Smoke, then Fire: Lung Cancer Screening Studies Under Further Scrutiny

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In the January 2008 issue of The Oncologist, we reported that the authors of a controversial article on CT screening for early detection of lung cancer had not revealed their financial interests in screening software and biopsy instruments [1]. We considered these interests relevant to the message of the article, and hence decided not to make the article available as a Continuing Medical Education (CME) course [2]. It was further revealed by Paul Goldberg, editor of The Cancer Letter, that the same authors, Claudia Henschke and David Yankelevitz of Weill Cornell Medical College, had not disclosed these interests in their many previous articles published in the New England Journal of Medicine (NEJM), the Journal of the American Medical Association, and elsewhere [3].

Goldberg [4] and, independently, Gardiner Harris of The New York Times [5] reported on March 25 and March 26, 2008, respectively, that Henschke and Yankelevitz financed some of their lung cancer screening work with a $3.6 million grant from Vector, the parent company of the Liggett Group, a major cigarette manufacturer. The tobacco money was filtered through a nonprofit foundation, the Foundation for Lung Cancer Early Detection, Prevention & Treatment, that was hastily established in late 2000. Henschke, Yankelevitz, Antonio Gotto (dean of Weill Cornell Medical College and a noted cardiology researcher), and Arthur Mahon (chair of the Weill Cornell Board of Overseers) are the foundation’s officers and directors. The foundation’s support was acknowledged in a few articles published by these authors, but the origin of the money was not obvious to the journals, as recently observed by Jeffrey Drazen, the editor-in-chief of the NEJM [6]. Goldberg further documents that the authors subsequently accepted grant support from the American Cancer Society and other sources that specifically prohibit projects that receive funding from tobacco companies. In fact, the authors neither acknowledged this funding from Vector nor their foundation in the paper published by The Oncologist [7].

Thus, smoke revealed the underlying fire. Clearly, tobacco companies can exploit the Henschke-Yankelevitz message that CT screening can prevent death from lung cancer. The subliminal message follows: “All a tobacco smoker has to do is get a CT every few years.” Disclosure of the real source of their funding would not only have been relevant, it could likely have prevented publication of these controversial results in any major journal. Had the editors of The Oncologist known about this, we would not have accepted the article, and we state unequivocally that this Journal will not knowingly publish articles from authors supported by tobacco money, whether that money is laundered through a foundation or given directly to the investigators. Our disclosure forms that must be submitted prior to publication of any new article with or without CME will so state.

As for the Henschke–Yankelevitz study itself, there are significant scientific reasons for concern about its conclusion that screening prevents deaths due to lung cancer. As a forthcoming letter to the editor from Peter Bach [8] and the accompanying commentaries point out in this issue of the Journal [9, 10], the methodology of their study was flawed. There was no simultaneously studied control group. The results were confounded by lead-time bias; the fact that many of the small cancers did not recur does not prove that the patients, unscreened, would have died of lung cancer. Their survival may or may not have been related to the screening. On the other hand, the majority of lesions detected by screening, and requiring diagnostic follow-up, are not cancers. The cost/benefit of CT screening is now the subject of a well-designed prospective trial by the National Cancer...
Institute and the American College of Radiology Imaging Network; the results are anticipated in two years [11]. Clearly, it is too early to accept the conclusions of Henschke–Yankelevitz’s work, and a significant pall has been cast over their studies. Because of the importance of the I-ELCAP study and the questions raised regarding its results and sources of funding, it would seem to be of highest priority to have an independent audit of the clinical outcomes of the study, and a full disclosure of all sources of support, direct or indirect. It does not appear, from the text of articles published or from the I-ELCAP website, that a comprehensive audit of clinical outcomes (deaths due to cancer, patients censored from the trial, etc.) was performed as part of this trial.

If anyone questions the importance of full revelation of conflicts of interest (COI), this episode should provide conclusive evidence of its vital role in placing research in context. The Cancer Letter and The New York Times have done an outstanding job of reporting a COI situation that taints the investigators, their medical school, and their published research.

The repercussions for the lung cancer field, for the journals, and for the individuals involved are likely to be significant. Further investigations of the overt or covert link(s) between tobacco companies and medical research are warranted.

What was once only smoke has now become a fire.

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REFERENCES
2. Editor’s note. Available at http://theoncologist.alphamedpress.org/cgi/content/full/13/1/65/DC1.
8. Editor’s note: Dr. Peter Bach’s letter to the editor will be published, along with a reply from Dr. Claudia Henschke, in the May issue of The Oncologist.
12. Dr. John N. Niederhuber and Dr. Frank M. Balis, senior editors of The Oncologist, as federal employees were recused from all discussions and/or editorial decisions regarding these particular matters.