

From the authors:

Lung cancer kills, the more advanced the disease the lower the chance of survival and therefore early diagnosis is key to improve survival [1]. Recent data from the largest screening study, including more than 50 000 high-risk patients, shows benefit with lung cancer screening, while data from other studies are awaited [2]. The joint white paper published by the European Society of Radiology (ESR) and the European Respiratory Society (ERS) on lung cancer screening is not a general recommendation to perform lung cancer screening in Europe, but a recommendation on how to do it right and under what circumstances [3].

According to the extensive review of all reported low-dose computed tomography (LDCT) lung cancer screening trials by SHLOMI *et al.* [4] and the NELSON study data from the first three screening rounds, as discussed in the paper (and accompanying online supplementary material) by HOREWEG *et al.* [5], the percentage of stage I lung cancer detected in prevalence screening rounds varies between 47.6% and 63.9% (if we omit the 81.8% of the LUSI trial). For the NELSON and NLST (National Lung Screening Trial) trials alone the percentage of stage I in the prevalence rounds were 64.9% and 58.3%, respectively [4, 5]. The average percentage of stage I lung cancer detected in incidence rounds in all LDCT trials varied between 53.1% and 76.5% (if we omit the 25% of the Lung Screening Study trial), while these data for NELSON and NLST were 74.3% and 66.4%, respectively. Therefore, we agree with the comment that downstaging as expressed by the difference in percentage of detected stage I lung cancer cases between incidence and prevalence is just below 10%.

According to our white paper most cancers detected by LDCT will be in a treatable stage (60–80% stage I) based on the NLST and NELSON as references [2, 5], and we agree that the interval of absolute results for these two trials better should correctly be between 58.3 and 75.8%. Based on the more variable results from all LDCT screening trials [4], it is probably rather optimistic to provide only the absolute values of NLST and NELSON for the percentage of stage I lung cancers as detected by LDCT screening, although these are the two largest screening trials.

Overdiagnosis and radiation exposure are always a challenge when screening programmes using imaging are performed. This was the case when screening for breast cancer was first established, and not just among women at risk but to the whole female population above 50 years old, at that time, the radiation exposure of mammography was quite high (up to 25 mSv) [6]. In the meantime mammography screening for breast cancer has been proven to be an important tool in diagnosing breast cancer early and saving lives, and only very few sceptics would go back to no screening for breast cancer, although the interval may now be longer than yearly. Overdiagnosis is dependent on the definition of positive screening results. As recommended in the white paper, overdiagnosis should be reduced using risk models to increase pretest probability. Moreover, the use of LungRADS (lung imaging reporting and data system) or LU-RADS (lung reporting and data system) will further decrease overdiagnosis and increase the positive predictive value of lung cancer screening.

The recommendation in the white paper is to reduce the radiation exposure to 1 mSv or less, which has recently become a reality [7]. 25 LDCT examinations are the maximum, which only a few participants of a longitudinal programme will undergo. As already stated in the white paper, longer scanning intervals have to be considered, *e.g.* depending on risk model assessment. Full diagnostic computed tomography (CT) has been strongly discouraged in the white paper; instead short-interval re-scans should be carried out with LDCT.

Cost-effectiveness has to be considered for the general decision to implement a screening programme; however, as already pointed out, this white paper focused on how to do it correctly, if deemed appropriate. This is why we did not discuss cost-effectiveness in depth. Cost is also highly dependent on the national healthcare systems which are highly variable in Europe. The cost estimates from the USA are certainly not applicable to Europe. It goes without saying that preventing people from smoking and encouraging people to stop smoking is highly effective with regards to remaining healthy. However, the success rates of smoking cessation through counselling or medication are still very poor [8], and they are higher if complemented with imaging. There is evidence that stopping smoking at any age, even if the diagnosis of lung cancer has been made is still efficient to prolong survival. This is why the white paper clearly calls for complementing CT lung cancer screening with a smoking cessation programme. However, even if all smokers quit smoking completely right now, which is unlikely to happen, there will still be patients at high risk of lung cancer in the next decades as ex-smokers who quit less than 15 years ago have a clearly increased risk to develop lung cancer and they deserve an evidence-based offer to have their disease detected early, regardless of a more cost-effective smoking prevention or cessation programme being in place for adolescents and young adults. The cost of the screening will be reduced as follow-up tests are performed in dedicated certified centres with high throughput, where fewer mistakes could be expected.

Currently available, less invasive diagnostic procedures and minimal surgical procedures, such as video-assisted thoracoscopic surgery, further reduce both the complications and the cost of all procedures.

Screening in a selected population of smokers using LDCT reduces mortality from lung cancer in comparison to screening using standard radiography. Even if the results are modest (one death from lung cancer avoided per 320 persons screened) [2], the physician has to take them into consideration and inform participants about the advantages and disadvantages of the screening programme as well as the conditions with which it should be performed, as stated in the white paper. The final decision should be left to the individual after adequate information and strong advice to quit smoking. In term of evidence-based medicine, the results of NLST cannot be ignored, and a general screening programme has already been established in the USA and many other countries are discussing establishing programmes, such as UK, Israel, Canada, Australia and Japan. Thus, we felt it was more than appropriate that the leading European medical societies in the field should provide recommendations on how and where it should be carried out. Early diagnosis in lung cancer is pivotal, and only if a screening programme is implemented properly with a high quality level can we expect positive effects.



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A lung cancer screening programme using CT will only yield positive effects if implemented properly with high quality <http://ow.ly/S1rGR>

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