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EDITORIAL

Screening for lung cancer in a high-risk group: but I still haven't found what I'm looking for…

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It seems so intuitive. Find early disease, remove it, and people will live long, productive lives. Screening for other cancers is commonplace already, isn't it? So why can't the pulmonary community just get on with it? We even have the advantage of targeting a ''high-risk'' group, namely smokers. Don't we get it? People are dying here. The overall 5-yr survivorship for lung cancer is ~14%, as opposed to 60–75% for those with resected early stage disease. Within the past several months, the International Early Lung Cancer Action Project (IELCAP), a single-arm observational study of >30,000 persons, screened with low-dose computed tomography (CT), reported an astounding 88–92% estimated 10-yr survival in 412 stage I patients resected with lung cancer discovered on screening [1]. The results must have merit. Or do they?

For the seasoned respiratory physician, this must feel like *déjà vu*. In the 1970s and 1980s, randomised controlled trials of screening with chest radiography were undertaken [2, 3]. More early stage lung cancers were detected and more patients were operated on, but paradoxically there was no reduction in lung cancer mortality. Possible explanations for these findings include lead, length and overdiagnosis bias. Perhaps the excess of small lesions detected on chest radiography are indolent or overdiagnosed cancers, which would not effect mortality. Without a reduction in mortality, mass screening with chest radiography was not endorsed by the healthcare community.

Excitement about screening was renewed by several large observational studies, which reported that most screen-detected cancers were treatable stage I tumours [4, 5]. These findings have lead to two large randomised controlled trials assessing the value of CT screening. The National Lung Screening Trial (NLST) has randomised 50,000 high-risk smokers in the USA, with the results due in 2009, while in the Netherlands and Belgium, 16,000 subjects have been randomised, with the results due in 2016. Only these trials can tell whether a true reduction in lung cancer mortality results from CT screening.

While awaiting the results of these trials, much interesting research has been undertaken. Several groups have attempted to estimate mortality using data from former and current screening trials [6, 7]. SWENSEN *et al.* [6] used data from 1,520 patients screened with CT for 5 yrs and found lung cancer incidence and mortality rates that were similar to those of persons screened with chest radiography in the previous Mayo Lung Project. PATZ *et al.* [7] modelled mortality rates for those undergoing screening with CT using the Mayo Clinic and IELCAP datasets and compared those with mortality estimates using radiographic screening. The estimated mortality rates were 4.1 and 5.5 deaths per 1,000 person-yrs using CT screening in the Mayo Clinic and IELCAP populations, respectively, compared with 4.4 and 3.9 deaths per 1,000 person-yrs using chest radiographic screening or usual care, respectively [7]. These findings do not appear to bode well for screening. Others have focused on cost-efficacy analysis. The results of these studies have varied wildly in their estimate of cost-effectiveness, from US$2,500 per life-yr gained to >$2,000,000 per quality-adjusted life-yr saved [8, 9]. Two clear findings emerge from these studies. The first is that if there is extensive lead time and overdiagnosis bias, screening becomes cost-ineffective. The second is that the individual risk of developing lung cancer will impact dramatically upon cost-efficacy. The higher the risk of developing cancer, the more cost-effective screening becomes. In one study there was a 17-fold difference in cost-effectiveness when comparing current smokers to ex-smokers [9]. Individual risk of developing lung cancer can vary greatly and is impacted by age, smoking history, sex, the presence of airflow obstruction and asbestos exposure [10, 11]. Thus, identification of an ''ultra high-risk'' group may improve the chances of a successful screening programme.

This brings us to the study published in this issue of the *European Respiratory Journal* by VIERIKKO *et al.* [12], who screened just such a high-risk group, namely asbestos-exposed persons, a subset of whom were also smokers. One would have thought that screening in this high-risk group would yield a greater number of malignancies. It did not, and this study mirrored other observational CT screening studies with the number of benign nodules (14%) far outnumbering the malignant ones (0.8%). Four patients had unnecessary thoracotomies and an additional 44% of those screened had incidental findings, some of which required further evaluation. It was surprising that in this asbestos-exposed smoking group more cancers were not detected. Certainly, the pack-yr history of smoking in this population was lower in this study than in other screening studies, but still, there was no statistical difference between the five subjects diagnosed with cancers and the rest of the screened group with respect to age, asbestos exposure and smoking history.

Are we sick and tired of seeing patients present to our clinics with advanced disease and unrelenting symptoms and being

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treated with toxic therapies only to go on to die within a year or two? We certainly should be. Do we hope screening will work? Absolutely. Unfortunately, so many questions remain and so few are as yet answered. Until the results of the randomised trials on screening are made available, when it comes to screening for lung cancer, I still haven't found what I'm looking for...[13].

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