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The (US) National Lung Cancer Screening Trial: intensifying the debate about the introduction of screening for lung cancer

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TITLE Reduced lung-cancer mortality with low-dose computed tomographic screening.

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SUMMARY

In November 2010 the National Lung Cancer Screening Trial (NLST), a large randomised trial of helical computed tomography (CT) screening for lung cancer versus chest radiograph, was stopped a year early as the required end point of a 20% reduction in lung cancer mortality had been reached.[1] This was the first conclusive evidence that was sufficiently free of lead time, length time and over-diagnosis bias, factors that had proven problematic in earlier randomised trials. The NLST enrolled 53,454 subjects aged 55–75 with at least a 30 pack-year smoking history who had quit smoking within the previous 15 years. Between 2000 and 2002 subjects were randomised to receive an annual CT or chest radiograph for three consecutive years. Subjects were found to be well matched to the US census data except that they were younger, better educated and more likely to be former smokers. Compliance with screening was over 90%. There were 247 deaths per 100,000 person years in the CT group compared with 309 deaths per 100,000 person years in the radiography group, representing a 20.0% reduction (95% confidence interval [CI], 6.8 to 26.7). The all-cause mortality was also reduced by 6.7% (95% CI, 1.2 to 13.6). In the first two screening rounds, 27% and 28% of scans respectively were classified as positive and of these, 96.4% were false positives. The level of physical harm reported was low and similar in the two arms; psychological harm was not reported.

OPINION

The NLST has shifted the emphasis of the screening debate from efficacy in reducing mortality to deciding on the applicability of the results to other populations and whether, and in what form, CT screening should be introduced.[2] If the results can be reproduced in the UK, it is likely that more than 3,000 lives will be saved each year. There remain however uncertainties that make it difficult to design a screening programme without significant financial risk or the prospect of excluding people that may benefit considerably. Key questions concern the selection of patients for screening programmes – should more detailed risk assessment scores be used to avoid screening groups where there is little benefit, as well as allowing a more permissive approach in those at greater risk by virtue of their age? The risk of cancer is much greater in the older age group, yet in the NLST 42.8% of participants were aged 55–59. Although age-specific cancer rates have not been published, it is likely that this high proportion of younger patients would have considerably diluted the impact of the three annual screens in the early years. Cost-effectiveness data have not yet been published on the NLST but there is at least one paper about a model based on the NLST and it shows incremental cost-effectiveness ratios (ICERs) well above the National Institute for Health and Clinical Excellence (NICE) thresholds, even when 6% smoking cessation rates are assumed.[3] Cost is also a key issue in deciding on the

optimal frequency and duration of screening. The NLST would suggest that screening should be annual from the age of 55 to 75 but other studies, including the Dutch-Belgian NELSON trial[4] and the United Kingdom Lung Screen trial[5] may clarify this. The optimal management of positive screening tests also needs to be determined to both reduce costs and minimise morbidity.[3]

Uncertainties notwithstanding, the NLST has reshaped our thinking about lung cancer screening and although the debate continues about the introduction of screening programmes, we are undoubtedly closer to seeing large lung cancer-specific mortality reductions, a change in the proportion of patients with curable lung cancer presenting to clinics and considerably more work for radiologists and radiographers.

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