EU Call for Evidence: Cancer Screening Recommendation update

Response from the International Association for the Study of Lung Cancer (IASLC)

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IASLC short response text (max 4000 characters including spaces and references)

The International Association for the Study of Lung Cancer is an international network dedicated to the study and eradication of lung cancer and other thoracic malignancies, founded in1974, with over 8,000 specialists from more than 100 countries.

We strongly recommend that targeted lung cancer screening, through low-dose CT (LDCT), be included in the forthcoming EU recommendations.

We feel that the clinical, economic and implementation research on LDCT has sufficient scientific evidence to justify this recommendation and have provided detailed evidence to support this position in the attached response document.

IASLC Full Response

The International Association for the Study of Lung Cancer (IASLC) is an international network dedicated to the study and eradication of lung cancer and other thoracic malignancies, founded in 1974, with over 8,000 specialists from more than 100 countries. The IASLC headquarters are based in the USA.

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Lung cancer is the leading cause of cancer mortality in EU and worldwide, accounting for one in five cancer deaths[1]. Early detection can have a significant impact on reducing mortality by shifting a large proportion of patients from late stage, largely incurable disease, to early stage with more options for curative treatment. Screening is also one of the best options for people who continue to smoke or had smoked heavily in the past but have quit smoking to decrease their chance of dying from persistent risk of lung cancer[2]. Detecting and treating lung cancer early will improve patients' quality of life and dramatically decrease its economic toll on society[2].

Lung cancer disproportionately effects underserved low SES populations due to higher smoking rates in these populations[3]. The ability to implement CT lung screening programs that reach all populations at risk is an additional consideration for designing lung screening programs. Studies in the UK using mobile screening vans and a lung health check approach were successful in screening underserved populations at high risk of lung cancer[4].

Of cancer costs in Europe, lung cancer has the highest economic cost (€18·8 billion, 15% of overall cancer costs), followed by breast cancer (€15·0 billion, 12%), colorectal cancer (€13·1 billion, 10%), and prostate cancer (€8·43 billion, 7%)[5].

The Call for Evidence notes that the updated recommendation should take account of the most up-to-date evidence. This is particularly relevant to lung cancer screening. Two major sufficiently powered randomised controlled trials (RCTs) have shown a statistically significant reduction in lung cancer mortality in participants; the NELSON trial (Netherlands and Belgium) found that LDCT screening is highly effective, with the potential to significantly reduce lung cancer deaths in high-risk individuals by 24%[6]. The NLST (USA) was the largest RCT lung cancer screening trial undertaken and demonstrated a 20% reduction in lung cancer deaths[7]. Further evidence has been provided from European RCTs, such as the ITALUNG, LUSI, MILD, DLCST and UKLS trials[8-13]. A meta-analysis of nine RCTs has also recently published by the *Lancet Regional Health – Europe*[12], providing support for undertaking lung cancer screening in high-risk groups.

A national analysis of U.S. patients recently published by the *British Medical Journal* showed that the introduction of LDCT screening in the U.S. was associated with significant improvements in survival at the population-level, demonstrating that the benefits of LDCT screening can be observed in a real-world, non-randomized, setting[14].

Policy documents have been previously presented to the EU Commission on taking LDCT screening forward in Europe, with specific recommendations on the management protocols, quality assurance, resource allocation and setting up an EU Expert group on lung cancer screening in 2017[15]. In addition, the Initiative for European Lung Screening (IELS) workshop report, also provided detailed recommendations[16].

The European Position Statement on lung cancer screening recommended the following actions: a risk stratification approach should be used for future lung cancer low-dose CT programmes; that individuals who enter screening programmes should be provided with information on the benefits and harms of screening, and smoking cessation should be offered to all people who currently smoke; that management of detected solid nodules should use semi-automatically measured volume and volume-doubling time; that national quality assurance boards should be set up to oversee technical standards; that a lung nodule management pathway should be established and incorporated into clinical practice with a tailored screening approach[17].

There is also strong evidence that the benefits of lung cancer screening demonstrably outweigh potential harms. High-quality LDCT screening shows a negligible risk from radiation exposure. The false-positive and over-diagnosis rates are similar to screening mammography[18,19]. LDCT screening has other benefits such as identifying COPD disease and detecting severe coronary artery calcification, providing an opportunity for cardiac disease risk reduction[20-24].

Targeted lung cancer screening through LDCT is cost-effective. When compared to other established screening programmes (breast or colorectal)[23,25], fewer people need to be screened for lung cancer to prevent one cancer death[26,27]. LDCT can also contribute to anti-tobacco agendas: when combined with smoking cessation programmes, targeted LDCT screening improves smoking cessation rates, thus having a synergistic effect[28,29]. CT lung screening can be a teachable moment resulting in increased quit rates helping heavily addicted individuals to quit smoking. International analysis of the cost effectiveness of LDCT-based lung cancer screening in the USA, Canada, UK, Switzerland, Italy and Germany have been considered cost-effective in most scenarios[28-32].

Over a decade of clinical trials and pilot studies from across Europe provides a wealth of learning on how to optimise the implementation of population based organized lung screening programmes.

Several EU Member States (Italy, Poland and Croatia) have now committed to implementing national organised LDCT screening programmes[33-35]. A major NHS England Targeted Lung Health Check programme was launched in England in 2019[36], which now has over 30 sites, utilising the two validated risk prediction models ($PLCO_{m2012}$ and LLP_{v2}) to select high risk participants[37,38]. Recently the base line performance of five UK lung cancer screening programmes comprising of over 11,000 individuals has been analysed, demonstrating a prevalence of 2.2 percent screen-detected lung cancers and a surgical resection rate of 66%. The reported harms including false-positives, benign surgical resection rates were found to be low[4].

The attached report outlines several key success factors that should be built into the development of lung cancer screening programmes. IASLC is developing a learning community around

implementation and seeks to ensure that lessons can be shared, and knowledge transferred effectively between new LDCT screening initiatives.

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