Are self-regulation and declaration of conflict of interest still the benchmark for relationships between physicians and industry?

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ABSTRACT

- Potential conflicts of interest do not imply wrongdoing, but can create bias, distort decision making, and create a perception that practitioners are being "bought "or "bribed" by industry.
- Transparency alone may not be sufficient to erase the doubts created when authors of clinical practice guidelines or editorials declare potential conflicts of interest. Can the subconscious obligation for reciprocation that exists when gifts are offered and accepted be fully negated?
- Analyses of published clinical cancer research studies have found a positive association between pharmaceutical industry sponsorship and reporting of positive outcomes, manipulation of clinical trials, and hiding of "preliminary data sets". More problematic is the issue of clinical researchers leaking preliminary results to the investment industry.
- Influential literature reviews and treatment guidelines have been associated with widespread declarations of conflict of interest.
- Some potential solutions are: regulating pharmaceutical companies to declare all gifts to clinicians, or ban such gifts; for clinicians to carefully declare potential conflicts of interest or to provide pro bono advice without accepting industry sponsorship; and for all gifts and payments from industry to academic physicians to be coordinated by an independent review committee.
- Journals should only allow reviews, editorials, guidelines and opinion pieces to be written by those without significant conflicts of interest.

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In an editorial in 2001, the Editor of the *Medical Journal of Australia* (*MJA*) found "a pressing need for an open inquiry and the formulation of national guidelines" to confront conflicts of interest in research organisations.[1] A subsequent editorial in 2002 tackled the issue of conflicts of interest in the formulation of clinical practice guidelines.[2] Articles by others echoed the Editor's concerns.[3,4]

Despite reaffirming many of the same concerns, another editorial in 2004 concluded that the aim of the *MJA* was "not to exclude anyone with a potential conflict of interest from publishing or reviewing — to do so would disqualify virtually everyone (including editors)".[5] In the light of increasing public and professional scrutiny of these issues, does this response still meet the "ultimate goal … to promote transparency, reduce bias, and maintain public trust in what we publish"?[5]

The impact of duality of interest

When clinical opinion leaders declare the receipt of financial or professional benefits in exchange for providing advice to a pharmaceutical company, but are then expected to give objective, unbiased interpretations of their industry-sponsored research or area of expertise in reviews, editorials or treatment guidelines, then a potential conflict, or duality, of interest exists. This does not imply wrongdoing, but it does create serious doubts.

We contend that leaving the interpretation of these declarations of potential conflicts of interest to consumers of these articles may be unnecessarily difficult, and that such transparency alone may not erase the doubts that are inevitably created. Others go further in suggesting that transparency may facilitate the creation of biased information because people may not sufficiently discount the influence of the declaration, and advisors may therefore feel licensed to exaggerate their position.[6] Does our diverse medical community[7] just "trust" the integrity and judgement of all authors or, conversely, should we dismiss all research findings and conclusions as biased when potential conflict of interest exists? As objective as authors with potential conflicts of interest try to be, can they fully negate the subconscious obligation for reciprocation that exists when gifts or other benefits are offered and accepted?[8] Self-regulation has rarely been shown to work effectively in any enterprise, be it politics or business reporting, as shown by Enron, HIH and many other examples.

Potential conflicts of interest are common in our field of clinical cancer research,[9,10] with complex financial relationships and conflicts of interest that may exist between the pharmaceutical industry and individual physicians,[9,11-14] academic institutions[7-9,11-15] and consumers,[16-18] and the potentially adverse effect that these relationships can have on individual patient care and public health. One author has gone as far as saying that, "We are compromising our integrity and the safety of research subjects, while engaging in unethical research practices and undermining ethical standards of research".[19]

Several studies in oncology have found a positive association between pharmaceutical industry sponsorship and the reporting of positive outcomes (even if not clinically significant),[20,21] manipulation of clinical trials,[22] hiding of "preliminary data sets"[19] and leaking of preliminary results to the investment industry by clinical researchers.[23] All such activities cast doubt on the trial results and the judgements involved in producing guidelines, when potential conflicts of interest are declared.[24] The best evidence-based guidelines are only as good as the quality of both the evidence and the evaluators.

The extent of the problem

In an editorial published in the *MJA* in 2006, Tattersall and Kerridge observed:

> The moral core of medicine and the therapeutic relationship has always been expressed in terms of the possession and expression of values such as honesty, integrity, benevolence, respect, compassion, courage and trustworthiness … Of those things that may damage trust in doctors, much of the attention in recent years has been on recognising and managing conflict of interest.[25]

However, does this always occur? For example, in the annually published analysis of significant clinical advances in oncology — as expert and ethical as each author of this document no doubt is, are there no alternative authors without conflicts of interest to take the place of the 10 authors (of the 20 overall) with declared potential financial conflicts, involving up to 13 different companies for one of them, and including ownership of shares of companies whose products they are charged with independently analysing?[26] Are there no alternatives for the expert Committee on Safety of Medicines, which advises the regulatory agency on new drug approvals in the United Kingdom, than 23 of the 29 committee members with potential financial conflicts of interest, including an association with at least five companies for 13 members, at least 10 companies for another four, and at least 20 companies for three?[27]

Regardless of the integrity of clinicians, such payments may be perceived as bribes or payments for favours received or expected.[28] The head of the Australian Competition and Consumer Commission (ACCC) views financial conflicts of interest as "grubby issues that act as an unpleasant stain on the professionalism and good name of Australia's medical practitioners …"[29] Professor Martin Tattersall, a leading Australian oncologist, has been quoted as saying that the "issue of buying the key opinion leaders is so overt these days".[30] In addition, concern about the profound influence of pharmaceutical companies on doctors is no longer confined to the developed world, as an alarming report from British organisation Consumers International reveals.[31] A former Editor of the *New England Journal of Medicine* (*NEJM*), Dr Jerome Kassirer, believes that these problems reflect the values of a rapacious society and a widespread decline in ethical standards, and are creating a fully justified loss of trust in the medical profession.[32]

Evidence-based data on the extent and impact on many integral parts of public health of potential conflicts of interest, particularly financial ones, have reached a new high point in 2008. As far back as 1970, the UK Department of Health first proposed that expert advisers to regulatory agencies suspend all conflicts of interest during their time in office.[33] However, over 30 years later, the industry's scientific experts continue to have extensive conflicts of interest while providing their advice.[27] We are conscious of the disturbing fact that the *NEJM*, which can currently claim to have the most stringent policy of the general medical journals for restricting and declaring potential conflicts of interest of authors, had to reverse its 12-year policy of precluding anyone with financial ties to industry from writing editorials or review articles in 2002 — simply because it couldn't find enough authors with no financial ties. As the Editor of the *BMJ* commented in a recent editorial:

> On the face of it, this is a pragmatic response to the world we live in. But looked at another way it's an indictment of medicine's culture. The evidence that industry funding biases the design and reporting of clinical research is overwhelming. So too is the evidence that paid opinion leaders increase prescription of the sponsor's drug. Why else would industry pay them?[34]

With recent increased public scrutiny, it is timely to review editorial and other policies.

Potential solutions

Increased transparency

We already have regulatory procedures, such as registers of clinical trials and ethics committees to approve and monitor research. In addition, in an effort to create more transparency and accountability in the often hidden relationships between physicians and the pharmaceutical industry in Australia, the federal government, through the ACCC, has recently ruled that Medicines Australia, representing pharmaceutical[35] companies in Australia, must publicly detail all gifts to physicians (updated regularly). After initially opposing this ruling, Medicines Australia has subsequently conceded that transparency alone may not be sufficient to maintain public trust in the important interface between physicians and their industry, and has appointed an external auditor to monitor these disclosures.[36]

This requirement for transparency should go further and, as with device makers and orthopaedic surgeons in the United States,[37] individual gifts to specific recipients should be publicly listed. Tight regulations on complete declaration and total transparency, with strict auditing by independent administrators, is the standard used in most sectors of society to try to counteract the effect of potential conflicts of interest. Doctors are paid from the public purse and should meet the same level of public disclosure and accountability as politicians and company directors.

Requirements by journals for opinion leaders to be free of dualities of interest

If we cannot control the design and seemingly over-enthusiastic conclusions of clinical trials by physicians with potential conflicts of interest that could conceivably be interpreted as slanted towards the interests of the product of the sponsoring company,[38-44] or find alternative sources to industry for the funding, design, data interpretation and reporting of clinical trials, then perhaps professional organisations and leading journals could retry a bold initiative and only use editorial writers, clinical guidelines committee members and reviewers with no potential conflicts of interest to declare. This still allows authors with potential conflicts of interest to publish their research, but requires others to make independent judgements of its impact.

Opinion leaders providing their expertise pro bono

Close collaboration and dialogue between industry and physicians are vital for the continued development of improvements in health care. However, many authors and reviewers demonstrate that this can occur very effectively without direct payments needing to be made from industry to individual clinicians. Some prominent clinicians have recently decided to stop accepting payments from industry and instead provide their expertise pro bono.[45] Would more clinicians consider this approach, or could industry be discouraged or prevented from offering such payments in the first place?[46]

Better medical student education

While better educating medical students about conflicts of interest and the sophisticated marketing techniques being used on them may help avert the problem at its genesis, as advocated by another former Editor of the *NEJM*, Arnold Relman,[47] much more is needed. Will our learned colleges, leading journals and academic

medical centres also help to provide the educational leadership required for practising physicians?

New guidelines for academic medical centres and opinion leaders

Now seems an ideal time to create a new set of guidelines to try to arrest the perception that some of the world's leading research organisations, journals and opinion leaders are becoming part of the marketing arm of the pharmaceutical industry.[48] The detailed recommendations of a 2-year study by the Association of American Medical Colleges taskforce on industry funding of medical education form a landmark document that should be read by all doctors, medical students and staff of academic medical centres in Australia.[49] It recommends bans on gifts, food and travel and strongly advises doctors against being on industry-sponsored speakers' bureaus to promote drug and device benefits. It advises medical schools to audit all medical education seminars given by faculty members for any "inappropriate influence". Most importantly, it advocates the establishment of a central continuing medical education office to coordinate and oversee all requests for — and offers of — industry funding, and to receive and distribute these funds. All educational scholarships and travel funding should also be coordinated through this independent office, which would evaluate and choose recipients.[49] The time has come to debate these ideas in Australia, as many of them directly affect all members of the medical profession.

The proliferating connections between physicians and the pharmaceutical industry have brought the credibility of clinical medicine to an unprecedented crisis.[50] Opinion leaders in cancer and medical treatment in general, such as the *MJA*, must continue to strive for "best practice". It is time to counteract the view that any "research deck is stacked".[51] This effort requires a bold shift from the current, largely inadequate strategies.[51] Medical care is a vocation, but it is now also a business. As with most businesses, it is essential to find the correct balance between an environment that fosters the creation, development and implementation of innovative ideas that benefit the public and the application of strict and independent oversight to protect the public.

The *MJA* threw down the gauntlet on this vital issue in 2001 and 2002. We urge that it now pick it back up. Consideration of these five strategies can help lead us forward.

Competing interests

None identified.

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