

## Tar-nished reputations

In March, 2008, *The New York Times* and *The Cancer Letter* reported a seminal lung-cancer screening study published in the *New England Journal of Medicine* on Oct 26, 2006, had been partly funded with money from a tobacco company. The International Early Lung Cancer Action Programme Investigators (I-ELCAP) study declared funding from the Foundation for Lung Cancer: Early Detection, Prevention and Treatment, but did not state that this charitable foundation was supported by US\$3.6 million from the Vector Group—parent company of the Liggett Group, which manufacture cigarettes. Of note, the foundation had been set up by the lead investigators of the I-ELCAP group who it now transpires also failed to disclose patents related to CT diagnostics in papers published in other journals. The I-ELCAP findings suggest lung cancer can be caught early and treated successfully, thereby potentially allowing tobacco companies to continue to peddle their products with impunity. So in light of these non-disclosures, can the I-ELCAP findings be trusted?

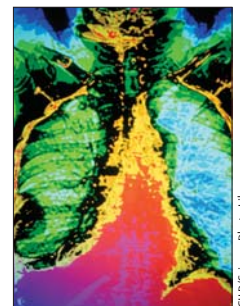
The I-ELCAP study was a large collaborative effort that assessed the stage distribution and subsequent survival of patients with lung cancer detected by low-dose CT screening of asymptomatic, high-risk participants. Of the patients identified, 85% had stage I disease. Patients with lung cancer are often diagnosed at advanced stages, thereby decreasing the efficacy of the limited treatment options available. In theory, any technique that identifies early-stage cancers should improve outcome, in particular by allowing more patients to undergo surgery with curative intent. However, the I-ELCAP study was criticised by experts for its design, which had no control arm, and because it used a survival rather than a mortality endpoint. Furthermore, at the 2007 American Association for Cancer Research annual meeting (Los Angeles, CA, USA), critics argued that the authors' interpretation presupposes small screen-detected cancers are clinically relevant and that the natural history of the disease is known. Screening programmes can result in overdiagnosis, in which some patients undergo unnecessary biopsies and treatment, and can lead to inflated survival rates. For example, a study published in the *Journal of the American Medical Association* in 2007 that screened a high-risk population with CT showed the number of screen-detected lung cancers was three-times higher than expected, and the

number of surgical procedures ten-times higher, but importantly, the number of patients with advanced disease at diagnosis, and the number of deaths, were similar to those expected in an unscreened population. These findings highlight that the risk-to-benefit ratio of any screening programme has to be considered carefully before national CT-screening schemes are introduced.

The Liggett grant was fully disclosed in a press release at the time it was awarded in 2000 and formed only a small part of the overall funding of the I-ELCAP study. But although scrutiny of funding sources in 2000 was not as rigorous as today, surprisingly, this public announcement was not reiterated when the paper was submitted to the *New England Journal of Medicine*.

So what is the issue? Research involves a degree of subjectivity. Consequently, the latest disclosures shed additional light on the already controversial interpretation of the I-ELCAP findings, in particular, the authors' conclusion that annual spiral CT screening detects lung cancer that is "curable". Many people have a fundamental problem with accepting that research funded by companies producing the causal instrument of a disease (eg, cigarettes), or advocating a test that the authors could financially benefit from, is truly impartial. Furthermore, this whole episode reflects badly not only on the authors of the *New England Journal of Medicine* paper, but also damages the reputations of their institute and the other journals that have become embroiled in the controversy. But who needs to take responsibility and how can a repeat of this sorry episode be avoided? Unfortunately, there are no simple answers, although increased scrutiny and vigilance at all stages of research from planning and execution through to publication is an advisory starting point.

Lung cancer is a difficult disease to treat and early detection could yield substantial benefits. Several randomised screening trials are underway that might provide more definitive answers on whether detecting early-stage lung cancer improves patient outcome, and at what cost—these trials might even confirm the I-ELCAP findings. However, until these studies are concluded, the I-ELCAP study, tarnished as it is by tobacco funding and other competing interests, must be viewed with scepticism, and any plans for immediate CT screening programmes must be put on hold until more evidence is available. ■ *The Lancet Oncology*



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For more on *The New York Times* and *The Cancer Letter* reports see [http://www.nytimes.com/2008/03/26/health/research/26lung.html?\\_r=1&oref=slogin](http://www.nytimes.com/2008/03/26/health/research/26lung.html?_r=1&oref=slogin) and <http://www.cancerletter.com/henschketobacco.pdf>

For more on the I-ELCAP study see *N Engl J Med* 2006; 355: 1763-71

For more on updated financial disclosures for 2006 paper see *N Engl J Med* published online Apr 2, 2008; DOI:10.1056/NEJMe0802618; DOI:10.1056/NEJMx080010; and DOI:10.1056/NEJMc086128

For more on the JAMA study see *JAMA* 2007; 297: 953-61