



Conflicting interests in biomedical research and medical practice

Suprotstavljeni interesi u biomedicinskim istraživanjima i medicinskoj praksi

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A conflict of interest exists when decisions made by a person or institution are affected by direct financial interests or by non-financial issues, such as personal relationships, business associations, and membership in political, national or other groups. These circumstances favor secondary interests over primary interests in medicine and can influence contributions to science and health. Regardless of individual life experiences and personal background, physicians and other health professionals should strive to remain conflict-free.

This paper illustrates conflicts of interests in biomedical research and medical practice caused by financial and non-financial influences. It also assesses how medical journals, professional organizations, healthcare, and government examine these issues.

Presented examples of potential conflicting interests are related to healthcare industry, psychiatry and psychology (e.g., 'enhanced interrogation techniques'), sports medicine, and in the publication process of biomedical journals (authors, editors and peer reviewers). In order to avoid potential conflicting interests, today majority of medical journals request from the authors to disclose any such interests in a written statement on a form prepared by the ICMJE on the journal. This disclosure includes payments for consulting, speaking, honoraria, research support, personal relationships, and institutional conflicts of interests that may influence the work presented in the submitted manuscript. The editor will decide on potentially relevant conflicting interest in the disclosure and publish it.

Conflicted interests and healthcare industries

Financial collaboration of individual researchers and/or medical institutions with the healthcare industry (pharmaceutical, medical device, and biotechnology companies) frequently benefits both medical practice and scientific research. For example, such collaborations have yielded new

drugs (e.g., ACE inhibitors, angiotensin receptor blockers, aliskiren) and monoclonal antibodies (e.g., abciximab, rituximab used for the treatment of non-Hodgkin's B cell lymphoma and other malignancies), as well as medications for human immunodeficiency virus (HIV) infection and various medical devices, especially those used in surgery and cardiology (e.g., catheters, cardiac pacemakers, venous filters, heart valves, annuloplasty rings).

The pharmaceutical and health product industries are highly profitable and influential, and financial relationships in these collaborations, like those involving tobacco and food industries could influence professional judgment and threaten objectivity. Between 1998 and 2005 the pharmaceutical and healthcare industries spent \$612 million on lobbying, and \$19 billion on marketing in the USA. Thus far, medical and psychological associations have failed to prevent the influence of these entities on the health care system.

Clinical trials and similar studies dependent upon financial support by the industry are more likely to produce favorable results for their sponsors than studies without industrial ties. Ultimately, discrepancies due to financial influence or conflicting interests could expose a large number of patients to less effective or unsafe clinical care and contribute to the loss of public trust in medicine. Publication of biased clinical research fails to maintain high-quality evidence based medicine (EBM) and clinical recommendations, which are important educational tools for clinicians¹. Regardless of the direct impact on clinical care, conflicts of interest in nonclinical research are also dangerous. They undermine scientific judgment and damage integrity of the research process, thus inhibiting improvement of clinical application.

Representatives of healthcare industry may attract practicing physicians with offers that promise to advance medical knowledge and patient care. However, the professionalism of participating physicians may be threatened when conflicts of interests arise. These conflicts could be as varied as accep-

tance of company gifts, sponsored travel to meetings, drug samples, fees for promotional speaking, or publishing on behalf of a particular company. More importantly, commercial interests could influence which products a physician prescribes, uses, or recommends. Physician ownership of health care facilities or his own practice presents a conflict of interest that is not easy for government to limit. Participation of community-based and/or academic physicians, residents, and fellows in industry-sponsored trials has the potential benefit of education, yet conflicts of interest can arise when payments to participants exceeds actual expenses or when a clinical study is designed to alter prescribing habits rather than to collect information.

Local medical associations sometimes regulate the gifts that a doctor can accept from industry, but their guidelines are only recommendations. Medical institutions (university hospitals and community-based health institutions) would be wise to include codes for the acceptance of gifts in contracts made between physicians and the institution. Most American hospitals allow gifts ranging from \$5 to \$25. The US Federal law does not limit the financial support of industry to individual physician, but industry must report each gift or payment to a physician with a value greater than \$10. This information is made public for every physician registered in the country. The Open Payments program, introduced in 2013, publishes financial relationships between the medical industry and physicians on free website and includes consulting, speaking, honorariums, gifts, travel, lodging and research support. Various specialties are included: medicine, dentistry, dental surgery, and osteopathy, optometry, chiropractic medicine, and podiatry. Cardiovascular specialists (78%) and neurosurgeons (77%) are most likely to receive general payments (per physician median \$100, interquartile range \$31–\$273). The least likely are pathologists (9%)².

In sports medicine, especially at the highest competitive level, physicians frequently have dual responsibilities: one to the athlete (as a patient) and second to his team³. Clinical decisions should always protect the player for his long-term health interest. However, a player's short term interest to win, pose conflict of interests for practicing physician. Drug misuse (doping) in elite sport is much bigger problem that faces a physician who is responsible for health of the athlete. To eliminate such temptation of the athletes, physicians should follow the World Anti-Doping Code.

Conflict of interests and psychology

Conflicts of interests in psychiatry and psychology are not different from those in other areas of medicine. Problems arise when industries such as tobacco, food, and pharmaceuticals fund activities to promote marketing, influence regulations, or advance industry interests.

Both public and biomedical media have addressed potentially damaging financial relationships between scientists and industry. One story concerned a senior researcher at the National Institutes of Health (NIH) who accepted unauthorized fees from 25 pharmaceutical and biotechnology companies in addition to government sponsored research in-

volving drugs. A second example was that of a senior scientist, a head of the geriatric psychiatry at the NIH, who admitted that he failed to disclose \$285,000 in fees from a pharmaceutical company⁴.

Conflicts of interests in practical psychology can raise serious ethical issues. For example, B.F. Skinner, a neo-behaviorist, thought that famines, wars, and the threat of a nuclear war could be solved by human behavioral modification⁵, and his plan for social engineering attracted funding from the American government *via* the Human Ecology Society. Neuroscientists, philosophers, and psychologists worked together on this controversial issue; one result was the theory of "learned helplessness" devised by Martin Seligman⁶. He discovered that giving dogs repeated shocks resulted in a state of passivity. This observation was translated to humans, who "in the face of events that seem uncontrollable, experience disruptions in motivation, emotion, and learning that amount to a sense of helplessness."

Seligman's theory became the basis for "enhanced interrogation techniques," developed by two psychologists (Bruce Jessen and James Mitchell) and sponsored by the Central Intelligence Agency (CIA) with \$81 million⁷. These techniques (sleep deprivation, hypothermia and waterboarding) are considered to be torture. According to an FBI interrogator,⁸ this form of torture yields no more information on crucial intelligence issues than can be obtained by more humane methods. Enhanced interrogation techniques were used on prisoners in Guantanamo Bay and Iraq, despite clear evidence that they were ineffective. The enormous financial gains enjoyed by participating psychologists in collaboration with government "to prevent terrorists from succeeding their goals" clearly constitute a conflict of interests⁷.

Conflict of interests in publishing

A notorious example of how conflicts of interest can affect dissemination of medical knowledge began when it was revealed that an adviser to a review board for the safety of pharmaceutical products in Canada had financial ties with producers of calcium-channel antagonists. These financial relationships resulted in an article favorable to the manufacturer's positions on the safety of calcium-channel antagonists⁹, although another, more careful study showed that calcium-channel antagonists considerably increased the risk of myocardial infarction in hypertensive patients treated with these medications. A television documentary, *The Fifth Estate*, suggested that the patients were not protected from dangerous adverse effects of calcium channel blocking drugs. This particular case raised a serious question of objectivity in assessing the safety of drugs, and the International Committee Medical Journal Editors (ICMJE) found an effective way to prevent a potential conflicting interests¹⁰.

It is well known-that all participants in the publication process of biomedical journals (authors, editors and peer reviewers) may have potential financial or non-financial interests related to the manuscripts under consideration. The author who submits a manuscript is responsible for accuracy and reliability of the presentation. In order to avoid any un-

due influence related to this contribution, most medical journals ask the authors to sign a form prepared by the ICMJE or the journal. This disclosure includes all financial, personal relationships, and institutional conflicts of interests that could influence the work presented in the submitted manuscript. The editor will decide if there are relevant conflicts of interest in the disclosure and indicate this under the heading 'Competing interests' or 'Conflict of interests' or 'Declaration of interests statement'. This section is generally placed above the references, or rarely as a footnote on the first page of the paper. Some journals publish this information under the title 'Additional information and declaration' where in addition to the competing interests, one can find funding, author contributions, and supplemental information.

The examples below show how various journals report conflicts of interest. Instead of author names, the journal uses initials in order to save space, and the entire section is usually printed in a smaller font than used for the body of the paper. Some journals report the exact amount of money the author received during the last three years in relation to his manuscript.

Examples

Author disclosure: Nothing to disclose.

Declaration of Interests: None declared

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Disclosures: the authors declare no conflicts of interest, financial or otherwise.

Conflict of interest statement: None declared.

Conflict of interest statement: KFC is a co-Editor-in-Chief of an online journal *Cough*. He was a co-organizer of the Fourth International Cough Symposium in 2006 that received educational grants from AstraZeneca, GlaxoSmithKline, and Novartis. He declares no other conflict of interest. IDP was one of the developers of the Leicester cough questionnaire. He receives occasional payments for the use of the questionnaire in commercially sponsored clinical trials. He declares that he has no other conflict of interest for this Series. SW declare no competing interests.

Conflict of interests: KHM has received unrestricted research support from Gilead Sciences. CB declares no competing interests. CB is a President of the International AIDS Society; KHM is a member of the International AIDS Society Governing Council.

Publishing a statement on conflicting interests alerts readers to recognize influence of financial or non-financial factors on the validity of research. However, it may affect readers in the opposite direction, causing them to find the article less interesting, relevant, or important than if published without declarati-

ons. In general, disclosure of potential conflicts of interest reduces bias and increases the transparency of scientific research.

When the editor of a medical journal concludes that the findings and conclusions of the authors are accurate and truthful, and that the paper may be interesting to readers, the process of manuscript evaluation moves ahead to select papers that contribute to science or improve medical practice. The peer-review process that includes the assessment and critique of the work is a crucial step in the evaluation^{11,12}. The reviewer (referee, manuscript assessor) advises the editor on the quality, originality, and suitability of the paper for publication. When a reviewer requests revision, a valid critique may improve the manuscript before publication, but a reviewer may also recommend rejection or acceptance of the paper without revision. It remains important for reviewers to know potential conflicting interests that could impact the conclusions of a paper under review. However, in a journal that is published in a local language for a "small scientific community"¹³ the reviewer's report might be uncritically positive or negative. Therefore, it falls to the editor to assess the objectivity of the selected reviewers.

Some journal editors ask the authors to recommend potential reviewers, and also to indicate those who should be excluded from the assessment of their manuscript. A reviewer should also disclose potential conflict of interests that could influence his review. Many journals use a blind review system, where author(s) and reviewer(s) remain unknown to each other. Nonetheless, editors should be alert to potential conflicts of interest and provide this information as needed to achieve the best assessment of the manuscript.

Consluson

Conflict of interests (both financial and non-financial) may influence medical practice, and reporting and evaluating of medical reasearch. Transparency is important for fidelity of scientific journals, researchers, and physicians. Professional and scientific cooperation between practicing and academic physicians with industry should be open and disclosed. It is the responsibility of medical journals, professional organizations, health care providers and government to create adequate safe-guards in the form of specific codes or rules that apply to collaborations with business interests. Simply becoming aware of the problem may help to prevent or reduce conflicts of interests.

Conflict of interests

The author of this paper accepted travel and local living expenses as Editor-in-Chief of the *Scripta Medica* (Banja Luka) from 2010 to 2013.

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