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WHAT'S HOT IN... MEDICINE , November/December 2008

Cancer Screening—When Will It Be the Lung's Turn?

by David W. Sharp



The principles of medical screening were set out 40 years ago in a World Health Organization paper (J.M.G. Wilson, G. Jungner, *WHO Chron.*, 22[11]: 473, 1968). They have been played around with over the years. For instance, these days you will find more emphasis on randomized trial evidence, and the health economics criteria may be stricter, but essentially the 10 principles have stood the test of time. Sadly, they have not always been adhered to, and screening often leads to lively debate. Cancer screening is no exception. Screening for breast cancer, and tests for cancer of the uterine cervix, are public-health policy in many countries, but neither has been free from controversy. Nor has prostate cancer screening. On lung cancer screening, the U.S. Preventive Services Task Force in 2004 found "evidence insufficient to recommend for or against" testing symptom-free individuals by any of the three techniques being explored (computerized tomography [CT], sputum cytology, and conventional chest radiography). A paper that is currently below the Top Ten but sure to rise higher in the Thomson Reuters citation rankings makes an important if not decisive contribution (at #18, The International Early Lung Cancer Action Program [IELCA] Investigators, *New Engl. J. Med.*, 355 [17]: 1763-71, 2006; total cites 154, latest bimonthly citation count 29).

The Early Lung Cancer Action Program published its first major finding, which has since been confirmed, in 2004. It appeared

Medicine Top Ten Papers

Rank	Papers	Cites May-Jun 08	Rank Mar-Apr 08
1	S.E. Nissen, K. Wolski, "Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes," <i>New Engl. J. Med.</i> , 356(24): 2457-71, 14 June 2007. [Cleveland Clinic, OH] *178DR	53	1
2	J. Yu, <i>et al.</i> , "Induced pluripotent stem cell lines derived from human somatic cells," <i>Science</i> , 318(5858): 1917-20, 21 December 2007. [Genome Ctr. Wisconsin, Madison; U. Wisconsin, Madison] *243HE	53	†
3	R.J. Motzer, <i>et al.</i> , "Sunitinib versus interferon alfa in metastatic renal-cell carcinoma," <i>New Engl. J. Med.</i> , 356(2): 115-24, 11 January 2007. [10 institutions worldwide] *124NE	49	4
4	L.J. Scott, <i>et al.</i> , "A genome-wide association study of type 2 diabetes in Finns detects multiple susceptibility variants," <i>Science</i> , 316(5829): 1341-5, 1 June 2007. [12 U.S. and Finland institutions] *173PS	49	5
5	R. Sladek, <i>et al.</i> , "A genome-wide association study identifies novel risk loci for type 2 diabetes," <i>Nature</i> , 445(7130): 881-5, 22 February 2007. [14 institutions worldwide] *138CR	48	2

that more than 80% of individuals who had had lung cancer diagnosed as a result of a baseline or follow-up spiral CT scan had clinical stage I disease (early), the only stage at which talk of cure is thought to be realistic. Participants were symptom-free at the time of screening but were at risk because they smoked (or were exposed passively to smoke) or were occupationally at risk because of, for example, exposure to asbestos. What happened later is the focus of paper #18. Screening of 31,567 people resulted in a diagnosis of lung cancer in 484, with an estimated lung-cancer-specific 10-year survival rate of 80%. However, this figure rose to 92% for the 302 stage I patients who underwent lung resection within a month of the diagnosis.

Good news, surely? Yes, but—which is where the criteria come in. We cannot assume that a cancer detected in this way will behave exactly the same as one presenting later on with symptoms (a problem that complicates prostate cancer screening). Any treatment given earlier than usual will have an apparent benefit on survival; this is the lead-time bias. Because smoking damages health in other ways, improved lung cancer-specific survival may not tell the whole story, as revealed in a modelling on data from the Mayo Clinic (P. M. McMahon, *et al.*, *Radiology*, 248[1]: 278-87, 2008). Other commentators emphasize the need for a control group as well as unbiased outcome measures (H.G. Welch, *et al.*, *Arch. Intern. Med.*, 167[21]: 2289-95, 2007).

The U.S. task force will want to look again at the case for this screening, but with so many other studies in the pipeline it may be as well to wait. The U.S. [Lung Screening Trial](#) is comparing spiral CT with chest radiography. Then in Europe there is the Netherlands-Louvain Lung Cancer Screening Study (R.J. van Klaveren, *et al.*, *Ned. Tijdschr. Geneesk.*, 152[4], 225-35, 2007) and the Cancer Research UK funded Lung-SEARCH study of spiral CT and fluorescence bronchoscopy in patients at risk by virtue of having chronic obstructive pulmonary disease. Randomized controlled trials of screening, especially in large numbers of people who do not think of themselves as patients, are difficult to carry out and interpret, and translating results into public policy is difficult too. Paper #18 usefully fuels the debate without resolving it. ■

A former deputy editor of *The Lancet*, Mr. David W. Sharp, M.A. (Cambridge), is a freelance writer living in Minchinhampton, Gloucestershire, U.K.

Keywords: lung cancer, cancer screening, Early Lung Cancer Action Program, spiral computed tomography, spiral CT, Lung-SEARCH.



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6	P.J. Rosenfeld, <i>et al.</i> , "Ranibizumab for neovascular age-related macular degeneration," <i>New Engl. J. Med.</i> , 355(14): 1419-31, 5 October 2006. [5 U.S. institutions] *090UA	46	†
7	E. Zeggini, <i>et al.</i> , "Replication of genome-wide association signals in UK samples reveals risk loci for type 2 diabetes," <i>Science</i> , 316(5829): 1336-41, 1 June 2007. [10 U.K. institutions] *173PS	45	7
8	B. Escudier, <i>et al.</i> , "Sorafenib in advanced clear-cell renal-cell carcinoma," <i>New Engl. J. Med.</i> , 356(2): 125-34, 11 January 2007. [15 institutions worldwide] *124NE	41	3
9	T. Sjoblom, <i>et al.</i> , "The consensus coding sequences of human breast and colorectal cancers," <i>Science</i> , 314(5797): 268-74, 13 October 2006. [11 U.S. institutions] *093TV	40	†
10	G. Hudes, <i>et al.</i> , "Temsirrolimus, interferon alpha, or both for advanced renal-cell carcinoma," <i>New Engl. J. Med.</i> , 356(22): 2271-81, 31 May 2007. [17 institutions worldwide] *172PO	38	†

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