European Alliance for Personalised Medicine

White Paper

Innovation, Screening, Guidelines: The Case of Lung Cancer
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Introduction

Around one billion people on the planet are regular smokers. And lung cancer is one of the biggest killers. We all now know that there is a direct connection in many cases. Non-smokers do get lung cancer, but the risks if you are a smoker are significantly.

Undoubtedly, tobacco smoking is the major risk factor for lung cancer, although passive smoking, and a family history of lung, head and neck cancer are, among other factors, also important.

Figures show that lung cancer causes almost 1.6 million deaths each year worldwide, representing almost one-fifth of all cancer deaths. Within the EU, meanwhile, lung cancer is also the biggest killer of all cancers, responsible for almost 270,000 annual deaths (some 21%).

It is at the very least surprising that the biggest cancer killer of all does not have a solid set of screening guidelines across Europe. Doctors need to quickly identify high quality, trustworthy clinical practice guidelines, in order to improve decision making for the benefit of their patients.

The Alliance has turned its attention to need for more guidelines across the arena of healthcare, especially in screening for lung cancer. There is a need for agreement and coordination across the European Union’s 28 Member States.

In the US, the American Cancer Society has stated that it had “thoroughly reviewed the subject of lung cancer screening” and issued guidelines that are aimed at doctors and other health care providers.

Europe, among other things, is looking at risk prediction models to identify patients for screening (i.e. Liverpool Lung Project risk model, i.e. LLPv2), plus determination of how many annual screening rounds are required.

The European Respiratory Society (ERS) and the European Society of Radiology (ESR) have both recommended screening for lung cancer under the following circumstances: “In comprehensive, quality-assured, longitudinal programmes within a clinical trial or in routine clinical practice at certified multidisciplinary medical centres.”

Meanwhile, the International Association for the Study of Lung Cancer (IASLC) Strategic Screening Advisory committee (SSAC) developed a consensus statement after the publication of the NLST trial identifying issues which required further research. These include effective risk assessment, and integrating screening with anti-smoking information.
Recently the SSAC experts have indicated that, while we wait, there is a good case for “immediate implementation of carefully designed and well targeted demonstration programmes”.

Of course, cost-effectiveness questions arise whenever population-wide screening is considered, especially in relation to frequency and duration.

The UK lung cancer screening trial (UKLS) has demonstrated that screening is cost effective by NICE criteria, in the modelling of their pilot screening trial. However, the potential benefit of low-dose CT lung cancer screening would almost certainly see an improvement in the lung cancer mortality rate in Europe.

Stakeholders are aware that screening for lung cancer also has potential harms. These include radiation risks (which are low but the potential for increased risk of other cancers); identification of often harmless nodules, which could lead to further evaluation (including biopsy or surgery); unnecessary fear in the patient and those close to him or her, and potential over-diagnosis.

On certain occasions, benign lesions are found that would not grow, spread, or cause death. This could lead to over-treatment, bringing about extra cost, anxiety and ill-effect (even death) caused by the treatment itself.

Clinically, it is now well recognised from multiple screening trials that if early Stage (1a/1b) lung cancer is identified and surgically resected, the patient has a very good five-year survival chance.

Unfortunately, at this time, most patients are diagnosed at an advanced stage (Stage III/IV), which is non-curable.

EAPM, along with other aforementioned stakeholders, believes that there is a strong case for lung cancer screening programmes across the 28 EU Member States to reduce the cases of advanced-stage lung cancer.

Among recommendations currently being discussed in European forums are the setting of minimum requirements, which should include standardised CT screening radiological procedures for low-dose imaging, risk prediction criteria for inclusion (or exclusion) for screening, together with the integration of smoking cessation programmes.

Also important are improving the quality, outcome and cost-effectiveness of screening, reducing radiation risks, and thorough assessments of other risks, such as co-morbidities.

IASLC-SSAC, ERS and ESR have stated that “the establishment of a central registry, including biobank and image bank, and preferably on a European level, is strongly encouraged”, and EAPM is in full support of this.
Current situation

The USA trial, NLST, demonstrated CT a 20% drop in lung cancer mortality in the CT screening arm.

In the USA, lung cancer screening has been the subject of major policy decisions based on the US Preventive Forces Task Force on CT screening and from Medicare. On the back of this, USA professional organisations have recommended the implementation of lung cancer CT screening.

In Europe, we are awaiting the NELSON RCT Trial undertaken in the Netherlands and Belgium which will provide data on mortality rates and cost effectiveness.

It is also planned to pool the data from the UKLS trial with the NELSON data set.

The NELSON study was designed to investigate whether screening for lung cancer by low-dose CT in high-risk subjects would lead to a decrease in 10-year lung cancer mortality of at least 25%. This to be looked at in comparison to a control group which was not undergoing screening.

The NELSON study began in 2003, using men aged 50–75 years from seven districts in the Netherlands and from both sexes from 14 close geographical areas in Belgium, their cancer history, and several other lifestyle and health factors.

Based on the smoking history, the estimated lung cancer mortality risk of the respondents was determined. Next, the required sample size including required participation rate was determined.

The NELSON trial have already made great contributions to our understanding of the CT screening process, especially in the use of volumetric analysis of suspicious CT detected nodules and in the definitions of positive and negative cases.

This has dramatically reduced the incidence of False Positives, which was a major issue in the NLST trial. The UKLS trial also utilised the use of volumetric analysis and has validated this workup procedure.

Other European studies like the Italian Cosmos study have provided important information on estimation of over-diagnosis, risk of radiation induced malignancies and role of CT/PET in the management of screening cancers.

The possibility to increase the interval between rounds in a selected population in a tailored prevention programme is under evaluation.
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Conclusions

Findings in both Europe and the US strongly suggest that lung cancer screening works. although debate continues about the best way to implement screening of this kind, and the NELSON trial ‘cost effectiveness’ data are awaited.

Ideally, guidelines could help to tether costs, by bringing in improvements to the efficiency of screening methodologies and, thus, programmes themselves.

Key to such a situation would be making the best use of efficient risk-assessment methods, top-of-the-range imaging technology utilising volumetric protocols, and clinical work-up guidelines that encourage the minimisation of invasive procedures and risk to the patient.

EAPM believes that the EU should put guidelines in place that will allow Member States to set-up quality assured early detection programmes for lung cancer, and that there is a need for increased public-private partnerships, such as IMI II.

There is clearly a need to:

- Raise awareness of the need for agreed recommendations over lung-cancer screening
- Improve the knowledge of policymakers and world health agencies so that effective lung-cancer screening guidelines and policies can be formulated on the international stage
- Work across national borders to ensure cooperation and collaboration in respect of much-needed guidelines in the fast-developing field of personalised medicine
- Advance parallel work done by professional groups, patient groups, healthcare funders, pharmaceutical companies and academic institutions to a new level

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Modern medicine is advancing swiftly and there are many areas trying to play catch up. Much can be achieved with consensus-based documents to ensure that effective screening can take place.

But Europe does not have a brilliant record when it comes to implementing screening.

As long ago as December 2003, EU health ministers unanimously adopted a Recommendation on cancer screening, which acknowledged both the significance of the burden of cancer and the evidence for effectiveness of breast, cervical and colorectal cancer screening in reducing the burden of disease.

This Council Recommendation outlined “fundamental principles of best practice in early detection of cancer” while inviting Member States to take common action to implement national cancer screening programmes with a population-based approach and with appropriate quality assurance at all levels.

At that point, EU guidelines updated and expanded for breast and cervical cancer screening had already been published by the Commission; while comprehensive European guidelines for quality assurance of colorectal cancer screening were, at the time, being prepared.

Thirteen years on and incidence and mortality rates of cancers still vary widely across the EU, reflecting a major health burden in various Member States, often splitting large and smaller countries along with richer and poorer nations. In fact, only six countries have implemented ALL recommended programmes even now in 2016.

This cannot be allowed to happen with the biggest killer of all cancers in Europe and beyond.

In the end, when it comes to the biggest cause of lung cancer - smoking - not enough people are kicking the habit. Governments everywhere are constantly telling us of the dangers of smoking and the costs of treatment.

But while information is vital no leaflet or poster, on its own, will stop a nicotine addict from doing what he or she does, although the message that smoking cigarettes is not a good lifestyle choice seems to be slowly getting through via a combination of things.

Of course knowledge of health risk, escalating costs and peer pressure are among the big ones. But even together they are not enough.

It is clear than any further delay to the implementation of the best form of lung cancer screening will mean many more unnecessary lives lost.

*Image*
About EAPM

The European Alliance for Personalised Medicine (EAPM), launched in March 2012, brings together European healthcare experts and patient advocates involved with major chronic diseases.

The aim is to improve patient care by accelerating the development, delivery and uptake of personalised medicine and diagnostics, through consensus.

As the European discussion on personalised medicine gathers pace. EAPM is a response to the need for wider understanding of priorities and a more integrated approach among distinct lay and professional stakeholders.

The mix of EAPM members provides extensive scientific, clinical, caring and training expertise in personalised medicine and diagnostics, across patient groups, academia, health professionals and industry. Relevant departments of the European Commission have observer status, as does the EMA.

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