3		29		
Organizational policies supporting issues for Cochrane to consider - Misc.					
Orga inter		nal policies supporting issues for Cochrane to consider - Non- financial/other	31		

1 Brief report

Cochrane's conflict of interest (COI) policy is vital to those who create and consume Cochrane content. The current <u>Commercial Sponsorship Policy</u> was last updated in 2014. In March 2018 the Governing Board approved a proposal to revise the current policy and develop a non-financial COI policy. This selective review of policies from organizations and biomedical journals is part of a larger project including a community survey and structured interviews with key stakeholders and COI experts.

We included policies from organizations that fell into the following six categories:

- 1. Funders of Cochrane Reviews and Cochrane Review Groups, e.g. the National Institute for Health Research (UK);
- 2. Users of Cochrane Reviews, e.g. the World Health Organization;
- 3. Guideline organizations, e.g. Guideline International Network;
- 4. Healthcare charities, e.g., the Wellcome Trust;
- 5. Academic institutions, e.g. the University of Edinburgh;
- 6. High-impact biomedical journals, e.g. the BMJ.

The review assessed 33 conflict of interest policies, which identified the following issues for Cochrane to consider when revising our COI policy:

- A clear statement of an organization's definition of conflict of interest is key to policy implementation and compliance, and was cited in the policies of six editorial publishing organizations, 14 healthcare research and guideline organizations, four funding organizations, and five other associated organizations.
- The need to publish accurate declarations was highlighted in the policies of four editorial publishing organizations, 10 healthcare research and guideline organizations, two funding organizations, and two other associated organizations.
- Financial thresholds are considered a useful tool by some other organizations to help grade judgements on financial COI. They were cited in the policies of one editorial publishing organization, four healthcare research and guideline organizations, one funding organization, and three other associated organizations.
- Some organizations now include non-financial interests in in their COI policies. This type of
 interest was cited in the policies of seven editorial publishing organizations, 12 healthcare
 research and guideline organizations, four funding organizations, and four other associated
 organizations. The types of non-financial interests most commonly mentioned are professional,
 intellectual and institutional interests, and personal relationships.
- The need for clarity about who is responsible for policy governance is cited as essential in the COI
 policies of one healthcare research and guideline organization, and one other associated
 organization.

- Best practice in COI policy management occurs when the policy is widely understood and the process is fully transparent from initial declarations to publication. Process management was covered in the policies of two publishing organizations, two funding organizations, and two healthcare research and guideline organizations.
- The management of policy breaches was discussed in the policies of one editorial publishing organization and one funding organization. It was also referenced in two academic papers to be part of their COI policy, including treating wilful non-disclosure as scientific misconduct.
- The importance of clear formatting and plain English in policy implementation was cited in the policies of two healthcare research and guideline organizations and referenced in one academic research article, which noted that policies should be publicly available.

In undertaking this review of organizational COI policies we sought to identify approaches that may be useful to Cochrane as it revises its own COI policy. There are elements of several organizational policies that merit consideration; some confirm where Cochrane's current policy is already strong and others suggest ways that we might strengthen our policy.

There has been an increasing focus on non-financial interests (Bero 2016) and some organizations now require disclosures of this type, alongside disclosures of financial interests. In the absence of any clear, empirical evidence about the impact of this type of interest we may wish to define "non-financial" interests in the context of Cochrane systematic reviews but not deal with them in the same way that we manage financial interests.

A clear, plain-English policy is essential to ensuring that the policy is widely understood and used. Authors should be encouraged to review their declarations, at least annually or when their circumstances change. It is also important that there is clarity about who is responsible for policy governance and that the consequences of non-compliance are clear. Openness and willingness to adapt to criticism and changing social and scientific norms is essential to creating a policy that is fit for purpose now and into the future.

2 Detailed report

2.1 Background

Having a robust conflict of interest (COI) policy is central to Cochrane's reputation as an organization that produces independent, high-quality systematic reviews. Cochrane's current Commercial Sponsorship Policy is one of the strongest in the biomedical publishing sector (Bero 2018). It is similar to those of some major guideline development organizations in that it not only requires interests to be declared, but also rules that some conflicts will lead to authors not being able to conduct Cochrane Reviews. The current policy affects anyone involved in Cochrane Review production - authors, editors, peer reviewers and all Cochrane Review Group (CRG) staff. It also covers the Governing Board, Geographic Groups, Fields, Method Groups, the Consumer Network and the Central Executive Team. The policy was last updated in May 2014, following a consultation exercise.

It is apparent from issues faced by the <u>Cochrane Funding Arbiters</u> that authors and CRGs are sometimes unclear about if and when it is a problem for an author to accept payments from a commercial organization. Audits requested by the Cochrane Governing Board in 2014 and 2017 suggest that adherence to the policy is inconsistent. This may be partly due to insufficient detail or ambiguous wording in the current policy. There has also been discussion within the Cochrane Co-ordinating Editor community and elsewhere about the impact of non-financial interests (academic, professional, intellectual and personal). These other types of interests have not so far been systematically addressed in Cochrane's policy. In March 2018 the Governing Board approved a project to revise the current Commercial Sponsorship Policy and to develop a non-financial COI policy. An <u>editorial</u> in the Cochrane Library sets out further information about the project, which includes this organizational policy review, a Cochrane community-wide survey and semi-structured interviews with key stakeholders and COI experts. Reports from all three exercises will inform a final report containing recommendations for the Governing Board.

2.2 Objectives

To situate Cochrane's current COI policy within the broader COI policy and practice landscape by reviewing the policies of organizations that are related to Cochrane, either as potential funders or consumers of Cochrane evidence or as presences in the biomedical research and publishing sectors.

2.3 Methods

This review examined the policies of the following types of organization:

- 1. Funders of Cochrane reviews and Cochrane Review Groups, e.g. the National Institute for Health Research (UK) and the National Health and Medical Research Council (Australia);
- 2. Users of Cochrane reviews, e.g. the National Institute for Health and Care Excellence (UK) and the World Health Organization;
- 3. Representative organizations for international healthcare guideline organizations, e.g. the U.S. Preventive Services Task Force, and the Guidelines International Network;
- 4. Healthcare charities, e.g. the Wellcome Trust;
- 5. Academic institutions, e.g. The University of Edinburgh and The University of Hong Kong;
- 6. High-impact biomedical journals, e.g. the BMJ, and PLOS ONE.

A list of organizations was suggested by the Funding Arbiters (FM and AW) and additional suggestions were made by KL. A final list of the 33 organizations for which policies were reviewed is shown in Appendix 1.

Only organizations with English-language policies were included and selection and synthesis were carried out by one person (KL). Where documentation allowed, the following information was extracted: 1) policy definitions; 2) approach to eliciting declarations; 3) approach to financial interests; 4) thresholds for

financial interests; 5) existence of a non-financial component; 6) policy governance; 7) COI management processes; 8) approach to misconduct; and 9) policy language and formatting. Many of the organizational policies were not publicly available and released on the understanding they would only be used for this review and not shared outside more widely. A glossary of terms and abbreviations is shown in Appendix 2.

2.4 Results

2.4.1 Financial Conflicts of Interest

Cochrane's current policy states that "Cochrane reviews must be independent of conflicts of interest associated with commercial sponsorship and should be conducted by people or organizations that are free of bias". Evidence suggests that financial support can consciously or unconsciously bias people and impact on study results (Bekelman et al 2003, Bero et al 2007, Brignardello-Petersen et al 2013, DeGeorge et al 2015, DeJong et al 2016, Mandrioli et al 2016, Perlis et al 2016, Wood et al 2017, Yeh 2016). Lee (2008) argues that the amount of money is not important in influencing an individual's decision-making and actions because "Gifts of any size from drug companies create feelings of reciprocity". Cochrane employs a range of methodological approaches aimed at minimizing the impact of any possible biases an author team might have. Lundh and colleagues (2017) suggest however that the Cochrane Risk of Bias tool cannot fully capture the impact of industry bias and recommend that Cochrane considers how to handle this potential source of bias in its reviews.

2.4.1.1 Definitions of Conflict of Interest

It is important to have a clear definition of conflict of interest to ensure wide understanding and compliance with a COI policy. Defining conflict of interest is linked to identifying possible conflicts. In revising Cochrane's policy we reviewed how other relevant organizations have defined COI.

<u>The International Committee of Medical Journal Editors</u>' (ICJME) definition of conflicts of interest, on which Cochrane's current definition is based, is: "A conflict of interest exists when professional judgment concerning a primary interest (such as patients' welfare or the validity of research) may be influenced by a secondary interest (such as financial gain). Perceptions of conflict of interest are as important as actual conflicts of interest."

<u>Committee on Publication Ethics</u> (COPE) uses a clear definition: "Conflicts of interest comprise those which may not be fully apparent and which may influence the judgment of author, reviewers, and editors. They have been described as those which, when revealed later, would make a reasonable reader feel misled or deceived. They may be personal, commercial, political, academic or financial. "Financial" interests may include employment, research funding, stock or share ownership, payment for lectures or travel, consultancies and company support for staff."

Some organizations use the Institute of Medicine (IOM) definition: "a set of circumstances that creates a risk that professional judgment or actions regarding a primary interest will be unduly influenced by a secondary interest" (IOM 2009).

The journal *Human Rights Law Review* uses this definition: "A conflict of interest is construed as a personal involvement in a case or other matter being reported; a meaningful financial interest in the matter, or a connection with an author, including personal relationships or direct academic competition, that might raise the question of bias in reviewing and judging work submitted for publication." (Human Rights Law Review 2019). This definition is inclusive and covers financial and non-financial interests.

The definition below is used in the <u>NIHR Evaluation</u>, <u>Trials and Studies Coordinating Centre</u> (NETCC), (2017) policy, and introduces the concept of "unfair advantage".

CONFLICT OF INTEREST AND UNFAIR ADVANTAGE

- A conflict of interest is defined as any situation in which an individual or organization is in a position to exploit a professional or official capacity for their personal or organizational benefit. Conflicts of interest are not themselves inappropriate and occur frequently. An issue of concern arises when an individual or organization acts in a manner that could reasonably be considered to be improper.
- Unfair advantage occurs when an advantage is given to an individual or organization (or a disadvantage imposed on another) in a way that could be considered improper or with wrongful intent. Having an advantage due to circumstances that could not reasonably be considered improper or use to wrongful intent would not constitute an unfair advantage.
- Most of the time we are dealing with the perception of conflicts of interest or unfair advantage. A perceived conflict of interest or unfair advantage occurs when an individual or organization could reasonably be perceived to have the potential to act improperly; the perception of which could still lead to embarrassment irrespective of whether improper action was actually taken.

Considerations for Cochrane: A clear statement of how the organization defines conflict of interest is key to policy implementation and compliance. This issue was cited in the policies of six editorial publishing organizations, 14 healthcare research and guideline organizations, four funding organizations, and five other associated organizations.

2.4.1.2 Declaring interests

If declarations are not published it will not be clear to the reader if there was nothing to declare, or if a declaration was purposefully omitted. Bou-Karroum et al (2018) undertook a cross-sectional study looking at reporting of conflicts of interest for authors of 200 systematic reviews published in 2015 in the health policy and systems research (HSPR) papers, stored in the Health Systems Evidence (HSE) database of McMaster Health Forum, from 152 different journals. The team found that 20% of the systematic reviews in this discipline did not include a COI disclosure statement, and the authors suggested that journals should strengthen and/or better implement their COI disclosure policies. The publication of declarations in systematic reviews is essential to ensure credibility in the results. NICE use a register to collate declarations of interests/conflicts of interest for guideline teams (see <u>Management of COI Process</u>).

Rasmussen (2018) found there were problems with the trustworthiness of self-declaration in trial publications by non-industry employed authors in Denmark, with inconsistencies between the conflicts disclosed in journal publications and the information provided by the same authors on the Danish Health and Medicines Authority's public disclosure. Lundh and colleagues (2012) found that authors involved in trials that were sponsored by industry rarely checked the sponsor's data analysis and summary by looking at the raw data themselves. A recent review (Bero 2018) of COI policies for 11 major medical journals which considered publishing industry-sponsored studies found that only JAMA and JAMA Internal Medicine would not publish studies which had not had independent data analysis.

In 2010 in the United States, a healthcare law – The Physician Payments Sunshine Act – was enacted to increase the transparency of financial relationships between healthcare providers and pharmaceutical manufacturers. <u>The Open Payments Data Register</u> can be very useful for checking declarations in the USA and may be helpful in verifying conflicts of interest and assessing misconduct. In Australia pharmaceutical companies have been required to report all the sponsored events since 2007 (Robertson 2009). This information is publicly available on the <u>Medicines Australia</u> website. In the UK, the General Medical Council (GMC) has promoted a public register of doctors collaborating with industry, <u>Disclosure UK</u>, but this information is given on a voluntary basis and many consider the list to be untrustworthy (Adlington 2016, Kmietowicz 2016, McCartney 2016). The Dutch have the 'Transparantieregister Zorg' (founded in 2013), which is being evaluated in 2019.

These registers and other means of checking financial payments are important as Zia et al (2018) found that only 37% of 100 doctors who received the highest amount of funding from device makers in 2015 disclosed funding from commercial sources. Associations between academic rank or productivity and industrial payments were not statistically significant (Zia at al 2018).

There may be a difference in the perceived importance of declaring based on where you live and work. A survey of Cochrane systematic review authors from low- and middle-income countries showed that 13% of the authors found it acceptable not to declare conflicts with a company involved in the research project (Rohwer et al 2017). Furthermore, 40% of responders were aware that under-reporting of conflicts with funders had taken place at their institution; so as Rohwer et al (2017) said, "Transparency is not a given". Geography and culture may present a challenge but Cochrane is not unique in its intention to apply a COI policy internationally. The <u>World Health Organization</u> states that its COI policy must be adhered to globally, and like Cochrane it has people working all round the world.

Considerations for Cochrane: The need to publish declarations was highlighted in the policies of four editorial publishing organizations, 10 healthcare research and guideline organizations, two funding organizations and two other associated organizations as a vital step in monitoring successful implementation of a COI policy. Consistency and accuracy of reporting is important but may be challenging to police.

2.4.1.3 Financial conflict of interest and approaches to authorship

Cochrane's current policy considers the same types of financial declarations as other medical journals. For instance, the policy of <u>The Lancet</u> simply states: "Financial relationships (such as employment, consultancies, stock ownership, honoraria, paid expert testimony) are the most easily identifiable conflicts of interest and the most likely to undermine the credibility of the journal, the authors, and of science itself." Cochrane's policy goes a step further however by prohibiting funding of reviews or financial support for authors by "commercial sponsors or sources with a real or potential vested interest in the findings or a specific review". Bero (2018) in her review did not find another medical journal which imposed a general ban on individuals with certain types of COI from authoring systematic reviews or primary research articles, regardless of topic. PLOS Medicine and the BMJ prohibit publication of research funded by tobacco companies only (Bero 2018). PLOS ONE state in their COI policy that they do not "publish commissioned or other non-research articles if [they] are aware of a competing interest that, in [their] judgment, could introduce bias or a reasonable perception of bias".

There are similarities between the types of conflicts of interest found in guidelines (Table 1) and those found in Cochrane reviews, with the important difference being that Cochrane reviews provide an objective summary of the evidence, whereas a guideline is making healthcare-resource-use decisions on behalf of a specific healthcare system or professional organization. While organizations such as the National Institute for Health and Care Excellence (NICE) UK have kept the wording organization-specific, all provide details of potential financial conflicts of interest.

Figure 1. Types and Examples of Conflicts of Interest in Guidelines

Table. Types and Examples of Conflicts of Interest in Guidelines

Type of Conflict	Domains*	Examples
Direct financial	Direct payments for service Stock options	Payments to participate in a study on an intervention that is subject to a recommendation Consultancy for a manufacturer of a relevant technology/intervention Payment for lectures and meeting attendance in support of a technology/intervention Paid board memberships, patent applications, and research grants† Honoraria and gifts
Indirect‡	Academic advancement Clinical revenue streams Community standing Scientific interest	Having published on a topic that expresses an opinion on the effectiveness of an interventio or doing research on a topic that could be affected by a recommendation§ Being an acknowledged expert in the intervention Gaining clinical income from the recommendation Leadership or board or committee memberships Involvement with an advocacy group that may gain from a guideline Writing or consulting for an educational company Personal convictions or positions

S For example, further funding decisions based on the direction and strength of a recommendation. Political, religious, ideological, or other.

Note. Reprinted from "Guidelines International Network: Principles for Disclosure of Interests and Management of Conflicts in Guidelines" by Schunemann et al(2015), Annals Intern Med; 163(7):548-553. (permission given).

2.4.1.4 Degrees of financial conflict of interest

Some organizations consider the level of remuneration as part of their COI policy, however many do not.

- The <u>Guidelines International Network (G-I-N</u>) policy (not publicly available) incorporates the value • of a grant or gift and takes into account whether personal benefit and/or institutional benefits are accrued. In addition, COI judgments are graded 'no conflict', 'low relevance/seriousness' or 'high relevance/seriousness'.
- The Society of General Internal Medicine COI policy includes thresholds under the "Extent of • Financial Relationship: Existence and Amount" section advising disclosure of both the existence of a relationship and the amount of any financial arrangement for four categories: none, \$10,000, \$10-\$50,000 and > \$50,000 received within the last three years.
- The National Institutes of Health (USA) COI policy (2018) describes a "significant financial interest" • as an amount in US Dollars that, when aggregated from one entity or any non-publicly traded entity, exceeds \$5,000 within the last 12 months.
- The Japanese Association of Medical Sciences sets a 500,000 Japanese yen (c4,500 USD) threshold • for articles, and a higher threshold of 1 million Japanese yen (c9,000 USD) per year for attending meetings.
- In the UK, the National Institute for Health Research (NIHR) policy also stipulates financial thresholds in pounds sterling:
 - "Personal remuneration (above £5k per year) from organizations including employment, pension, consultancies, directorships and honoraria.
 - Shareholdings and other financial interests in companies valued greater than £10k or greater than 1% of the issued share capital held by panel members or their close family.
 - Non-financial or unremunerated involvement with organizations, such as Scope directorships of companies or organizations, which benefit from support by the NIHR."

The application of thresholds must take into account changing exchange rates and the relative value of a payment in one country vs. another (e.g. £1k in a low-income country is likely more significant than the

same amount in a high-income country). Another challenge is that thresholds, even when carefully considered and agreed, are inevitably arbitrary.

Considerations for Cochrane: Financial thresholds are considered a useful tool to grade judgements about financial COIs by some other organizations. They were cited in the policies of one editorial publishing organization, four healthcare research and guideline organizations, one funding organization, and three other associated organizations.

2.4.2 Non-financial Conflicts of Interest

Cochrane's current <u>Commercial Sponsorship Policy</u> refers to two types of activity that might be considered to constitute non-financial interests: "involvement in primary research in the subject area of the review" and "any other interests that others may judge relevant". The impact of non-financial interests has been debated within Cochrane but defined policy approach has not yet been developed.

Interest in the need to declare non-financial interests has been increasing and organizations ranging from <u>local councils</u> to national governments and international organizations like the <u>World Health Organization</u> are encouraging transparency and seeking to manage non-financial declarations. Interest ranges from discussion about nutritional research and the importance of the researchers declaring their own dietary preference (Ioannidis 2018) to the influence of religious beliefs on assisted dying and abortion (Smith 2018). Both research teams argue for disclosure of interests if they are relevant to the work being undertaken. This approach has been criticised however because of concerns about discrimination. While it is acknowledged that non-financial conflicts can influence medical research, some believe they "cannot be avoided or eliminated" (Wiersma 2018).

Separating non-financial from financial interests can be challenging and it is important to understand any possible links. Dunn (2016) recommended "precise, structured and comprehensive reporting of such interests so that we can treat them like any other confounder" and suggested ideology, religion, politics or personal relationships were as important as financial interests in influencing research. Attempting to determine a relevant interest – financial or otherwise – is not always easy and so Wiersma and Lipworth (2019) define an interest as: "a commitment to oneself or others that affects our attitudes, judgements and actions".

The main non-financial interests that have been included in COI policies of other journals are personal, professional, intellectual and institutional. Bero and Grundy set out a more detailed list of non-financial interests specifically relevant to systematic review production (Table 1).

Table 1. Examples of Interests in Biomedical Research (that may be relevant to systematic reviews)

Type of training: professional or academic education
Profession or discipline
Institutional affiliation or academic associations
Advocacy or policy positions of the researcher or organization with which they are affiliated
Academic competition or rivalry
Role as investigator on study included in a systematic review
Professional relationships - dominant or dominated researcher in area of research –
Career advancement or promotion
Intellectual, theoretical, or school of thought commitments
Personal, religious, or political beliefs
Published opinions, essays or commentaries on topic of research
Personal experiences
Personal experience with subject of the disease

Personal relationship with someone who has the disease or condition under study Personal recognition (glory seeking or desire for fame)

Note. Adapted from "BOX 1, Examples of Interests in Biomedical Research. "Why having a (Nonfinancial Interest) is Not a Conflict of Interest" by Bero LA and Grundy Q (2016), PLOS Biology;14(12) (permission given).

Shawwa et al (2016) found that all but one of the 117 National Library of Medicine (NLM) peer-reviewed "core clinical journals" had COI policies, with over half of them (66) incorporating non-financial interests. This category was described as "other" in 44 journals (66%) but other descriptions were also used: "academic association" (14%), "professional" (8%) and "intellectual" (3%). Only two (3%) journals referred to "intellectual" interests. There did not appear to be consensus on having a COI policy that integrated both non-financial and financial conflicts, with discussion on how disclosure or non-disclosure would be managed by the journals in their editorial policy.

Khamis (2017) found that 81% (54/67) of the health policy and systems research (HSPR) journals examined required some aspect of non-financial COI disclosure. The top three categories were "personal relationship" (54%), "non-financial COI" (33%) and "professional" (28%). COPE or ICJME membership did not affect the explicit requirement for disclosure of non-financial interests. Khamis et al (2017) also described the COI policies of 54 journals that include non-financial interests for which disclosure is required (Figure 2). A journal may have more than one option that applies.

Non-financial COI terms	n (%)
Personal relationship	29 (54)
Other	21 (39)
Non-financial COI	18 (33)
Professional	15 (28)
Academic competition	12 (22)
Personal opinion	10 (19)
Academic	9 (17)
Intellectual passion	9 (17)
Religious views	8 (15)
Political	8 (15)
Personal	8 (15)
Intellectual	7 (13)
Ideological	7 (13)
Competing loyalties	5 (9)
Advocacy groups/institutional advocacy	5 (9)
Institutional	3 (6)
Legal relationship	3 (6)
Governmental	1 (2)

Figure 2. Descriptors used to refer to non-financial conflicts of interest (COI) for which disclosure is required (n=54)

Note. Reprinted from "Requirements of health policy and services journals for authors to disclose financial and nonfinancial conflicts of interest: a cross-sectional study" by Khamis AM et al (2017), Health Research Policy and Systems,15:80 (permission given).

A simpler list of non-financial interests has been developed by Akl et al (personal communication 2018) building on the framework used in the paper by Bou-Karroum (2018). These non-financial and financial interests are integrated, and the classification system is divided into individual (financial, intellectual and personal) and institutional affiliation (financial, intellectual and cultural) interests (Figure 3). In this framework, COI is conceived as a risk of bias associated with a specific relationship. They propose that the level of risk will vary from low to high across and within the categories. One major challenge is how to assess the level of this risk qualitatively or semi-quantitatively (Personal communication Akl et al 2018).



Figure 3. Framework to assess individual and institutional COI including non-financial interests

Note. Reprinted from Personal communication by Akl (2018) (permission given).

Bero and Grundy (2016) argue that a reflexive process with individuals considering carefully what has influenced their work, with institutional support, could assist management of potential conflicts. They caution however that focussing on non-financial interests could distract from the significant and well-documented impact of financial conflicts. They argue that having an *interest* should be distinguished from having a *conflict of interest* and only situations where there is a genuine conflict should be disclosed. There is currently no empirical evidence to indicate that non-financial interests have the same impact as financial interests.

In sub-sections 5.2.1.1 to 5.2.1.4 specific types of non-financial interest are outlined.

Considerations for Cochrane: Healthcare research and funding organizations are beginning to incorporate non-financial interests in their policies. This type of interest was cited in the policies of seven editorial publishing organizations, 12 healthcare research and guideline organizations, four funding organizations, and four other associated organizations. The types of non-financial interests most commonly mentioned are professional, intellectual and institutional interests and personal relationships, but currently there is no empirical evidence to show that non-financial interests have the same impact as financial interests.

2.4.2.1 Personal relationships

In the study by Khamis et al (2017) 54% (29/54) of journals included "personal relationships" as a category in the non-financial policy. However, defining a personal relationship in a COI context can be difficult. Many people would agree that relationships with family and close friends or colleagues are personal. The National Institute for Health and Care Excellence (NICE) states that "indirect interests can arise from people (such as close relatives, close friends and associates and business partners)". The BMJ has two clauses in its COI policy which focus on editorial matters which may be influenced by a personal relationship:

- Non-financial interests: Personal relationships with authors or editors of material, including having held grants, co-authored articles or papers, or worked together.
- Interests of related parties: Conflicts of interest may also arise where a related party (spouse, partner, or other close family member) has a financial or non-financial interest as described above that could be seen to conflict with the task a person is being asked to do for BMJ.

Bero and Grundy (2016) argue that a "personal relationship with someone who has the disease or condition" could be perceived as something that might influence conclusions.

Other organizations have referred to personal relationships in the following ways:

- U.S. Preventive Services Task Force (USPSTF): "All members are expected to provide full disclosure of their own interests as well as the interests of immediate family members (which includes their spouse/partner, dependent children, and parents) and those of other close personal relationships." Personal communication indicated "business partners" were also included.
- The Research Grants Council in its COI policy stated: "Close personal relationship (e.g. partner, spouse, immediate family member, long-term close friend)".
- The Japanese Association of Medical Sciences (JAMS): "Whether to include spouses, first degree relatives, or subjects who share income or financial benefits (inherited benefits) of those above subjects should be determined depending on the situation of each affiliated society. However, in cases where the spouses, first degree relatives are not included as subjects of COI disclosure, if there is possibility of COI due to indirect or uneconomical factors that might affect the carrying out or interpretation of the results of the medical science research, they may be required to disclose such COI using the designated form".
- The National Institutes of Health (USA): "...and those of the Investigator's spouse and dependent children".
- The Association of the Scientific Medical Societies in Germany (AWMF): "...personal/professional partners for non-financial and financial policy".
- The University of Edinburgh: "Relative or friend: Any member of an employee's close family (i.e. spouse, parents, siblings or children): his/her partner (i.e. boy/girlfriend, sexual or romantic partner); close personal friends; and any other person with whom the employee has a relationship which is likely to appear, to a reasonable person, to influence his/her objectivity."
- The Charity Commission (2014) uses the term "connected person" to give a comprehensive list to assist individuals in fulfilling their duties to declare, manage and avoid conflicts of interest.

People in positions of authority must be acutely aware of the perception of bias that attaches to any type of interest. They must not let friendships or relationships lead to biased and anti-competitive decisions (Bero and Grundy 2016). It is uncertain to what degree relationships with friends, family, students and colleagues may influence systematic reviews but arguably it might be helpful to readers if these relationships were declared, particularly when they relate to a pharmaceutical company employee or a trialist working in an area relevant to the review.

Considerations for Cochrane: personal relationships are covered in the policies of six editorial publishing organizations, 11 healthcare research and guideline organizations, four funding organizations, and five other associated organizations. Some are more inclusive than others.

2.4.2.2 Professional interests

One of the key non-financial interests identified by Khamis et al (2017) is professional. This interest is included in 15 out of 54 (28%) HSPR journal policies. According to Bero and Grundy (2016) being a healthcare professional or an academic researcher is an interest but not necessarily a *conflict* of interest as this is part of the individual's personal identity. When a person has undergone extensive training and accumulated a great deal of clinical experience in a particular speciality, their career becomes part of their

individual essence and is impossible to remove. Bero and Grundy (2016) argue that a conflict of interest is something that can be removed, for instance shares in a drug company can be sold but it is not possible to step aside from being, for example, a paediatric nurse or orthopaedic surgeon with a professional interest in this speciality. Cochrane's current Commercial Sponsorship Policy states that income from private clinical practice should be declared but this does not prevent an individual from being a review author, editor, or peer reviewer.

Both NICE and the WHO have included "professionalism" in their COI policies. The NICE policy (2018) states that "care is needed around any indirect reputational interest related to positions held in other organizations, and publications authored, or public statements made, which could reasonably be interpreted as potentially prejudicial to an objective interpretation of the evidence." Both organizations emphasize balancing the risk that comes from being a "professional" with the benefit of access to a person's expertise. Involvement in guidelines developed in accordance with international criteria does not usually lead to people being excluded from the meeting, but they cannot be the chairperson in committees (<u>NICE 2018, WHO 2018</u>).

Considerations for Cochrane: Professional interest is cited in the policies of six editorial publishing organizations, seven healthcare research and guideline organizations, three funding organizations and four other associated organizations as an influencing factor on the perspective of a person involved in producing a Cochrane review.

2.4.2.3 Intellectual interests

Working in a speciality field in academia or healthcare and building on a personal interest and passion for a particular subject is key to professionalism and research (Bero and Grundy 2016). Described as "intellectual passion" Khamis (2017), this type of interest was referenced in 17% (9/54) of HSPR journals. Bero and Grundy (2016) also called this "Intellectual, theoretical, or school of thought commitments". Focussing in on a speciality area may result, however, in "a blinkered approach", leading to a lack of awareness or the ability to acknowledge other viewpoints which demand recognition. This issue can be magnified if several professionals of similar backgrounds and viewpoints work together. There may not be a real problem, but perceptions are important where potential COIs are concerned. Being self-aware and acknowledging bias through declarations is vital so that this can be managed.

Exclusion because of intellectual interests can be a potential problem in decision-making; the Food and Drug Administration (FDA) Advisory Committees had a policy of excluding experts on the basis of intellectual COI and discovered that industry benefited. Interestingly there was no policy for exclusion based on favouring a drug or device (Lenzer 2016). NICE (2018) in their recent COI policy update did include information on what should be declared regarding intellectual interests: "(1) has published a clear opinion about the matter under consideration; and (2) has authored or co-authored a document submitted as an evidence publication to the relevant NICE advisory committee." NETSCC, NIHR (2017) (COI policy not publicly available) states that it is "important that there are sufficient committee members who have the appropriate knowledge and skills to make an informed decision. Each decision to exclude someone from a committee must balance these competing risks of bias due to conflict of interest versus wrong decisions from lack of expertise."

Considerations for Cochrane: The need to declare a specific intellectual interest is cited in the policies of four editorial publishing organizations, six healthcare research and guideline organizations, two funding

organizations, and four other associated organizations.

2.4.2.4 Institutional interests

Bero and Grundy (2016) included "institutional affiliation or academic association" as a non-financial interest, highlighting the need for institutions to carefully consider the possibility of reputational damage which may arise from entering into partnerships with commercial organizations. Akl et al (2018 personal communication) describe intellectual COI as something "which arises when an organization, to which an individual belongs, focuses or funds research on a specific topic, or arises when an individual (paid employee or unpaid member) belongs to an institution/organization that clearly advocates for the issue under consideration." They further define potential institutional COI as "institutional participation in research" and "institutional advocacy" in addition to "cultural COI: arising when an individual (paid employee or unpaid member) belongs to an institution/organization that has a specific cultural identity (e.g. Catholic university)" (Akl 2018 personal communication).

Khamis et al (2017) found that only 6% (3/54) of HPSR journals included the term "institutional" as part of their assessment of non-financial COIs. In addition, advocacy groups or institutional advocacy was included by 9% (5/54) of HPSR journals. Bou-Karroum et al (2018) suggest that conflicts of interest should be specified by journals as either individual or institutional and as either financial or non-financial. The COI framework by Bou-Karroum et al (2018) (Figure 4) was developed from a review of the literature, the ICMJE disclosure form and recent studies by Hakoum (2016, 2017). Disclosure of these institutional interests does not necessarily indicate bias. Bou-Karroum et al (2018) note that full declaration and careful management, promote trust and credibility in the research findings for policymakers and the public.

	Financial	Professional	Scholarly	Advocatory	Personal
Individual	Individual financial	Individual professional	Individual scholarly	Individual advocatory	Individual personal
nstitutional	Institutional financial	Institutional professional	Institutional scholarly	Institutional advocatory	

Figure 4. Conflicts of Interest Framework.

Note. Reprinted from "Reporting of Financial and Non-Financial Conflicts of Interest in Systematic Reviews on Health Policy and Systems Research: A Cross Sectional Survey" by Bou-Karroum et al(2018), International Journal of Health Policy and Management; 7(8), 711–717.

Considerations for Cochrane: Institutional conflicts of interest are considered in the policies of two editorial publishing organizations, nine healthcare research and guideline organizations, and one funding organization.

2.4.2.5 Non-financial interests within three key Cochrane stakeholder organizations

Non-financial interests that should be declared have been detailed by three organizations with which Cochrane has important relationships – the National Institute for Health and Care Excellence (NICE), the NIHR Evaluation Trials and Studies Coordinating Centre (NETSCC) and the World Health Organization (WHO). These three organizations have been selected for two reasons:

- 1. Evidence from Cochrane systematic reviews is used in NICE and WHO clinical guidelines and is sometimes specifically commissioned for that purpose.
- 2. The NIHR funds the majority of Cochrane review production in the UK.

NICE, NIHR and WHO have addressed non-financial COI in their policy updates (2018). NIHR is currently updating its COI policy for the whole organization (personal communication, 2018).

The <u>NICE COI Policy</u> defines non-financial interests as follows:

When a person has a non-financial professional or personal benefit, such as increasing or maintaining their professional reputation.

This can include situations where the person:

- Is an advocate for a particular group or is a member of a lobbying or pressure group with an interest in health or social care.
- Holds office or a position of authority in a professional organization such as a royal college, a university, charity, or advocacy group.
- Is actively involved in an ongoing or scheduled trial or research project aimed at determining the effectiveness of a matter under review.
- Has published a clear opinion about the matter under consideration.
- Has authored or co-authored a document submitted as an evidence publication to the relevant NICE advisory committee.

The NETSCC definition of personal non-financial interests includes "honorary contracts, unpaid academic collaborations, memberships, charities, Trustees [and] pressure groups" and states:

- Members must declare any unremunerated involvement with, or membership of, any other body in connection with medical, bio-medical, pharmaceutical, healthcare provision and similar activity, including relevant: (i) appointments at a university or research institute or similar body; (ii) directorships or employment or other connection with companies in any field where the company might benefit from support by the NIHR either as a collaborator or in some other way; (iii) positions of authority in charities and other bodies providing research funding or science or health policy/communication.
- Members are expected not to occupy paid party-political posts, or to hold particularly sensitive or high-profile unpaid roles in a political party, pressure group or similar organization. Any political/pressure group associations should be declared.

The WHO definition of non-financial interests is as follows:

- Personal vs. non-personal (department or institution) nature of the declared interest.
- If non-personal, the position and role of the expert in the department or institution.
- Relationship of the expert's institution with WHO.
- The relevance and specificity of the declared interest in view of the subject matter of the meeting or work to be undertaken.
- The timeliness of the interest. Is it still current i.e. has it occurred within a period of 4 years from the foreseen WHO meeting or activity.
- Whether the interest relates to an expert's immediate family member

- Whether the interest could be attributed to a professional bias reflected repeatedly as part of expert testimony in a regulatory or judicial proceeding or by reason of the expert's office.
- Whether the participation of the expert in the meeting or work provides, or may provide him or her, with clear actual and direct financial or pecuniary benefit or enable him or her to obtain access to a competitor's or potential competitor confidential proprietary information.

Considerations for Cochrane: NICE, NIHR (NETSCC) and WHO all include non-financial interests in their policies.

2.4.3 Policy Governance

The Cochrane Funding Arbiters provide guidance on conflict of interest in the context of Cochrane review production and adjudicate in cases where there is doubt or disagreement about policy breaches. Currently the Funding Arbiters answer to Cochrane's Governing Board but work closely with the Editor in Chief of the Cochrane Library. The term 'Funding Arbiter' is not used in other COI policies and suggests a focus on funding and a commercial policy rather than a conflicts of interest policy. Wellcome use the term "Conflicts manager", while NICE use the title "Conflict of interest reference panel" to describe a body which resolves contentious COI issues (NICE 2018). WHO uses the term "responsible officer", a person who is assisted by the "Office of Compliance, Risk Management and Ethics" to resolve COI problems. JAMS uses an ethics committee to discuss COI issues.

Considerations for Cochrane: The need for clarity about who is responsible for policy governance is cited in the policies of one healthcare research and guideline organization, and one other associated organization. The title 'Funding Arbiter' may need to be reviewed.

2.4.4 Policy Management Processes

Several of the COI polices examined include a description of how conflicts are managed (e.g. BMJ, G-I-N, NICE, PLOS ONE, WHO). NIH and PLOS ONE have online information for members, while the U.S. Preventive Services Task Force (USPSTF) conducts face-to-face discussions with new members, discussing their declarations and using the member's resumé as well as <u>The Open Payments Data Register</u>. International organizations may have additional obstacles in managing disclosures and implementing their policies consistently across jurisdictions, regions and countries. A strong process is one which is comprehensive, aiming to identify and manage conflicts for everyone involved in delivering the main objectives of the organization.

The <u>NICE COI policy</u> states that there must be complete transparency in declarations of interest for all members of every NICE guideline. The project team for each guideline collates the COI statements which are then published as a Corporate Risk Register as part of a Risk Management Strategy (<u>NICE COI policy</u> 2018). This information is available on the NICE website. After discussing declarations with new members, USPSTF chairs grade potential conflicts from Tier 1 to 3. Tier 1 and 2 are not published but Tier 3 is online and includes financial interests over \$1000, being primary investigator on studies in a particular topic, and non-financial interests. In the BMJ policy there is a "Dealing with declarations" section. The WHO uses "COI Assessment – Description of Steps", which includes a "Balancing test" to ensure that the input of an individual does not affect the integrity and independence of the decision-making process.

The <u>PLOS ONE COI policy</u> describes how editors deal with author declarations under "Editorial Actions and Decisions":

- PLOS editors must take all competing interests into account during the review process and ensure that any relevant ones are declared in the published article.
- PLOS editors will not publish commissioned or any other non-research articles if they are aware of a competing interest that, in their judgment, could introduce bias or a reasonable perception of bias.
- PLOS editors do not consult reviewers who have competing interests that, in the editors' judgment, could interfere with unbiased review.

Declaring interests is crucial, but different organizations have different time periods for which interests should be declared (Table 2) ranging from 1 year to 5 years, with the BMJ also requesting information on the next 12 months. The USPSTF has a three-year time span for funding but this does not count for publications and opinion pieces related to the topic; there is no time limit on that.

Table 2: Time Period for Declarations of Interests for different organizations and journals.

Organization	Time period for Declarations of Interest (years)
Bill & Melinda Gates Foundation, NICE, SIGN	1
Cochrane Library	3
The Lancet, BMJ, SGIM, JAMS, NIHR ICJME	3
WHO	4
PLOS ONE	5

Bou-Karroum (2018) highlights the importance of going back to the beginning and not only encouraging authors to declare but ensuring that potential conflicts of interest are correctly managed to minimize bias and ensure research integrity. The reader needs sufficient information to judge for themselves if the conclusions might be biased by the declared interest(s). Khamis (2018) also included "choosing what to disclose" as an important step.

<u>The American College of Physicians</u> has a useful phrase, often used in teaching ethics, "When in doubt, err on the side of disclosure". The WHO applies the concept of a "reasonable person in the street". NICE also use the phrase "reasonable person" in its declaration advice and to determine COI: "There is a conflict of interest when a reasonable person would consider that an individual's ability to apply judgement or act in the work of NICE is, or could be perceived to be, impaired or influenced by one of their interests." <u>PLOS</u> <u>ONE</u> uses the phrase "reasonable perception of bias" to encourage declaration of competing interests.

Rare diseases may be more strongly impacted by a COI policy as there is limited public funding for research and it is pharmaceutical companies that are investing money in clinical trials, with a limited number of people involved in the work (Yarborough 2017). The Australian National Health and Medical Research Council specifically states in its Australian Code for the Responsible Conduct of Research, 2018 policy that: "Situations will arise in which the pool of individuals able to provide a high level of specialist input is relatively small. Therefore, judgements need to be made which balance the benefit of having persons with expertise against the risks of their interests biasing a process."

Considerations for Cochrane: Best practice in COI policy management arises when the policy is widely understood and the process is fully transparent from initial declarations to publication. Process management was covered in the policies of two publishing organizations, two funding organizations, and two healthcare research and guideline organizations.

2.4.4.1 Misconduct

Without honest declarations of interest, research outputs cannot be properly evaluated by readers. Godlee (2009) argues that "we need to make it easy for people to declare their COIs and painful for them if they are found out not to have done so". Similarly, Botkin (2018) argues that there should be repercussions for falsehood when declaring interests, whether or not it was intentional. In this spirit, some organizations include information about how to manage breaches of their policy. For instance, the NICE policy mentions that breaches may occur either accidentally or on purpose and details the process for managing them. The Japanese Association of Medical Sciences describes the management of members who violate the COI policy and bring the organization into disrepute. The ICJME recently updated its recommendations to include wilful non-disclosure of COI declarations (2018) and consider "purposeful failure to disclose conflicts of interest" as a form of misconduct. COPE advises that, when a reader suspects undisclosed conflicts in a published article, in subsequent publications the journal editors should get signed COI statements from all authors and reviewers before publication (COPE 2018).

A transparent policy should make clear to everyone what the consequences are for not declaring conflicts and for making inaccurate declarations. Regular audits and follow-up could be one way of identifying misconduct. A recent New York Times article, *What These Medical Journals Don't Reveal: Top Doctors' Ties to Industry*. (Ornstein and Thomas 2018) argues that for a minority of journals self-reporting and self-policing do not work. A policy could include: mandating full disclosure; ensuring these disclosures are publicly available and searchable online; and, at its most extreme, publishing all violators prominently, banning them from publication for life, and formally notifying all violators' employers and medical boards. Independent assessment of implementation of an organization's COI Policy can assist in identifying problems.

Considerations for Cochrane: Treating failure to disclose conflicts fully was cited in the policies of one editorial publishing organization and one funding organization.

2.4.5 Policy Presentation

Searching for COI policies for various organizations gave helpful insight into how challenging it can be to find such documents. Having a COI policy that is easy to find, downloadable in PDF format and easy to read is important to ensuring that a policy is used. One of the most navigable, concise documents is from <u>Wellcome</u> and includes a header on each page which allows the reader to jump to different sections. The policy also displays its date on the front cover so that the reader knows when it was created or checked and last updated. For Wellcome this is at least every two years. The NICE policy includes a "Date effective from" and also the "Review date". The <u>Bill and Melinda Gates Foundation</u> had this information at the end of its policy. Clearly indicating that a policy is routinely reviewed can give readers confidence. None of the COI organizational policies reviewed here could be described as "continuously evolving documents", a concept proposed by Shanahan et al (2015). This would require users getting into the habit of continuously referring to the policy and not relying on possibly outdated knowledge. However, it would also ensure that user feedback and case law arising from COI disputes could be implemented with immediate effect.

Another useful resource found in several organizations, including NICE, was a "Frequently Asked Questions" document, which may be helpful in addition to the <u>Scenarios</u> information that Cochrane already provides. The NETSCC policy has a register of "persistent potential COI which are predictable" to help users.

The format of the NETSCC document (2017) provides a useful template (Figure 5):

Figure 5: NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC) COI policy structure

- 1. Who is the policy relevant to
- 2. Policy
- 3. Underlying principles
- 4. Direct and indirect conflicts of interest
- 5. Examples of what could constitute financial or commercial conflicts of interest
- 6. Declaring potential conflicts of interest
- 7. Handling potential conflicting interests
- 8. Advisory committees providing strategic advice, broken down by stage
- 9. Purpose of the document
- 10. Purpose of policy
- 11. Scope
- 12. Terminology
- 13. Overall Responsibility

3 Conclusions

This selective policy review highlights common elements in policies across organizations as well as areas of divergence. An organization must consider an approach to declaring interests and managing conflicts that suits its particular needs, bearing in mind that a COI policy is open to scrutiny and the way that an organization deals with this issue may have a significant effect on its reputation. Cochrane does not have the luxury of distancing itself from author declarations. The 'declare and leave it to the reader to decide' approach is not compatible with the aspiration to present the highest quality, most unbiased evidence. In this regard Cochrane is closer to guideline development organizations, but Cochrane Reviews in their raw state are not intended to dictate clinical practice in the way a clinical guideline is. Taking the same approach to COI as a guideline developer, then, is not necessarily ideal. Nevertheless, there are elements of many organizational policies that merit consideration; some confirm where our policy already adheres to good practice and others suggest ways in which we can strengthen the policy.

Despite the lack of empirical evidence about the impact of non-financial conflicts, several of the organizations included in this review ask contributors to declare both financial and non-financial interests. With debates and research about non-financial interests ongoing, Cochrane may wish to take a common-sense approach by covering this type of interest in the new policy but not necessarily treating non-financial interests.

Conflicts of interest range from subtle to self-evident. A clear, plain-English policy that helps Cochrane authors and Review Groups determine what should be declared and what types of conflict represent a barrier to authorship is essential to ensuring that the policy is widely understood and used. Authors should be encouraged or mandated to review their declarations at least annually or when their circumstances change. It is also important that the policy be clear about who is responsible for policy governance and what the consequences of non-compliance might be. Many organizations and journals are seeking to improve processes for declaring and managing potential conflicts and for ensuring that their policies are accessible and transparent. Openness, and willingness to adapt to criticism and changing social and scientific norms, is essential to create a policy that is fit for purpose now and into the future. A well-understood and well-used COI policy helps to ensure the integrity of both individuals and the organization.

4 Bibliography

Adlington K, Godlee F. Disclosure UK: transparency should no longer be an optional extra. *BMJ* 2016;354:i3730.

Bastian H. A reader's guide to conflicts of interest in biomedicine. May 2016. <u>blogs.plos.org/absolutely-maybe/2016/05/31/a-readers-guide-to-conflicts-of-interest-in-biomedicine</u> (accessed 14 January 2019).

Bekelman JE, Li Y, Gross CP. Scope and impact of financial conflicts of interest in biomedical research: a systematic review. *JAMA* 2003;289(4):454-65.

Bero LA. More journals should have conflict of interest policies as strict as Cochrane. November 2018. <u>blogs.bmj.com/bmj/2018/11/12/lisa-bero-more-journals-should-have-conflict-of-interest-policies-as-</u> <u>strict-as-cochrane</u> (accessed 13 November 2018).

Bero L, Oostvogel F, Bacchetti P, Lee K. Factors associated with findings of published trials of drug-drug comparisons: why some statins appear more efficacious than others. *PLoS Medicine* 2007; 4(6):e184.

Bero LA, Grundy Q. Why having a (nonfinancial interest) is not a conflict of interest. *PLOS Biology* 2016;14:e2001221.

Botkin JR. Should failure to disclose significant financial conflicts of interest be considered research misconduct? *JAMA* 2018;320(22):2307-8.

Bou-Karroum L, Hakoum MB, Hammoud MZ, Khamis AM, Al-Gibbawi M, Badour S, et al. Reporting of financial and non-financial conflicts of interest in systematic reviews on health policy and systems research: a cross sectional survey. *International Journal of Health Policy and Management* 2018;7:711-7.

Brignardello-Petersen R, Carrasco-Labra A, Yanine N, Ulloa C, Araya I, Pintor F, et al. Positive association between conflicts of interest and reporting of positive results in randomized clinical trials in dentistry. *Journal of the American Dental Association* 2013;144(10):1165-70

Charity Commission. Conflicts of interest: a guide for charity trustees. May 2014. www.gov.uk/government/publications/conflicts-of-interest-a-guide-for-charity-trustees-cc29.

Committee on Publication Ethics. Conflicts of interest/competing interests. <u>publicationethics.org/competinginterests</u> (accessed on 3 January 2019).

Committee on Publication Ethics. What to do if a reader suspects undisclosed conflict of interest (CoI) in a published article. <u>publicationethics.org/files/COI%20published.pdf</u> (accessed on 3 January 2019).

Committee on Publication Ethics. COPE consultation/guidance document on handling competing interests. <u>publicationethics.org/forum-discussion-topic-comments-please-5</u> (accessed on 3 January 2019).

DeGeorge BR, Holland MC, Drake DB. The impact of conflict of interest in abdominal wall reconstruction with acellular dermal matrix. *Annals of Plastic Surgery* 2015;74(2):242-7.

DeJong C, Aguilar T, Tseng C-W, Lin GA, Boscardin JW, Dudley, RA. Pharmaceutical industry–sponsored meals and physician prescribing patterns for Medicare beneficiaries. *JAMA Internal Medicine* 2016;176:1114-22.

Dunn AG, Coiera E, Mandl KD, Bourgeois FT. Conflict of interest disclosure in biomedical research: a review of current practices, biases, and the role of public registries in improving transparency. *Research Integrity and Peer Review* 2016;1:1.

Guyatt G, Akl EA, Hirsh J, Kearon C, Crowther M, Gutterman D, et al. The vexing problem of guidelines and conflict of interest: a potential solution. *Annals of Internal Medicine* 2010;152:738-41.

Hakoum MB, Anouti S, Al-Gibbawi M, Abou-Jaoude EA, Hasbani DJ, Lopes LC, et al. Reporting of financial and non-financial conflicts of interest by authors of systematic reviews: a methodological survey. *BMJ Open* 2016;6:e011997.

Hakoum MB, Jouni N, Abou-Jaoude EA, Hasbani DJ Abou EA, Lopes JLC, et al. Authors of clinical trials reporting individual and financial conflicts of interest more frequently than institutional and non-financial ones: a methodological survey. *Journal of Clinical Epidemiology* 2017;87:78-86.

Human Rights Law Review. Conflict of interest policy. <u>academic.oup.com/hrlr/pages/Conflict_Of_Interest</u> (accessed 9 January 2019).

Institute of Medicine. Conflict of Interest in Medical Research, Education, and Practice. Washington, DC:National Academies Press; 2009.

Ioannidis JPA, Trepanowski JF. Disclosures in nutrition research: why it is different. JAMA 2018;319:547-8.

Khamis AM, Hakoum B, Bou-Karroum B, Habib JR, Ali A, Guyatt G, et al. Requirements of health policy and services journals for authors to disclose financial and non-financial conflicts of interest: a cross-sectional study. *Health Research Policy and Systems* 2017;15:80.

Khamis AM, Hakoum MB, El-Rayess HM, Haddad S, Akl EA. Verification of conflicts of interest disclosures in health research: a conceptual analysis [abstract]. In: Proceedings of the Cochrane Colloquium, 2018 Sept 16-18; Edinburgh. Poster ID:116.

Kmietowicz Z. Disclosure UK website gives "illusion of transparency," says Goldacre. BMJ 2016;354:i3760.

Lee K. Has the hunt for conflicts of interest gone too far? No. BMJ 2008;336:477.

Lenzer J. When is a point of view a conflict of interest? BMJ 2016;355:i6194.

Lundh A, Lexchin J, Mintzes B, Schroll JB, Bero L. Industry sponsorship and research outcome. *Cochrane Database of Systematic Reviews* 2017;(2):MR000033.

Lundh A. Conflicts of interest in biomedical publishing (2012). Graduate School of The Faculty of Health and Medical Sciences, University of Copenhagen. PhD Dissertation.

Mandrioli D, Kearns CE, Bero LA. Relationship between research outcomes and risk of bias, study sponsorship, and author financial conflicts of interest in reviews of the effects of artificially sweetened beverages on weight outcomes: A systematic review of reviews. *PLoS ONE* 2016; 11(9); e0162198. doi:10.1371/journal.pone.0162198.

McCartney M. Optional disclosure of payments is pointless. *BMJ* 2016;354;i3692.

Norris SL, Burda BU, Holmer HK, Ogden LA, Fu R, Bero L, et al. Author's specialty and conflicts of interest contribute to conflicting guidelines for screening mammography. *Journal of Clinical Epidemiology* 2012;65:725-33.

Ornstein C, Thomas K. What these medical journals don't reveal: top doctors' ties to industry'. New York Times. 8 December 2018. <u>nyti.ms/2G8UXvq</u>

Panagiotou OA, loannidis JP. Primary study authors of significant studies are more likely to believe that a strong association exists in a heterogeneous meta-analysis compared with methodologists. *Journal of Clinical Epidemiology* 2012;65:740-7.

PLOS Medicine Editors. Making sense of non-financial competing interests. PLOS Medicine 2008;5:e199.

Rasmussen K. Collaboration between academics and industry in clinical trials: cross-sectional study of publication and survey of academic authors (2018). Graduate School of Health and Medical Sciences, University of Copenhagen. PhD Dissertation.

Rasmussen K, Schroll J, Gøtzsche PC, Lundh A. Under-reporting of conflicts of interest among trialists: a cross-sectional study. *Journal of the Royal Society of Medicine* 2015;108:101-7.

Robertson J, Moynihan R, Walkom E, Bero L, Henry D. Mandatory disclosure of pharmaceutical industry-funded events for health professionals. *PLOS Medicine* 2009;6:1000128.

Rohwer A, Young T, Wager E, Garner P. Authorship, plagiarism and conflict of interest: views and practices from low/middle-income country health researchers. *BMJ Open* 2017;7:e018467.

Schunemann HJ, Al-Ansary LA, Forland F, Kersten S, Komulainen J, Kopp IB, et al. Guidelines International Network: principles for disclosure of interests and management of conflicts in guidelines. *Annals of Internal Medicine* 2015;163:548-53.

Schwab T. Dietary disclosures: how important are non-financial interests? *BMJ* 2018;361:k1451.

Shanahan DR. A living document: reincarnating the research article. *Trials* 2015;16:151.

Sharma T. Effects of selective serotonin reuptake inhibitors (SSRIs) and serotonin -norepinephrine reuptake inhibitors (SNRIs) on suicidality, violence, and quality of life (2018). Graduate School of The Faculty of Health and Medical Sciences, University of Copenhagen. PhD Dissertation.

Shokraneh F, Adams CE, Clarke M, Amato L, Bastian H, Beller E. Why Cochrane should prioritise sharing data. *BMJ* 2018;362:k3229.

Shawwa K, Kallas R, Koujanian S, Agarwal A, Neumann A, Alexander P et al. Requirements of clinical journals for authors' disclosure of financial and non-financial conflicts of interest: a cross sectional study. *PLOS One* 2016;11:0152301.

Smith R, Blazeby J. Why religious belief should be declared as a competing interest. *BMJ* 2018;361:k1456.

Standards Commission for Scotland. Non-financial interests. www.standardscommissionscotland.org.uk/about-us/who-we-are/notes/non-financial-interests (accessed on 5 November 2018).

Taichman DB. Data sharing statements for clinical trials. *BMJ* 2017;357:j2372.

Wiersma M, Kerridge I, Lipworth W, Rodwin M. Should we try to manage non-financial interests? BMJ 2018;361:k1240.

Wiersma M, Lipworth W. Should scientists declare non-financial conflicts of interest? *Australasian Science* 2019; Jan/Feb. www.australasianscience.com.au/article/issue-janfeb-2019/should-scientists-declare-non-financial-conflicts-interest.html

Wood SF, Podrasky J, McMonagle MA, Raveendran J, Bysshe T, Hogenmiller A, et al. Influence of pharmaceutical marketing on Medicare prescriptions in the District of Columbia. *PLOS One* 2017;12;0186060.

Yarborough M. Conflict of interest challenges. Translational Science of Rare Diseases 2017;2:175-94.

Yeh JS, Franklin JM, Avorn J, Landon J, Kesselheim AS. Association of industry payments to physicians with the prescribing of brand-name statins in Massachusetts. *JAMA Internal Medicine* 2016;176:763-8.

Ziai K, Pigazzi A, Brian R, Smith BR, Nepomuceno H, Carmichael JC, et al. Association of compensation from the surgical and medical device industry to physicians and self-declared Conflict of Interest. *JAMA Surgery* 2018;153(11):997-1002.

Appendix 1

List of organizations

Organization	Country	URL links to COI policy
American College of Physicians	USA	<u>Available online</u>
Association of the Scientific Medical Societies in Germany	Germany	Not publicly available
Bill and Melinda Gates Foundation	USA	<u>Available online</u>
BMJ	UK	<u>Available online</u>
Campbell Collaboration	International	<u>Available online</u>
Canadian Institutes of Health Research	Canada	<u>Available online</u>
Canadian Medical Association Journal	Canada	<u>Available online</u>
Centers for Disease Control and Prevention	USA	<u>Available online</u>
Cochrane	International	<u>Available online</u>
Committee on Publication Ethics	UK	<u>Available online</u>
The European Code of Conduct for Research Integrity	Europe	<u>Available online</u>
Guidelines International Network	International	<u>Available online</u>
Haute Autorité de santé	France	<u>Available online</u>
Research Grants Council	Hong Kong	<u>Available online</u>
University of Hong Kong	Hong Kong	<u>Available online</u>
Institute for Quality and Efficiency in Health Care	Germany	<u>Available online</u>

Organization	Country	URL links to COI policy		
International Committee of Medical Journal Editors	International	<u>Available online</u>		
The Japanese Association of Medical Sciences	Japan	<u>Available online</u>		
The Japanese Society of Internal Medicine	Japan	Not publicly available		
National Health and Medical Research Council	Australia	<u>Available online</u>		
The National Institute for Health and Care Excellence	UK	<u>Available online</u>		
National Institute for Health Research	UK	Not publicly available		
National Institutes of Health	USA	<u>Available online</u>		
PLOS ONE	USA	<u>Available online</u>		
Scottish Intercollegiate Guidelines Network	Scotland	Not publicly available		
Society of General Internal Medicine	USA	<u>Available online</u>		
The Lancet	UK	<u>Available online</u>		
United Nations	USA	<u>Available online</u>		
U.S. Preventive Services Task Force	USA	<u>Available online</u>		
Wellcome	UK	<u>Available online</u>		
World Health Organization	International	<u>Available online</u>		

27

Appendix 2

Glossary of terms and abbreviations

AWMF:	Association of the Scientific Medical Societies in Germany		
COI:	Conflict of Interest		
COPE:	Committee on Publication Ethics		
DOI:	Declarations of Interest		
FDA:	The Food and Drug Administration		
G-I-N:	Guidelines International Network		
GMC:	General Medical Council		
HPSR:	Health Policy and Systems Research		
ICJME:	International Committee of Medical Journal Editors		
IOM:	The Institute of Medicine		
JAMS:	The Japanese Association of Medical Sciences		
NETSCC:	NIHR Evaluation Trials and Studies Coordinating Centre		
NICE:	The National Institute for Health and Care Excellence		
NIH:	National Institutes of Health		
NIHR:	National Institute for Health Research		
SGIM:	Society of General Internal Medicine		
WHO:	World Health Organization		

Appendix 3

Organizational policies supporting issues for Cochrane to consider - Misc.

Organization	Statement of organization's definition of COI	Specify that declarations are published	Sets financial thresholds (amounts above XX should be declared)	Indirect financial interests arising from personal relationships
American College of Physicians	Yes	Yes	Yes	Yes
Association of the Scientific Medical Societies in Germany	Yes	-	-	Yes
Gates Foundation	Yes	Yes	Yes	Yes
ВМЈ	Yes	Yes	-	Yes
Campbell Collaboration	Yes	-	-	Yes
Canadian Institutes of Health Research	Yes	-	-	-
Canadian Medical Association Journal	-	Yes	Yes	-
Centers for Disease Control and Prevention	Yes	-	-	Yes
Charity Commission	Yes	Yes	-	Yes
Chinese Medical Journal	Yes	-	-	Yes
СОРЕ	Yes	Yes		Yes
The University of Edinburgh	Yes	-	Yes	Yes
The European Code of Conduct for Research Integrity	-	-	-	-
Guidelines International Network	Yes	Yes	Yes	-
Research Grants Council	Yes			Yes

Cochrane Conflict of Interest Review 2019	30			
Organization	Statement of organization's definition of COI	Specify that declarations are published	Sets financial thresholds (amounts above XX should be declared)	Indirect financial interests arising from personal relationships
The University of Hong Kong	Yes	-	-	Yes
Institute for Quality and Efficiency in Health Care	Yes	Yes	-	-
International Committee of Medical Journal Editors	Yes	Yes	-	Yes
The Japanese Association of Medical Sciences	Yes	Yes	-	Yes
National Health and Medical Research Council	Yes	-	-	Yes
The National Institute for Health and Care Excellence	Yes	Yes	-	Yes
National Institute for Health Research	Yes	Yes	Yes	Yes
National Institute of Health	Yes	Yes	Yes	Yes
PLOS ONE	Yes	-	-	Yes
Scottish Intercollegiate Guidelines Network	Yes	-	-	Yes
Society of General Internal Medicine	Yes	Yes	-	Yes
The Lancet	Yes	Yes	-	Yes
United Nations	Yes	Yes	Yes	Yes
U.S. Preventive Services Task Force	Yes	Yes	Yes	Yes
Wellcome	Yes	-	-	Yes
World Health Organization	Yes	Yes	-	Yes

31

Organizational policies supporting issues for Cochrane to consider - Non- financial/other interests

Organization	Professional interests	Intellectual interests	Institutional interests	Section/wording in the policy that mentions non- financial/other interests
American College of Physicians	-	-	Yes	Yes
Association of the Scientific Medical Societies in Germany	Yes	Yes	Yes	-
Gates Foundation	Yes	Yes	-	Yes
ВМЈ	Yes	-	-	Yes
Campbell Collaboration	Yes	Yes	-	Yes
Canadian Institutes of Health Research	Yes	-	-	Yes
Canadian Medical Association Journal	Yes	Yes	-	Yes
Centers for Disease Control and Prevention	Yes	Yes	-	Yes
Charity Commission	Yes	-	Yes	Yes
Chinese Medical Journal	Yes	-	Yes	Yes
COPE	Yes			Yes
The University of Edinburgh	Yes	Yes	-	Yes
The European Code of Conduct for Research Integrity	-	-	-	Yes
Guidelines International Network	Yes	Yes	-	Yes
Research Grants Council	Yes			Yes
The University of Hong Kong	Yes	Yes	-	Yes
Institute for Quality and Efficiency in Health Care	-	-	Yes	Yes

Organization	Professional interests	Intellectual interests	Institutional interests	Section/wording in the policy that mentions non- financial/other interests
International Committee of Medical Journal Editors	-	-	Yes	Yes
The Japanese Association of Medical Sciences	Yes	-	Yes	Yes
National Health and Medical Research Council	Yes	Yes	Yes	Yes
The National Institute for Health and Care Excellence	Yes	Yes	-	Yes
National Institute for Health Research	-	Yes	-	-
National Institute of Health	-	-	-	-
PLOS ONE	Yes	Yes	Yes	Yes
Scottish Intercollegiate Guidelines Network	-	-	Yes	Yes
Society of General Internal Medicine	-	-	Yes	Yes
The Lancet	-	Yes	-	Yes
United Nations	-	-	-	-
U.S. Preventive Services Task Force	Yes	Yes	-	Yes
Wellcome	-	Yes	-	Yes
World Health Organization	Yes	Yes	Yes	Yes

32