

Managing Moral Hazards in Funded Research

Robin N. Fiore, PhD

rfiore@miami.edu

I. Moral Hazard (MH)

In law and economics, moral hazard refers to the increased risk of morally problematical behavior and negative outcomes because the person responsible for the hazard doesn't suffer the consequences and may actually benefit. Originally associated with risk transfer contracts such as insurance, it is now frequently invoked these days in connection with financial bailouts. And the American League's Designated Hitter.

II. Conflicts of interest (COI)

A. Definition: Conflict of Interest (COI)

A conflict of interest is an objective fact situation. COI exists whenever one's interests or commitments compromise one's independence or professional judgment. COI's can influence action, but are not themselves acts. COI's are distinct from breaches of obligation.

B. Conflict of Interest vs. Breach

A breach of trust occurs when researchers violate known obligations. COI's have the potential to cause avoidable harm: the risk is not potential. COI's do not guarantee improper conduct, however they do increase the risk that researchers will compromise their independence.

III Funded Research

Following technology transfer legislation in 1980, scientific research became increasingly funded by industry, with clinical research (and medical education) heavily sponsored by the pharmaceutical industry and medical device manufacturers: 80% by some estimates. A number of studies confirm a significant association between industry funding and research conclusions. These financial relationships benefit the researcher and the hazard affects the integrity of research and the safety of human research subjects and consumers. Thus, COI is a species of "moral hazard."

IV. Management Strategies

A. Prohibition/Limitation

Prohibition does not prevent research from being conducted; it prevents researchers from conducting clinical trials on products or techniques in which they have significant financial interests. Absolute prohibitions (on stock ownership/options in sponsoring company; etc., are a practical impossibility in that implementation on a global scale would be necessary to avoid a disastrous "race to the bottom" that would result from an uneven playing field.

B. Disclosure

Disclosure is a preferred strategy by regulators, researchers, and administrators. However, studies suggest that disclosure may not be the panacea for conflicts of interest: for a number of reasons, including that patients are unable to correct for the biasing influence. [Cain DM, Lowenstein G, and Moore DA. 2005. The Dirt on Coming Clean: Perverse Effects of Disclosing Conflicts of Interest. *Journal of Legal Studies* 34: 1-25.] Patients in cancer research trials believed that close collaboration between academic researchers and pharmaceutical companies was necessary for progress against major diseases and expressed little worry about researchers' financial relationships with drug companies; their overriding interest was access to "the best" care. [Hampson LA et al. Patient's Views on Financial Conflicts of Interest in Cancer Research Trials. *NEJM* 2006; 355: 2330-2337.]

C. Oversight

More patients preferred information/disclosure about the oversight system than of researchers' financial interests. [Cain DM, Lowenstein G, and Moore DA. 2005].

V. Spiral CT Lung Cancer Screening Controversy

International Early Lung Cancer Action Project (I-ELCAP)/Dr. Claudia Henschke and colleagues (Presbyterian/Weill Cornell Medical Center) report "increased survival" from CT screening. (NEJM 2006; 355: 1763-1771). I-ELCAP conclusions refuted; no change in "mortality" (JAMA 2007; 297: 953-961)

Cascading Disclosure of Financial Relationships/Interests:

1. Dr. Claudia Henschke and colleagues (Presbyterian/Weill Cornell Medical Center) originally declared I-ELCAP report support from the Weill Cornell Medical Center's Foundation for Lung Cancer: Early Detection, Prevention and Treatment. In March 2007 the *New York Times* reported that the Weill Cornell Medical Center Foundation was almost entirely underwritten by the parent company (Vector Group) of Liggett Group, which produces a number of brands of cigarettes. Weill Cornell Medical Center claims that Vectors grant was disclosed through a press release to the lay media.

2. *Cancer Letter* (2008; 34 [2] details patents issued to Dr. Claudia Henschke and colleagues for technology used in spiral CT scanning (software, biopsy needle), for which royalties are paid to Weill Cornell Medical Center by GE, a licensee. These royalties were not mentioned in the 2006 NEJM paper although GE was mentioned among funding sources in a January 2007 paper in *The Oncologist*. Royalties were paid to Cornell Research Foundation, a subsidiary of Cornell University, which distributed funds to Cornell University which made the payments to Dr. Henschke and Dr. Daniel Yankelevitz. NIH rules do not require disclosure of "payments from employer institutions" (42CFR 50.603).

3. Dr. Henschke and Dr. Yankelevitz respond that since I-ELCAP did not require the use of GE products, these patents and licensing agreements played no role in their research; they claim that disclosure was not relevant because these technologies were not mentioned in the papers at issues or related papers published in JAMA. JAMA editor Catherine DeAngelis disagreed and added the financial disclosures as corrections to the original publications. The editors of *The Oncologist* withheld CME availability and published a notice of potential conflict of interest, commenting that the adoption of the study recommendations re widespread CT screening would increase the commercial value of these patents and products and the authors could reasonably be expected to benefit from the publication. NEJM found no specific conflict of interest but a former editor of NEJM (Kassirer) took an opposing view in a *Boston Globe* editorial.

VI. Discussion

In their analysis of the Henschke/Weill Cornell Medical Center controversy, *The Oncologist* editors expressed difficulty interpreting "what actually represents a conflict of interest. Is it the explicit and direct promotion of one's own financial interest or a *potential* [emphasis in the original] personal benefit...at some future date?" The answer is that both are conflicts of interest. However, each presents a different type of moral hazard and calls for a different management strategy. The first sort of hazard, direct self dealing, can be mitigated by familiar and prosaic human subjects protection protocols: appropriate enrollment criteria and strict adherence to those standards, as well as restricting payment of reasonable compensation for study services rather than referral, and so forth. The second type of hazard is more difficult. The actions of the researcher contribute to whether or not the bet pays off and we should expect that the researcher, unconsciously or consciously, will prefer the outcome that is a "win" for her.

The emerging research on disclosure redirects us to concentrate on oversight. The practical impossibility and undesirability of prohibition and limitations on financial interests confirm that direction. IRB's can effectively address the protection of human subjects in particular research but are less well positioned to address institutional conflicts of interest and the creation of financial structures that elude outdated regulatory definitions. In the case presented, the recommended approach would require research institutions to "assure" publication disclosure, analogous to their "assurance" of regulatory compliance. For example, rather than permit researcher interpretation and possible gaming of the varied journal and meeting disclosure requirements, a Financial Conflict of Interest Committee could determine a single, comprehensive standard of disclosure of relevant financial relationships for publications and in presentations; the standard would be binding for all venues and for all subsequent uses of the data; IRB's would continue to manage disclosure of hazards to subjects. Given the institutional financial interests in research and the institutional relations with industry, the development of quasi-independent entities to perform the necessary research oversight may be required.