

Perspectives on '*Conflicts of interest*'

A report of a one-day workshop held by
the Academy of Medical Sciences on 27
November 2015

Disclaimer

This report does not represent a formal Academy of Medical Sciences position on conflicts of interest. Rather this document is a summary of the wide-ranging discussions that took place at the workshop and does not necessarily represent the views of all participants. The report of this meeting will feed into the Academy's workstream on '*How can we all best use evidence to judge the potential benefits and harms of medicines?*'.¹

We would welcome feedback on the report. For further information, please contact Rachel Brown, Policy Officer at the Academy of Medical Sciences (rachel.brown@acmedsci.ac.uk, 020 3176 2184).

We are most grateful to Professor Onora O'Neill CH CBE HonFRS FBA FMedSci for Chairing this workshop, and for all individuals who contributed to the meeting and the report.

All web references were accessed in January/February 2016

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1. Led by Professor Sir John Tooke FMedSci, the workstream also includes workshops on evaluating evidence in health and communicating evidence about medicines. For further information, please see: <http://www.acmedsci.ac.uk/policy/policy-projects/how-can-we-all-best-use-evidence/>

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Executive summary

Actual and perceived conflicts of interest undermine confidence in the generation and interpretation of scientific evidence. The financial relationship between industry and academics has come under particular scrutiny, although conflicts of interest can be financial and non-financial, direct and indirect.

The *'Conflicts of interest'* workshop was held on 27 November 2015 as part of the Academy of Medical Sciences' wider project exploring the question *'How can we all best use evidence to judge the potential benefits and harms of medicines?'*. It brought together representatives from academia, clinical practice, the pharmaceutical industry, other areas of business, the legal sector, patient support organisations, the media, and other interested parties to discuss how sources of funding (or other potential conflicts of interest) might impact on the generation or interpretation of medical evidence, and how conflicts can be effectively managed. The discussions were wide-ranging, and although the meeting was not designed to reach a consensus on all topics, several key themes emerged.

The distinction between interests and conflicts of interest is important. It was widely agreed that **an interest in itself does not always inherently present a conflict** as conflicts are context dependent. For example, whether the funding source for academic research (e.g. industry or government) presents a conflict of interest will depend on the degree of influence that the funder has on the design, analysis, and publication of the research as well as the personal benefit (e.g. financial) derived by the researcher. Public declarations of interests, regularly updated, provide tools for assessing whether a conflict of interest might arise in a specific decision-making situation or during the generation of evidence.

Conflicts of interest are important to recognise as they are one potential source of bias in the medical evidence base. However, **care should be taken not to routinely conflate conflicts of interest with bias**. Conflicts do not inherently lead to bias, and other sources of bias also exist, for example sub-conscious 'cognitive biases'.

Much of the discussion during the workshop centered on the **mechanisms by which both real and perceived conflicts of interest could be managed** in order to safeguard against this potential source of bias.

In decision-making situations, not including individuals with particular interests (e.g. those with industry funding) could remove an important source of expertise, potentially leading to committees and advisory groups lacking sufficient knowledge or experience. It was generally agreed, therefore, that efforts should focus on the management of conflicts of interest rather than on their avoidance. While in some cases it may be necessary to remove a conflicted individual from the decision-making process, in other cases the decision-making processes could accommodate input from individuals declaring a conflict of interest. In this case their input should be subject to scrutiny and group discussion. While the onus is on individuals to identify potential conflicts arising from an interest, which management mechanism is ultimately required should be determined by those responsible for the decision-making process. In any case, **the simple act of declaring an interest should not lead to a false reassurance that any resulting conflict has been managed effectively**; more active steps are necessary.

With respect to the generation of evidence, a couple of participants argued that the impact (and perceived impact) of commercial conflicts of interest on the medical evidence base was so serious that they need to be eliminated completely, for example by preventing direct financial connections between industry and academia. Many were concerned, however, that this could damage what some see to be beneficial outcomes of the relationship between academia and industry, such as the accelerated development of new products that benefit patients. A number of participants felt that an **agreed framework** to define what constitutes a conflict of interest and to provide guidance on their management in the context of academic-industry relationships would be beneficial. This would be similar to those already established in many companies and professional bodies within the wider public sector. Although the precise form this framework could take was not agreed - particularly whether it would be prescriptive or establish high level principles - many participants felt a body such as the Academy of Medical Sciences would be well placed to develop it.

Some participants raised concern that a person's interests (even in cases where any conflicts are appropriately managed) were sometimes being incorrectly used - particularly in the media - as a proxy for bias or as a means by which to undermine the credibility of research. As an example, it was suggested that it would be beneficial, particularly for the public, if the **rationale behind the value of industry-academia collaborations were communicated more effectively**, something that some participants felt has to date been neglected.

This report does not represent a formal Academy of Medical Sciences position on conflicts of interest. Rather this document reflects the wide-ranging discussions that took place at the workshop. The report of this meeting will feed into the Academy's workstream on '*How can we all best use evidence to judge the potential benefits and harms of medicines?*'.²

We would welcome feedback on the report.

References and notes

2. Led by Professor Sir John Tooke FMedSci, the workstream also includes workshops on evaluating evidence in health and communicating evidence about medicines. For further information, please see: <http://www.acmedsci.ac.uk/policy/policy-projects/how-can-we-all-best-use-evidence/>

Introduction

Evidence-based medicine is fundamentally dependent on the availability of high-quality evidence to guide decision-making. Concerns have been expressed that parts of the medical evidence base is biased because of flaws at multiple stages of the evidence generation and analysis pathway, and during the downstream interpretation of such evidence. Although various sources of bias exist, conflicts of interest may represent one factor contributing to this bias.

Many major funders of medical research - including research councils, medical charities, and Government departments such as the Department of Business, Innovation and Skills and the Department of Health - have stressed the importance of closer working between academia and industry in order to accelerate the translation of research to generate patient benefits and greater wealth for the country. The Academy recognises that these relationships will be increasingly important as the process of drug development evolves to limit the time and cost associated with late stage failures in drug development. More precise definition of potential drug targets derived from academically driven discovery science and experimental medicine will be core features of such a strategy.

On the other hand, there are concerns that commercial interests may jeopardise the development of a reliable evidence base on which to base health policy-making and clinical decision-making. Commercial pressures may influence what research is carried out, how it is carried out, whether and how it is disseminated, and the analysis of evidence in decision-making. With closer links between academia and industry, there are concerns that these pressures may also influence those working within the academic sector.

On 27 November 2015, the Academy of Medical Sciences held a one-day workshop on '*Conflicts of interest*' as part of a wider Academy project exploring the question '*How can we all best use evidence to judge the potential benefits and harms of medicines?*'.³ Led by Professor Sir John Tooke FMedSci, this wider project has already hosted a workshop on '*Evaluating evidence in health*' which discussed the strengths and limitations of different forms of evidence and further explored the opportunities to enhance the generation and use of medical evidence, and its communication to wider groups.⁴ The wider project is also organising a meeting on communicating evidence about medicines.⁵ The '*Conflicts of interest*' workshop brought together representatives from academia, clinical practice, the pharmaceutical industry, other areas of business, the legal sector, patient support organisations, the media, and other interested parties to discuss how sources of funding (or other potential conflicts of interest) might impact on the generation or interpretation of medical evidence, and how conflicts can be effectively managed. The discussions held at this meeting will be used to inform the report that is produced as part of the wider '*How can we all best use evidence to judge the potential benefits and harms of medicines?*' workstream. We would welcome feedback on this report as a means to gather further views on this topic.

After an introductory presentation by Baroness Onora O'Neill of Bengarve CH CBE HonFRS FBA FMedSci, Emeritus Professor of Philosophy, University of Cambridge, and Chair of the Equality and Human Rights Commission, the workshop was organised around three panel sessions with short presentations from invited speakers. Each panel discussion was followed by audience discussion. Annex 1 provides details of the workshop agenda and list of attendees, and Annex 2 summarises speakers' presentations. The following is a summary of the main points raised by participants during discussions; they do not necessarily represent the views of the Academy and should not be taken as agreed outputs from the workshop.

References and notes

3. The Academy of Medical Sciences. *How can we all best use evidence to judge the potential benefits and harms of medicines?* <http://www.acmedsci.ac.uk/policy/policy-projects/how-can-we-all-best-use-evidence/>
4. The Academy of Medical Sciences. *Evaluating evidence in health workshop.* <http://www.acmedsci.ac.uk/more/events/evaluating-evidence-in-health/>
5. The Academy of Medical Sciences. *Communicating evidence about medicines workshop.* <http://www.acmedsci.ac.uk/policy/policy-projects/communicating-evidence-workshop/>

Overview: Introductory presentation by Baroness O'Neill

Introducing the workshop, Baroness O'Neill made the clear case for the importance of managing conflicts of interest in public decision-making. Decision-making, she suggested, can bear upon both public goods and individual goods; it is important that individuals do not influence decision-making to favour their own interests over these goods.

Reflecting on the 'Nolan principles', established to guide behaviour in public life, Baroness O'Neill suggested it is reasonable to expect public figures to act in the public interest rather than on the basis of self-interest.⁶ While individuals with public responsibility might be expected to take it upon themselves to act with professionalism and integrity, systems and procedures can also be put in place to encourage and support good practice.

Baroness O'Neill argued that individuals with interests do not inherently have a conflict of interest as these are context dependent. However, the first step in avoiding or mitigating the impact of conflicts of interest is for individuals to identify all their interests, thereby facilitating the identification of those that might present a conflict. Such a 'declaration of interests' should be made public, readily accessible, and regularly kept up to date. There are many possible types of interest, some pecuniary (such as salary or other direct financial support, share holdings, and hospitality) and some not (individuals may, for example, have an interest in an institution, particularly if they hold a governance role).

However, it is not always easy to decide what constitutes an interest. Difficult areas include indirect financial interest (such as financial interests held by a spouse or family member) and levels of hospitality (being bought an occasional coffee probably does not constitute an interest, while a day out at a major sporting event almost certainly does, but many examples may fall between these extremes). It may also be unclear when an interest ceases to exist – individuals may retain an interest even when their formal association has ended, but the exact period may vary considerably from case to case.

Nonetheless, everyone has interests of some kind and it would be a mistake to consider only financial interests when formulating lists of interests. For example, the pressure to publish and other academic pressures on career progression can create interests. Interests may also arise if individuals stand to gain financially from increasing personal visibility (for example, in traditional or social media). Many organisations provide guidelines on what they consider it appropriate to declare. Baroness O'Neill suggested it was generally advisable to err on the side of caution and to declare interests if in any doubt.

Public declarations of interests provide tools for assessing whether a conflict of interest might arise in a specific decision-making situation. However, it is only a first step and because it is relatively easy to achieve, there are dangers that the transparent declaration of an interest alone becomes a proxy for having fulfilled conflict of interest obligations. Instead, when a potential conflict is identified appropriate actions should be taken to manage it.

There is a particular onus on committee chairs or others with responsibility for a decision-making process to be mindful of potential conflicts of interest and to ensure that the appropriate steps are taken to manage them. They have a duty to protect the integrity of the decision-making process. While that may mean excluding conflicted individuals from discussions, it may also mean allowing their input while recognising its potential to be influenced by their interests. Allowing input may be particularly important in situations where decision-making relies on expert knowledge but it has proved difficult to identify experts without any conflicts of interest.

Baroness O'Neill concluded by pointing out that financial conflicts of interest are just one possible factor potentially biasing the health evidence base. In particular, researchers (or others with an interest in a product) may have an emotional attachment that subconsciously influences their thinking or behaviour. Such 'cognitive biases' may simply reflect 'wishful thinking' on the part of a researcher rather than a conscious desire to subvert evidence generation or analysis. However, while acknowledging the undoubted influence of cognitive biases, she suggested that it is challenging for conflict of interest measures to be the main mechanism for minimising all bias in the medical evidence base. Some issues are better dealt with through other mechanisms addressing the methodologies of health evidence generation and evaluation. It is important, she suggested, that managing conflicts of interest is not seen as a way of solving all problems of bias in the health evidence base.

References and notes

6. <https://www.gov.uk/government/publications/the-7-principles-of-public-life>

What constitutes an interest and when do interests present a conflict?

Following the introductory presentation, participants engaged in further discussion about interests and their distinction from conflicts of interest.

There was widespread agreement that this distinction is important, with many reiterating that in many situations an interest does not pose a conflict of interest. There was also support for the public declaration of interests as a first step in the identification of those that may pose a conflict in a particular situation. Declarations of financial interests should detail not only the source of funding, but also the size of the contribution and what the money was used for. Many participants felt that such a process should be practiced more widely, and all parties involved in evidence generation, analysis or dissemination – such as researchers, journalists, commentators, medical journals, and others – should routinely declare their interests. It was however noted that care should be taken to balance complete transparency with the risk of over-disclosure, which could lead to pertinent information being lost among a mass of irrelevant detail or to the normalisation of conflicts of interest within the community. Deciding which interests to declare and which might be considered conflicts requires judgment on the part of the individual; in doing so it may be helpful to consider the perceptions of ‘a reasonable person’.

When are conflicts of interest 'real' and what is the impact?

- Using industry funding as an example, it was noted that whether a particular interest gives rise to a conflict depends in part on the nature of the relationship with industry (for example, whether a researcher has complete freedom to analyse and publish findings), the scale of industry support, and how that support is used (for example, whether it benefits researchers personally, is used to support their research, or is donated to charity).
- Nonetheless, there is published evidence that researchers with industry links are more likely to publish favourable findings on medicinal products.^{7,8} Similarly, one panellist detailed a study on academic researchers' comments in the media during the recent swine flu epidemic which revealed that those with reported conflicts of interests were more likely to make heightened risk assessments and promote the use of antiviral drugs.⁹
- Therefore, conflicts of interest are one factor potentially contributing to bias in the medical evidence base, and can influence all stages of evidence generation and evaluation, including the choice and framing of research questions, the design of experimental studies, the disclosure of results, and the analysis of evidence. Participants were keen, however, to emphasise that conflicts of interest do not inevitably lead to bias: conflicts can be managed and an individual may still be able to maintain objectivity despite having relevant interests.
- In addition to the role of industry in the funding of academic research, one participant raised a concern about industry's attempts to build relationships with influential medical academics ('key opinion leaders') who hold positions of influence and authority.¹⁰
- As well as true conflicts of interest, perceived conflicts of interest can also be damaging, particularly to an organisation's reputation. This may again encourage organisations to adopt a cautious approach to minimise and manage even remote risks of conflicts of interest.

References and notes

7. Perlis RH, *et al.* (2005). *Industry sponsorship and financial conflict of interest in the reporting of clinical trials in psychiatry.* *Am J Psychiatry* **162**(10):1957–60.
8. Wang AT, *et al.* (2010). *Association between industry affiliation and position on cardiovascular risk with rosiglitazone: cross sectional systematic review.* *BMJ* **340**:c1344.
9. Mandeville KL, *et al.* (2014). *Academics and competing interests in H1N1 influenza media reporting.* *J Epidemiol Community Health* **68**(3):197–203.
10. Moynihan R. (2008). *Key opinion leaders: independent experts or drug representatives in disguise?* *BMJ* **336**(7658):1402–3.

Mechanisms to manage and mitigate the impact of conflicts of interest

Following short presentations from invited speakers (see Annex 2), extensive discussion centered on both the avoidance and the management of conflicts of interest in the context of evidence generation and decision-making as means to safeguard against this potential source of bias.

Managing conflicts of interest during evidence generation

- One speaker suggested that conflicts of interest had such insidious effects on the generation of evidence that they needed to be eliminated entirely by removing all direct financial connections between companies and researchers.
- It was suggested that companies could contribute to a central fund which would support independent evaluations of products (e.g. phase III trials) and comparative studies that individual companies would be unlikely to conduct. The Italian Medicines Agency (AIFA) was highlighted as one organisation that had introduced a scheme along these lines (although some queried how sustainable the scheme is).¹¹ Some 5% of the marketing budget of pharmaceutical companies operating in Italy is used to support such studies.
- Another historical example given was an initiative run by the British Thoracic Society beginning in the inter-war years on behalf of the Medical Research Council (MRC), particularly to evaluate treatments for tuberculosis: UK doctors were reluctant to work directly with industry on trials, so the Society acted as an intermediary, deciding which treatments merited further evaluation.
- However, other participants questioned whether it was desirable – or feasible – to eliminate close academia–industry interactions entirely, reiterating that there are mutual benefits to industry and academia working together, and that in the long run patients benefited from more rapid development of medicines.
- Participants felt it would be useful to have a supportive framework in place to provide guidelines on responsibilities and good practice in industry-academia relationships. Such guidelines could provide clarity on best practice for industry-funded research in academia (e.g. independent design of research, full disclosure of results), detail what could be considered a conflict of interest, and advise on how issues relating to conflicts of interests should be dealt with. Some participants felt that such a governance framework should focus on general principles or values, while others suggested a more rules-based framework (including definitions on the precise value at which industry funding could become a conflict) would be valuable.
- It was suggested that a body such as the Academy of Medical Sciences would be well placed to develop such a framework or ‘code of conduct’ to cover interactions between industry, academics, and higher education institutions. Medical journals should also be involved in this process, so that there is clarity regarding the processes that need to be followed in order for journals to consider publication of findings.
- Such guidelines would need to take account of the international nature of medical research. Ideally, the principles adopted and approaches used would be consistent across different countries.¹²
- It was more specifically noted that the publication of contractual arrangements between academia and industry would enhance transparency, encourage the adoption of good practice, and provide reassurance about key principles such as academic freedom to analyse and publish data.

Managing conflicts of interest during decision-making processes

- Excluding individuals with particular interests (e.g. industry funding) from decision-making committees could remove an important source of knowledge and experience from discussions. Excessively robust rules to avoid conflicts of interest could also unwittingly hamper attempts to include the patient voice in discussions, as patient groups often receive charitable industry support.
- There is a similar argument that such rules could mean that the dissemination of evidence, for example through the media, would fall to individuals who lack the relevant expertise.
- Therefore, rather than attempting to avoid conflicts of interest by severing all connections between interested stakeholders, a better approach may be to establish transparent and robust mechanisms to manage potential conflicts of interest should they arise.
- While the first step is the declaration of interests, thereby facilitating the identification of conflicts, the simple act of declaring an interest should not lead to a false reassurance that any resulting conflict has been managed effectively; more active steps are necessary.
- For example, in some cases mechanisms such as leaving the room may be needed to limit the potential impact of conflicts of interest on decision-making processes. It is not always necessary, however, to go to such extents. Other mechanisms exist that support full and open debate, with participants declaring their interests in advance and presenting their perspective for independent scrutiny by others in the decision-making group.
- Examples were given where such mechanisms were used to reach agreement in highly contentious areas (including nuclear waste disposal: Nirex adapted a 'group consensus elicitation methodology' to facilitate discussions and achieve agreement between stakeholders with very different interests).¹³
- Such mechanisms highlight the important role played by the 'process owner', or committee Chair, who has the responsibility to ensure that good conflicts of interest practice is followed in order to ensure a reliable decision is reached.

Conflicts of interest: the need for greater public communication

- Several participants expressed concern that the media in particular use conflicts of interest as a short-hand heuristic to undermine the authority of individuals by implying that their contributions are inevitably unreliable or biased.
- Others described how researchers can be unfairly labelled as having conflicts of interest despite having complete independence to design and carry out industry-funded studies and publish their findings (Box 1).
- It was widely felt that academics face conflicting pressures since the Government, funders, and their institutions promote closer contact with industry, but some commentators and the public subsequently criticise them or devalue their input because they are considered too closely connected to industry. It was noted that this could discourage researchers from contributing to evidence appraisal or public discussions even though they have valuable knowledge and experience.

Box 1: Food industry funding

To what extent does food industry funding of research create conflicts of interest?

The food industry has been accused of wielding excessive influence on policy-making. In early 2015, a series of features in the *BMJ* suggested that industry funding was being used systematically to distort the evidence base and to influence the thinking of academics involved in public policy-making.¹⁴ It was argued that there was a '*network of relationships between key public health experts and the sugar industry*' and that '*these sorts of links create bias... [and] weaken public health efforts to tackle the harmful effects of sugar on the diet*'.

These *BMJ* articles reflect concerns that the food industry has undue influence on policy-making. They imply that any form of industry funding creates conflicts of interest and has the potential to influence the thinking or behaviour of individuals with an advisory role in policy-making.

Some researchers believe that encouraging relationships between academics and industry may help promote a commercial environment in which health-encouraging behaviours can develop. Others argued that there are many ways in which academics can receive funding from industry, and it is debatable whether all of these can be truly considered conflicts of interest. Indeed, in response to such criticism, several scientists involved in academic research part-funded by industrial contributions have pointed out instances where all industry funding had been declared, had been used to support research rather than personal remuneration, represented only a very small proportion of total research funding, and where the researchers had been fully responsible for study design and analysis, and maintained an independent right to publish any data regardless of the findings.¹⁵

- The inappropriate use of conflicts of interest as a proxy for bias or unreliability could also exclude some patient organisations from important forums, or pressure them to decline a potentially important source of income.
- Further still, concern was raised that a disproportionate focus on conflicts of interest has the potential to detract attention from more valid underlying issues around the evidence and its interpretation (Box 2).
- It was noted that this situation may have arisen because the reasoning behind encouraging close ties between industry and academia (i.e. to accelerate medical innovation and translation of research) has not been communicated effectively to the general public. It was felt that those who support such collaboration should take greater responsibility for communicating their reasoned benefits to the media and wider public.
- Being entirely open about interests, and the precise situations in which conflicts of interest arise, may lead to a more nuanced public understanding of what they mean in practice and aid in the proper critical appraisal of evidence. Journalists and commentators should be similarly open about their interests.

Box 2: e-cigarettes evidence appraisal

A recent analysis of evidence relating to e-cigarettes has led some to question how conflicts of interest considerations are being used.

A group of researchers recently undertook a 'comparative harm analysis' of e-cigarettes and conventional nicotine-containing products such as cigarettes, concluding that the former were considerably less harmful than the latter.¹⁶ This analysis was cited prominently in a report from Public Health England, which argued in favour of e-cigarettes as a health-improvement measure.¹⁷

The group included some members with e-cigarette industry connections. However, it used a methodology (multi-criteria decision analysis, MCDA) based on an objective criteria-based framework enabling expert opinion to be discussed and challenged in an open forum.

Nevertheless, the group's work was subject to both a critical *Lancet* editorial and a commentary in the *BMJ*.^{18,19} Both focused heavily on the make-up of the analysis group and possible bias owing to their perceived conflicts of interest, as well as the fact that the project's funders received support from the tobacco industry.

As well as arguing that the MCDA approach is a good way of minimising the impact of conflicts of interest, members of the group have also suggested that the focus on conflicts of interest in the critical commentaries failed to address the substantive issues raised in the original analysis or provide any alternative assessment of the evidence.²⁰

References and notes

11. The Italian Medicines Agency. <http://www.agenziafarmaco.com/en/node/4111>
12. Amongst other reasons, the need for such a framework to be international in nature is in recognition of the finding that UK researchers are highly collaborative and rates of international co-authorship are high. UK Department of Business, Innovation and Skills (BIS). (2013). *International Comparative Performance of the UK Research Base – 2013*. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/263729/bis-13-1297-international-comparative-performance-of-the-UK-research-base-2013.pdf
13. A procedure for data elicitation in support of performance assessments. (Nirex report N/132). 2006. Harwell: United Kingdom Nirex Ltd.
14. Gornall J. (2015). *Sugar: spinning a web of influence*. *BMJ* **350**:h231; h215; h219; h220
15. The Guardian. (2015). *Obesity advisor rejects conflict of interest claim*. <http://www.theguardian.com/society/2015/feb/11/obesity-adviser-rejects-conflict-of-interest-claim>

16. Nutt DJ *et al.* (2014). *Estimating the harms of nicotine-containing products using the MCDA approach*. *Eur Addict Res.* **20**(5):218–25.
17. McNeill A, *et al.* (2015). *E-cigarettes: an evidence update*. London: Public Health England.
18. McKee M, Capewell S. (2015). *Evidence about electronic cigarettes: a foundation built on rock or sand?* *BMJ* **351**:h4863. doi:10.1136/bmj.h4863.
19. Anon. (2015). *E-cigarettes: Public Health England's evidence-based confusion*. *Lancet* **386**(9996): 829.
20. Nutt DJ. (2015). *Evidence about electronic cigarettes: a foundation built on rock or sand? Reply*. *BMJ* **351**:h4863; <http://drugscience.org.uk/blog/2015/08/27/blinded-smoke-why-do-e-cigarettes-provoke-such-irrational-reactions/>

Concluding remarks

The '*Conflicts of interest*' workshop demonstrated that this topic remains an impassioned area of divergent views.

A few participants felt strongly that there are serious, systemic flaws in the processes used to acquire, analyse, and disseminate medical evidence, and that conflicts of interest are a fundamental contributor to such bias. Others reasoned that conflicts of interest are just one source of bias, and it is therefore better to consider them in a more restricted sense and use additional mechanisms to address wider issues relating to the integrity of the medical evidence base.

Regardless, there is clearly a tension between calls for greater engagement between academia and industry on the one hand, and public concern regarding the pervasive impact of conflicts of interest on the other. Some call for complete disengagement to preserve the independence of academia and to eliminate any scope for conflicts of interest to influence evidence generation and analysis; others argue that disengagement would itself be damaging to medical progress.

There was a widespread sense that the public is currently being ill-served by a focus on conflicts of interest that is being exploited to (in many cases inappropriately) undermine individuals without addressing underlying points of substance. While it is undoubtedly important to recognise and manage conflicts of interest, over-zealous interpretation can also be damaging – for example by leading to the exclusion of knowledgeable voices from discussions which in turn can lead to decision-making becoming dependent on groups lacking sufficient knowledge and expertise.

While participants disagreed on the degree to which conflicts of interest can be minimised or eliminated, there was a widespread feeling that a governance framework needs to be developed to establish and promote good practice in industry–academia relationships. Such a document could also support more effective communication with the public about the nature of conflicts of interest and the medical evidence base.

The exploratory discussions held at this '*Conflicts of interest*' workshop will feed into the Academy of Medical Science's wider workstream on '*How can we all best use evidence to judge the potential harms and benefits of medicines?*' and its final report.²¹

References and notes

21. Led by Professor Sir John Tooke FMedSci, the workstream also includes workshops on evaluating evidence in health and communicating evidence about medicines. For further information, please see: <http://www.acmedsci.ac.uk/policy/policy-projects/how-can-we-all-best-use-evidence/>

Annex I Agenda and participants list

Friday 27 November 2015, 09.00 – 17.00

Academy of Medical Sciences, 41 Portland Place, London, W1B 1QH (John Newsom-Davis Council Chamber)

09.00 – 09.30	Registration
Introductory session: What constitutes an interest and when do they present a conflict?	
09.30 – 09.40	Welcome from the Chair Baroness Onora O’Neill CH CBE HonFRS FBA FMedSci , Emeritus Professor of Philosophy, University of Cambridge
09.40 – 10.00	Dealing with interests Baroness Onora O’Neill CH CBE HonFRS FBA FMedSci , Emeritus Professor of Philosophy, University of Cambridge
10.00 – 10.45	Q&A and discussion Chair: Baroness Onora O’Neill CH CBE HonFRS FBA FMedSci , Emeritus Professor of Philosophy, University of Cambridge <ul style="list-style-type: none"> • What constitutes an interest? • When and why should interests be declared? • How to identify when an interest presents a conflict? • What actions should be taken when a conflict is identified?
10.45 – 11.00	Refreshment break
Panel discussion sessions: What actions should be taken when conflicting interests are identified?	
11.00 – 12.30	Panel discussion 1: Interests when funding studies, and generating and analysing findings Chair: Professor Jonathan Montgomery , Chair, Health Research Authority; Chair, Nuffield Council on Bioethics; Professor of Healthcare Law, University College London Panellists: <ul style="list-style-type: none"> • Funding body: Dr Tony Peatfield, Director of Corporate Affairs, Medical Research Council • Industry: Wendy Harrison, Ethics and Compliance Programme Director, Shell • Systematic reviews: Sir Iain Chalmers FMedSci, Co-founder, Cochrane Collaboration; Co-ordinator, James Lind Initiative

12.30 – 13.15	Lunch
13.15 – 14.45	<p>Panel discussion 2: Interests when disseminating findings Chair: Professor Dame Nicky Cullum DBE FMedSci, Professor of Nursing, University of Manchester</p> <p>Panellists:</p> <ul style="list-style-type: none"> • Publishing: Dr Fiona Godlee, Editor in Chief, The BMJ • Researcher: Dr Kate Mandeville, Wellcome Trust Clinical Research Fellow, London School of Hygiene and Tropical Medicine • Media: Fiona Fox OBE, Chief Executive, Science Media Centre • Industry: Dr Marilyn Metcalf, Senior Director, Benefit Risk Evaluation, GlaxoSmithKline
14.45 – 15.00	Refreshments
15.00 – 16.30	<p>Panel discussion 3: Interests when using evidence to inform practice/policy Chair: Baroness Onora O’Neill CH CBE HonFRS FBA FMedSci, Emeritus Professor of Philosophy, University of Cambridge</p> <p>Panellists:</p> <ul style="list-style-type: none"> • Third sector: Tracey Brown, Director Sense About Science • Regulatory sector: Jonathan Mogford, Policy Director, Medicines and Healthcare products Regulatory Agency • Patient group: Jeremy Taylor, Chief Executive, National Voices • Consumer Champion: Nick Ross, President, HealthWatch
16.30 – 17.00	<p>Identification of key questions and uncertainties, and/or common principles, in declaring and managing interests Chair: Baroness Onora O’Neill CH CBE HonFRS FBA FMedSci, Emeritus Professor of Philosophy, University of Cambridge</p>
17.00	Close

- Michael Blastland*, Journalist
- Eleanor Boddington, Senior Legal Counsel, Wellcome Trust
- Tracey Brown, Director, Sense about Science
- Professor Nancy Cartwright FBA[†], Professor of Philosophy, Durham University and University of California
- Sir Iain Chalmers FMedSci, Co-founder, Cochrane Collaboration; Co-ordinator, James Lind Library
- Professor Sir Rory Collins FRS FMedSci, Professor of Medicine and Epidemiology; Head of the Nuffield Department of Population Health, University of Oxford
- Professor Dame Nicky Cullum DBE FMedSci[†], Professor of Nursing, University of Manchester

- Professor David Delpy CBE FRS FEng FMedSci, Professor of Biomedical Optics, University College London; Chairman, Defence Scientific Advisory Council; Chair, UK Quantum Technologies
- Dr Jon Fistein, Head of Clinical Ethics and Data, Medical Research Council
- Phillippa Foster-Back CBE, Director, Institute of Business Ethics
- Fiona Fox OBE, Chief Executive, Science Media Centre
- Dr Fiona Godlee, Editor in Chief, BMJ
- Dr Stephanie Harriman, Medical Editor, BioMed Central
- Wendy Harrison, Ethics and Compliance Programme Director, Shell
- Dr Farah Jameel, General Practitioner; Member of the GP Clinical and Prescribing sub-committee, British Medical Association
- Professor Susan Jebb, Professor of Diet and Population Health, University of Oxford
- James Lawford Davies, Solicitor, Hempsons
- Dr Kate Mandeville, Wellcome Trust Clinical Research Fellow, London School of Hygiene and Tropical Medicine
- Dr Marilyn Metcalf, Senior Director Benefit Risk Evaluation, GlaxoSmithKline
- Jonathan Mogford, Policy Director, Medicines and Healthcare products Regulatory Agency
- Professor Jonathan Montgomery*, Chair, Health Research Authority; Chair, Nuffield Council on Bioethics; Professor of Healthcare Law, University College London
- Dr Jo O’Leary, Head of Innovation and Skills Delivery Unit, Biotechnology and Biological Sciences Research Council
- Baroness Onora O’Neill CH CBE HonFRS FBA FMedSci (Chair)*, Emeritus Professor of Philosophy, University of Cambridge;
- Dr Tony Peatfield, Director of Corporate Affairs, Medical Research Council
- Professor Lawrence Phillips, Emeritus Professor of Decision Sciences, London School of Economics and Political Science
- Professor Mark Philp, Director of Research (History), University of Warwick; Chair, Research Advisory Board to the UK Committee on Standards in Public Life
- Charmaine Roberts, Funding Policy and Governance Manager, Strategy and Research Funding, Cancer Research UK
- Dr Elizabeth Robertson, Director of Research, Breast Cancer Now
- Nick Ross, President, HealthWatch
- Professor Sir Michael Rutter CBE FRS FBA FMedSci*†, Professor of Developmental Psychopathology, King’s College London; Chair of the ‘Methods of evaluating evidence’ Working Group, Academy of Medical Sciences
- Dr Daniel Schiff, Board Member, International Association of Scientific, Technical and Medical Publishers; Vice President and Publisher, Journals, Thieme
- Heather Simmonds, Director, Prescription Medicines Code of Practice Authority
- Derek Stewart OBE, Associate Director for Patient and Public Involvement, National Institute for Health Research Clinical Research Network
- Tony Sumner, Founding Director, Patient Voices
- Dr Ed Sykes, Senior Press Manager and Head of Mental Health and Neuroscience, Science Media Centre; Chair, Stempla
- Jeremy Taylor, Chief Executive, National Voices
- Aileen Thompson, Executive Director of Communications, Association of the British Pharmaceutical Industry
- Dr Matina Tsalavouta, Head of Communications and Public Engagement, Rothamsted Research
- Professor John Uff CBE, Barrister, Keating Chambers
- Dr David Warriner, Clinical Research Fellow, University of Sheffield

Secretariat

- Dr Rachel Brown, Policy Officer, Academy of Medical Sciences
- Dr Claire Cope, Senior Policy Officer, Academy of Medical Sciences

- Elizabeth Gothard, Policy Intern, Academy of Medical Sciences
- Nick Hillier, Director of Communications, Academy of Medical Sciences
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Annex II Summary of panel presentations

Panel 1: Interests when funding studies, and generating and analysing findings

Dr Tony Peatfield, Director of Corporate Affairs, Medical Research Council (MRC), provided a funders' perspective, based on the principles and practices adopted by the MRC (most of which are likely to be shared by other research councils and major funders).

Dr Peatfield identified three stages in the grant review process when conflicts of interest are important. Recently, applicants have begun to be asked if they have pecuniary or other interests in the research they are proposing or its outcomes. Potential reviewers are asked to declare their interests, which are borne in mind when reviewers are selected or their reviews received (it can be difficult to identify reviewers without any relevant interests). Well-established procedures exist for decision-making panel meetings, with conflicted members leaving the room for particular discussions or not being sent paperwork. Panel chairs have an important role to play in ensuring good practice is followed, and all actions are formally recorded.

Dr Peatfield argued that transparency and established procedures are crucial, but are only part of the solution to ensure that conflicts do not bias decision-making; individual judgement is necessary as it is difficult to impose hard and fast rules. To some degree, trust is required as it can be challenging to identify hidden interests.

Wendy Harrison, Ethics and Compliance Programme Director at Shell, provided an industry perspective from a different business sector, Oil and Gas. An important cornerstone of Shell's Ethics and Compliance programme is for staff to avoid both real and perceived conflicts of interest – even the latter may be damaging in terms of a company's reputation and loss of public trust.

Shell is a large global company and has to consider the complexity of both the cultural context in which business is being conducted – accepted practices may vary widely between countries – and the many different types of people engaging with external contractors. It does however apply one Code of Conduct globally.

Although it necessarily deals with complex issues, Shell has aimed for simplicity in its Code of Conduct, with a focus on specific risk factors, how problems can be avoided, and where to seek advice.²² Its Code of Conduct combines a set of values, mandatory rules, and guidance (such as *'don't get involved in situations where the average person may question your objectivity* and *'don't make decisions based on personal considerations'*) with a supportive framework that encourages staff to identify potential interests (including a conflicts of interest register) and to raise them with their manager when appropriate. A manager can decide how to handle the situation or escalate and seek advice from compliance officers. Although hard and fast rules are again difficult to define, specific guidance and financial thresholds are provided in areas such as corporate hospitality.

However, given there are many grey areas, the general principles and supportive framework for identifying and managing conflicts of interest is important. She suggested that a similar framework might be useful in the medical sciences.

Sir Iain Chalmers FMedSci, Co-founder of the Cochrane Collaboration and Coordinator of the James Lind Initiative, emphasised the importance of the reliability of the evidence generated by medical research, and the potential for patients to be harmed because of biases, perceived or real, in the evidence base. The ultimate goal of eliminating these biases is better health.

He argued that biases have been introduced within medical academia because of systemic flaws in the way that evidence is generated and evaluated. He felt that this issue has not received the attention it deserves, and commented that many, including the Academy of Medical Sciences, have long been too accepting of its existence. He suggested that conflicts of interest were one source of such bias and detailed there is a large body of evidence showing that papers from authors with industry funding tend to publish more favourable assessments of commercial products.

As steps in the right direction, Sir Iain identified a workshop organised by the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) on biased reporting of animal research, and a recent report from the Academy on reproducibility and reliability of biomedical research, an outcome of a symposium organised in partnership with the MRC, Biotechnology and Biological Sciences Research Council (BBSRC) and the Wellcome Trust and led by Professor Dorothy Bishop FRS FBA FMedSci.^{23,24} Nevertheless, he maintained his argument that much more needs to be done, especially to tackle conflicts of interest in senior levels of medical academia.

Panel 2: Interests when disseminating findings

Dr Fiona Godlee, Editor in Chief of the *BMJ*, emphasised the importance of an unbiased evidence base open to independent scrutiny, and suggested that we are some way from achieving these objectives. She argued that financial conflicts of interest were distorting all stages of evidence generation and analysis, including the framing of research questions, the design of research, whether or not findings were published, and access to data.

Dr Godlee highlighted a 2009 report from the US Institute of Medicine, *Conflict of Interest in Medical Research, Education, and Practice*, which argued that researchers should not undertake research in which they had a financial interest.²⁵ The *BMJ* has a policy of not publishing studies funded by the tobacco industry, is likely to introduce a similar policy for research funded by the food and drink industry, and is considering how to handle studies supported by the pharmaceutical and medical device industry. She also argued that research conducted by researchers in academia should be subject to the same scrutiny and challenge as that carried out by industry-based scientists.

Dr Godlee also argued that conflicts of interest also apply to authors of commentary and review articles, and authors had a responsibility to declare such interests. The *BMJ* has gone a step further and instigated a 'zero tolerance' policy to conflicts of interest for authors of its clinical educational articles, refusing to publish such articles from authors with a relevant financial conflict of interest.

In terms of possible solutions, she suggested that pharmaceutical companies should not be allowed to directly evaluate their own products. Instead they could contribute to a central fund that would support independent research on their products. A small-scale initiative along these lines has been established by the Italian Medicines Agency (AIFA).²⁶

Dr Kate Mandeville, Wellcome Trust Clinical Research Fellow at the London School of Hygiene and Tropical Medicine, described her studies identifying a correlation between researchers' conflicts of interest and the viewpoints expressed in the media about the recent UK swine flu epidemic and use of antiviral drugs.

Dr Mandeville and colleagues examined newspaper coverage of the swine flu epidemic and analysed the interests of all academics quoted. The studies revealed that academics were widely called upon to comment – they were the most common voice after ministers of health – but those with industry interests were significantly more likely to stress high-impact pandemic scenarios and to promote the use of antiviral drugs.²⁷

Dr Mandeville suggested that academics are seen as trusted and independent sources of information, but public trust could be compromised if conflicts of interest are not declared and could be perceived to be influencing their thinking. She suggested that scientists should be open in declaring their interests and journalists should seek to identify whether any conflicts exist.

Fiona Fox OBE, Chief Executive of the Science Media Centre, argued that the malicious misuse of conflicts of interest were beginning to discourage scientists from engaging with the public through the mainstream media, and that they were being used as a tool to undermine public confidence in scientists.

She emphasised that some of the media exposure of conflicts of interest have been truly revelatory and in the public interest, changing the way scientists behave in a positive way. However, she suggested that an unfortunate situation was developing in which any link with industry was automatically seen as evidence of bias, rendering viewpoints of some of the best scientists as unreliable. This could have damaging consequences on the quality of public debate, with potential consequences for public health. Furthermore, commentators dismissing input as 'tainted' on the basis of conflicts of interest may themselves have undeclared conflicts of interests, such as membership of single issue campaign groups. The upshot, she argued, was that knowledgeable experts were sometimes being unfairly criticised for having industry connections, even when there is no evidence these connections affected their scientific findings or advice. Meanwhile, less expert opinion from potentially conflicted commentators was being presented by some sections of the media as more credible and subjected to less rigorous scrutiny. As an example, she explained that if the public place greater trust in celebrity campaigners (despite their good intentions) than senior academics with industry connections, this could lead to poor decision-making.

To address this issue, the Science Media Centre is promoting a culture of openness. Every scientist who issues a comment declares their conflicts of interest, and material provided at press briefings provides a full disclosure of relevant speakers' interests. The Science Media Centre also encourages journalists to be skeptical and questioning, and challenges weak associations about links to industry. Finally, she argued that, although academics were being encouraged to work with industry, the rationale for this policy has not been communicated well to journalists or the public, and needs to be communicated more effectively.

Dr Marilyn Metcalf, Senior Director of Benefit Risk Evaluation at GlaxoSmithKline (GSK), provided a perspective from the pharmaceutical industry. She suggested that biases were intrinsic to everyone – they are simply a fact of human nature. Standards and processes applicable to all interested parties can be put in place to minimise the risk that these biases influence decision-making.

GSK, she suggested, had taken steps to promote robust processes of evidence generation and analysis. It is a supporter of the AllTrials initiative which has called for full disclosure of all clinical trials and publication of clinical trial data, and has developed a platform to provide bona fide researchers with access to GSK clinical trial data (with due regard to participants' privacy rights).^{28,29} It is also actively conducting collaborative research in pre-competitive spaces and continues to engage with patients, for example to identify trial endpoints that matter to patients.

Panel 3: Interests when using evidence to inform practice/policy

Tracey Brown, Director of Sense About Science, suggested that the current focus on conflicts of interest is doing the public a disservice. She argued that the public is, in many areas, apparently comfortable with the idea that industry pays for research and development of new products (and would be unlikely to favour increased taxes or a reduction in other public spending to replace this with public funding).

She also summarised a range of questions that members of the public typically have about new scientific developments, such as *'should we worry?'*, *'what do scientists actually know?'*, *'do all scientists agree?'*, and *'is it a proper study and how can I tell?'* She suggested that the focus on conflicts of interest is not addressing these questions. Indeed, it is proving a distraction and not helping the public get to grips with the reliability of research findings or cases of actual, rather than alleged, bias. Furthermore, there is a risk of 'false reassurance' if a lack of conflicts of interest was seen as a proxy for trustworthiness.

She argued that there is a need for more engagement with the public about what is gained by academia–industry partnerships and the nature of the conflicts of interest that might thereby arise. Strong institutional leadership is needed to support researchers who are increasingly expected to work with industry but can then find themselves subject to public criticism. This should include specifying the ideal contract for protecting research from funder interests. Currently, she suggested, there is huge variation in practice between institutions. Standard guidelines would encourage the spread of good practice and enable researchers and institutions to demonstrate how their work sits within an approved governance framework. The public would then be able to question whether such standards were in operation and move on to issues of substance about the value of the research itself.

Jonathan Mogford, Policy Director at the Medicines and Healthcare products Regulatory Agency (MHRA), discussed the implications of conflicts of interest for regulatory agencies. Conflicts of interest, he suggested, form part of a wider set of governance questions and also need to be seen in an international context.

Decision-making in regulatory agencies relies heavily on scientific advice from expert committees. Selection processes for membership of expert committees need to be mindful of the potential risks

posed by conflicts of interest but it is also important that committees have the expertise to make truly informed decisions.

Regulatory agencies are now typically drawing on a wider set of resources to inform decision-making, including 'real world' data, raising new conflicts of interest issues. However, he also argued that it is important that conflicts of interest policies and procedures do not only have a negative or excluding function, and that enabling mechanisms also need to be put in place to ensure appropriate input into decision-making. He also noted that it is essential that there is professional and public confidence in regulatory processes, emphasising the importance of the integrity of the evidence base used to inform decision-making and of transparency in decision-making procedures.

Mr Mogford suggested that transparency and clear practical guidance were required to manage conflicts of interest. Importantly, however, these provided a tool to support good governance, and there were limits to what could be achieved even by careful management of conflicts of interest. There is also a risk that over-zealous application of conflicts of interest could be counterproductive, in terms of eliminating input from experts whose knowledge would benefit the process. Furthermore, he suggested, conflicts of interest policies would not provide a mechanism to counter deliberate acts of subterfuge or law-breaking.

Jeremy Taylor, Chief Executive of National Voices, provided a patient group perspective. His organisation has worked with the Association of the British Pharmaceutical Industry (ABPI) to develop a set of guidelines for charities working with industry. A key principle of these guidelines is that it can be appropriate for charities to collaborate with industry and receive industry funding, but they need to be transparent, exercise caution and consider any possible implications for their independence and reputation.

Mr Taylor noted that NHS England's Patient and Public Voice Advisory Group, which feeds into specialised commissioning policy, had been asking members to declare potential conflicts of interest, casting its net very widely (for example, to include interests of family members and friends). He suggested that there was an important distinction between declaring and managing conflicts of interest on the one hand, and seeking to eliminate them on the other. A focus on the latter risks excluding individuals or organisations that could make a useful contribution to decision-making.

More generally, he pointed out that companies and patients affected by a condition naturally have a shared interest in developing new treatments, and in ensuring these treatments are implemented. At what point, he asked, does this natural alignment of interests become a conflict of interests?

Mr Taylor also noted that the absence of conflicts of interest does not automatically mean an individual is unbiased. People might for example have strong views either in favor of or against medical models of care and pharmacological approaches, based on their own values, experience or other personal factors.

Nick Ross, Honorary President of HealthWatch, argued that subconscious cognitive biases pose a significant threat to the reliability of the scientific evidence base for medicines. He suggested that many individuals have a considerable emotional investment in their work, and naturally hope that their efforts will have practical impact. These perfectly natural desires may subconsciously

influence their thinking – they may genuinely believe they are acting in the public interest or interpreting evidence impartially.

To guard against these natural tendencies, it is important that mechanisms exist to minimise sources of bias in medical evidence. Industry needs to acknowledge the importance of methodologies such as formalised protocols, full data release, and other mechanisms that support impartial assessment of an unbiased evidence base. He also argued that it would be beneficial for individuals and organisations to publish details of the measures they have taken to minimise and manage conflicts of interest.

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