'*Conflicts of interest*' workshop

This briefing document provides the background to, and purpose of, the Academy's '*Conflicts of interest*' workshop that will be taking place on Friday 27 November 2015. It has been informed by the responses to our call for written evidence, which is still open for further input (please see www.acmedsci.ac.uk/call-for-evidence for further information). It also details relevant documents pertaining to the management of conflicts of interest and fictional scenarios, which we hope will stimulate discussion during the meeting. **We would be particularly grateful if you could consider these documents and scenarios prior to the workshop to ensure productive and stimulating discussions on the day.**

Background

Over the past few years, questions have been raised in both the general and scientific media about the evidence underlying decisions about treatment options (for example the use of statins and Tamiflu). The validity of different ways of collecting and analysing evidence has been part of this debate. At the same time, broader discussion of issues such as overmedicalisation (or the reliance on prescribing drugs over lifestyle changes) and conflicts of interest in the way that evidence collection is funded and/or analysed has led to wider questions surrounding trust in academic researchers, clinicians, the media and the pharmaceutical industry. The Academy is therefore undertaking a project to examine '*How society uses evidence to judge the risks and benefits of medicines*' (please visit our website for further details: www.acmedsci.ac.uk/evidence-for-medicines). This '*Conflicts of interest*' workshop is one of three sub-projects that will inform the overall workstream.

As part of this project we issued a call for written evidence, which asked the following questions related to this workshop:

- How should conflicts of interest be addressed?
- How important is industry funding in the generation and analysis of evidence?
- What are the other potential sources of conflicts of interest, other than industry sponsorship?

The responses revealed that, although industry funding calls impartiality into question and is a commonly cited source of conflict of interest, it is widely believed that collaboration with industry can be beneficial to all parties involved. For example, industry funding and collaboration is thought to increase the innovative potential of research and its capacity: the involvement of pharmaceutical companies supports the funding of trials of a sufficient size and scope to provide robust conclusions, which would be too expensive to conduct if supported only by the public sector. Reponses also highlighted that some aspects of research may be impossible without input from industry, and that the evidence base around medicines would be considerably smaller if research were restricted to organisations without a vested interest.

The written evidence also highlighted that industry is not the sole source of conflicts of interest. Researchers themselves are not devoid of conflicts, regardless of any associations with industry, with factors such as the pressure to publish and financial incentives from non-industrial funders to work in specific areas of research also playing a role. Institutional priorities, for example

universities' focus on maximising REF scores, may also influence the research that academics choose to pursue and publish. Similarly, academic journals can contribute to conflicts of interest by favouring manuscripts that present positive findings and creating publication bias. GPs may experience conflicts of interest arising from: financial incentives, which may encourage inappropriate prescribing practices; income generated by publishing books and articles that take a controversial stance; and payments received for acting as an expert witness in legal cases.

Broad strategies for conflict management outlined in the written evidence ranged from calls for transparency in disclosing conflicts of interest, to insisting on complete independence (for example by excluding conflicted individuals from panels and requiring that industry outsources aspects of its research). It was noted that all proposed management strategies may need to be underpinned by legal reinforcement to ensure they are implemented consistently.

With regards to publishing, management strategies included encouraging the wider dissemination of negative data and replication studies. It was suggested that compulsory trial registration, and the publication of protocols before a trial begins, would increase accountability to publish the final results in their entirety. Central repositories for clinical trial data, accessible to researchers, are being developed.[1,2]

It was also suggested that conflicting interests in general practice could be alleviated by replacing financial incentives for doctors to prescribe certain types of medicines with an incentive for shared doctor-patient decision-making.[3]

Purpose

The purpose of this workshop is to further explore this complex topic by bringing together experts from academia, industry, the media, journals, patient groups, and the wider regulatory and healthcare sectors to:

- Consider what interests impact on the validity (or perception of the validity) of evidence about medicines and decisions about their use.
- Understand how these interests might be identified, communicated and managed.
- Identify key questions, uncertainties and/or common principles in declaring and managing interests.

During the day, we will use panel discussions to explore what constitutes an interest and when this might present a conflict, before considering how interests can be best managed when: funding research, and generating and analysing data; disseminating findings; and using evidence to inform policy and practice. We are keen to consider the **broad spectrum of sources of interests**, including, but not limited to, the source of funding. The outputs from this workshop will feed into the Academy's workstream on '*How does society use evidence to judge the risks and benefits of medicines?*'.

[1] https://clinicalstudydatarequest.com/Default.aspx
[2] https://medicine.yale.edu/core/projects/yodap/
[3] The Quality and Outcomes Framework (QOF) has been cited as an example of a financial incentive for doctors to prescribe certain types of medicines. It is a voluntary incentive scheme for GP practices in the UK, to which many practices subscribe, and rewards contractors '*for the provision of quality care*'. It contains groups of indicators, against which practices score points according to their level of achievement: the higher the score, the higher the financial reward for the practice. For more information, please see: http://www.nice.org.uk/standards-and-indicators

Elements to consider ahead of the meeting

Literature on conflicts of interest

The following documents are particularly relevant to this workshop, and you may wish to familiarise yourself with their content ahead of the meeting:

- The National Audit Office's guidance on '*Conflicts of interests*' (attached separately) [4]
- The Nolan principles (attached separately) [5]
- The Universal Ethical Code for Scientists (attached separately) [6]
- Two published analyses demonstrating an element of bias in trials where authors declared a financial conflict of interest [7,8]
- The US Institute of Medicine's report on '*Conflict of Interest in Medical Research, Education, and Practice*' [9]
- The House of Commons Health Committee report on the '*Influence of the Pharmaceutical Industry*' [10]
- A Times Higher Education article entitled '*Is industry funding undermining trust in science?'*, which includes a section on the psychology of indebtedness [11]
- Article 26 of the World Medical Association Declaration of Helsinki:
  'In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information.

  After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed.

  All medical research subjects should be given the option of being informed about the general outcome and results of the study.'

If you have trouble accessing any of these documents, please contact Rachel Brown (Rachel.Brown@acmedsci.ac.uk; 020 3176 2184) who will be able to assist.

---

[4] https://www.nao.org.uk/wp-content/uploads/2015/01/Conflicts-of-interest.pdf
[5] https://www.gov.uk/government/publications/the-7-principles-of-public-life
[6] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/283157/universal-ethical-code-scientists.pdf
[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**, 1957-1960
[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] http://www.ncbi.nlm.nih.gov/books/NBK22942/
[10] http://www.publications.parliament.uk/pa/cm200405/cmselect/cmhealth/42/42.pdf
[11] https://www.timeshighereducation.com/features/is-industry-funding-undermining-trust-in-science

Scenarios

In preparation for the meeting, we would also be grateful if you could consider the scenarios and related questions (attached in the Annex), which have been designed to stimulate discussion and debate during the meeting.

The Academy of Medical Sciences

The Academy of Medical Sciences has a strategic aim to enhance links between academia, industry and the healthcare sector.[12] We believe that industry has been at the heart of establishing many breakthroughs in pharmacological therapy, and plays a major role in generating evidence (for example through clinical trials) by increasingly partnering with academia.

As the Academy does not benefit from a permanent endowment or significant sources of unrestricted income, we must seek external funding for the majority of our activities. A large part of our work is funded by voluntary donations that augment funds we receive from a grant-in-aid from the Department of Health and the Department for Business, Innovation & Skills, and subscriptions from our Fellowship. The Academy also receives funding from the pharmaceutical industry, which contributed less than 1% of our total funding in 2014/15.[13]

The conduct and scope of our policy projects, such as our workstream on '*How does society use evidence to judge the risks and benefits of medicines?*' and its sub-projects, is decided by the Academy. This includes deciding the Terms of Reference and Working Group members in consultation with our Council. The Fellows on our Council, including the Officers of the Academy, provide robust governance of the process to ensure that our outputs are thorough and considered. Our major policy reports are peer reviewed by a committee, chaired by a Fellow, before they are submitted for approval by Council. Funders do not approve the conclusions and recommendations and are not sent a draft of the report for approval.

[12] http://www.acmedsci.ac.uk/about/objectives/

[13] Most of the industry funding that the Academy receives is from organisations that make an annual donation to the FORUM, which is a major component of the Academy's work to deliver its strategic objective of 'linking academia, industry and the NHS'. For further information, please visit: http://www.acmedsci.ac.uk/about/how-we-are-funded/.

Annex: Scenarios for '*Conflicts of interest*' workshop

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

Scenario 1: Principal Investigator A holds equity in pharmaceutical company B, from which he has applied for funding for his academic project.

Questions to consider are:

- Does Principal Investigator A have an interest?
- In what contexts should this interest be declared (e.g. when applying for funding, when publishing the research, etc.)? How can the declaration of such interests be encouraged?
- If a conflict of interest has occurred, how should it be managed and at what stage?
- Is the situation changed if Principal Investigator A provides unpaid advice to pharmaceutical company B but does not hold shares (e.g. so will not financially benefit from the company)?
- Is the situation changed if Principal Investigator A used to hold equity (or provide advice) to pharmaceutical company B, but no longer does so?
- Is the situation changed if Principal Investigator A has no involvement with pharmaceutical company B, but his wife works for the company?
- Can it be envisioned that the management strategies designed to mitigate these interests instead create a different conflict of interest? (e.g. would the declaration of an interest allow Principal Investigator A to feel 'morally licensed' to act immorally because he has declared his interests).

Scenario 2: Reviewer C sits on a research council funding committee, and has been asked to review a submission from applicant D, who is a current collaborator.

Questions to consider are:

- Does Reviewer C have an interest, and when should it be declared? How can the declaration of such interests be encouraged?
- If a conflict of interest has occurred, how should it be managed?
- Can it be envisioned that the management strategies designed to mitigate these interests instead create a different conflict of interest (e.g. would blinding of the reviewers to the applicants (and vice versa) help, or simply encourage people to keep interests that become apparent during the review process undeclared as they cannot be sure that there is a conflict)?
- Is the situation changed if Reviewer C previously collaborated with applicant D, but no longer does?
- Is the situation changed if Reviewer C works at the same institution as applicant D, but does not work directly on the same topic?
- Is the situation changed if Reviewer C knows applicant D in a personal rather than professional capacity?

Scenario 3: Reviewer E sits on a research council funding committee, and holds equity in a spin-off company owned by applicant F. The research project of applicant F is unrelated to the company, and will not be used to develop the company in any way.

Questions to consider are:

- Does Reviewer E have an interest, and when should it be declared? How can the declaration of such interests be encouraged?
- If a conflict of interest has occurred, how should it be managed?

Scenario 4: Researcher G has secured funding from pharmaceutical company H to research a disease for which pharmaceutical company H develops treatments. Pharmaceutical company H will allow researcher G full control on the data collection, analysis, and dissemination of the evidence.

Questions to consider are:

- Does Researcher G have an interest, and when should it be declared?
- If a conflict of interest has occurred, how should it be managed?
- How is the situation, and its management, changed if pharmaceutical company H imposes some guidelines on the data collection, analysis, or dissemination of the evidence?

Scenario 5: Researcher I is performing a systematic review on publications that focus on a currently controversial topic. Researcher I does not have any interests to declare. However, some of the authors of the papers (s)he will include in the review have declared interests, and there are others which (s)he now knows to have been written by authors who, at the time of writing, had undeclared conflicts of interest.

Questions to consider are:

- How should the interests declared in papers included in systematic reviews be managed?

Scenario 6: Researcher J has spent three years researching a particular topic which has led to the creation of a large database of raw data. On investigating his/her initial hypothesis, the results are unequivocal and (s)he does not consider it to be worthy of publication. However, in order to secure another grant, (s)he feels it necessary to publish a set of results emanating from the data set. On reviewing the data a second time, (s)he finds evidence to support a hypothesis that was not developed before the generation and analysis of the data.

Questions to consider are:

- Does Researcher J have an interest, and when should it be declared?
- If a conflict of interest has occurred, how should it be managed? How can the discussion of individual cognitive, financial, and career interests be encouraged and mitigated? Are they as important to the validity of evidence as large organisational conflicts of interest (i.e. the source of funding?).

Scenario 7: Researcher K works on a disease from which a close friend suffers. Researcher K has received funding for their work from a small medical charity that also performs a patient advocacy role.

Questions to consider are:

- Does Researcher K have an interest, and when should it be declared?
- If a conflict of interest has occurred, how should it be managed? How can the discussion of individual moral interests be encouraged and mitigated? Are they as important to the validity of evidence as large organisational conflicts of interest (i.e. the source of funding)?

Panel discussion 2: Interests when disseminating findings

Scenario 1: Peer Reviewer A has been asked to review a manuscript submission from author B, who is a current collaborator.

Questions to consider are:

- Does Reviewer A have an interest, and when should it be declared? How can the declaration of such interests be encouraged?
- If a conflict of interest has occurred, how should it be managed?
- Can it be envisioned that the management strategies designed to mitigate these interests instead create a different conflict of interest (e.g. would blinding of the reviewers to the applicants (and vice versa) help, or simply encourage people to keep interests that become apparent during the review process as they cannot be sure that there might be a conflict)?
- Is the situation changed if Reviewer A previously collaborated with author B, but no longer does so?
- Is the situation changed if Reviewer A works at the same institution as author B, but does not work directly on the same topic?
- Is the situation changed if Reviewer A knows author B in a personal rather than professional capacity?

Scenario 2: Principal Investigator C's work shows that pharmaceutical D is beneficial for disease E, although it is an area of contention and other work has disputed his findings. Principal Investigator C has been asked to speak to the media about the current, and general, state of research into disease E.

Questions to consider are:

- Does Principal Investigator C have an interest, and when should it be declared?
- If a conflict of interest has occurred, how should it be managed?
- Is there a responsibility for the media to further investigate interests, and present a balanced view?

Scenario 3: Researcher F is funded by a research council to work on disease G. (S)he volunteers in his/her spare time for a charity that supports patients with disease G, and they have asked her to speak about her project at a patient engagement event.

Questions to consider are:

- Does Researcher F have an interest, and when should it be declared?
- If a conflict of interest has occurred, how should it be managed?
- Does the situation change if Researcher F is funded by the charity who has asked her to speak?
- Does the situation change if Researcher F is funded by a pharmaceutical company who is developing treatments for disease G?

Scenario 4: Principal Investigator H has had a publication detailing some basic, cutting edge research accepted. The university press office would like to draft a press release, and are keen to emphasise the potential implications of Researcher H's work for future treatments, even though this would require decades of further research. It is thought that by doing so, the university will attract more prestige and more funding from a wider range of funders. Increased publicity for Principal Investigator H may also be beneficial for attracting further funding and researchers to his/her lab.

Questions to consider are:

- Does Principal Investigator H have an interest, and when should it be declared?

- Does the press office have an interest, and when should it be declared?
- If a conflict of interest has occurred, how should it be managed?

Scenario 5: Researcher I has published a paper showing that a certain activity increases a person's absolute risk of disease to 0.1%. A mainstream paper would like to cover the story, but conscious that they need to attract readers, would prefer to cover the paper by stating that the activity increases a person's relative risk of disease by 20%.

Questions to consider are:

- Does either party have an interest, and if so, how should they be declared and managed?
- How can opposing interests (and potential conflicts of interest) be managed to the satisfaction of both parties?

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

Scenario 1: Researcher A is an expert in disease area B and works on developing a drug that may be beneficial in the treatment of this disease. (S)he also sits on a regulatory advisory board for treatments in this area.

Questions to consider are:

- Does Researcher A have an interest, and when should it be declared?
- If a conflict of interest has occurred, how should it be managed?
- Should (s)he be allowed to provide expert opinion? Would this situation change if (s)he has industry funding?

Scenario 2: General Practitioner C sits on a Clinical Commissioning Group (CCG) governing body, and makes commissioning decisions about services (s)he provides within their practice.

Questions to consider are:

- Does General Practitioner C have an interest, and when should it be declared?
- If a conflict of interest has occurred, how should it be managed?

Scenario 3: A patient group, which receives funding from pharmaceutical company D, is lobbying for the adoption and use of medicine E produced by pharmaceutical company F.

Questions to consider are:

- If the evidence base of the medicine is well founded, has been reviewed by experts, and looks compelling does the pharmaceutical funding constitute a conflict of interest?
- How should it be managed?

Scenario 4: General Practitioner G has accepted a travel grant from pharmaceutical company H to attend their conference about the management of a common disease I, of which many patients seen by General Practitioner G suffer from.

Questions to consider are:

- When prescribing drugs for disease I, does General Practitioner G have an interest?
- If a conflict of interest has occurred, how should it be managed?
- Is the situation exacerbated or changed if the management of disease I falls under the Quality and Outcomes Framework (QOF)?