# Does UKLS strategy increase the yield of screen-detected lung cancers? A comparison with ITALUNG

The optimal strategy to increase the benefit of low dose computed tomograph (LDCT) screening of lung cancer in terms of as high as possible number of discovered cancers and to reduce the costs, in terms of as low as possible number of LDCT examinations and of interventions on benign lesions, is not established.

Field and co-workers recently reported[1] the results of lung cancer screening with LDCT in the UKLS RCT pilot study that selected eligible subjects with a validated individual risk prediction model, invited potential candidates by mail and applied the Wald Single Screen Design[2] with nodule management based on volumetry.[1]

We compared (table 1) some data of UKLS RCT pilot study with those of ITALUNG RCT that selected eligible subjects based on age and smoking history, invited potential candidates by mail and involved four annual LDCT screening rounds with nodule management based on diameter measurement.[3 4]

In the UKLS pilot study, higher rates of screen-detected primary lung cancers (2.1% vs 1.7%) and of stage I–II lesions (86% vs 68%) were observed. These features may be accounted for different population's characteristics including older age (mean 67 vs 61 years), higher male/female ratio (3.01 vs 1.79), higher frequency of asbestos exposure (36.0% vs 6.6%), higher prevalence of respiratory disease (52.1% vs 35.1%) and familial history for lung cancer (24.6% vs 16.8%) in UKLS screens. In particular, prevalence of lung cancer at LDCT screening can be as high as 4.2% in subjects exposed to asbestos.[5] On the other hand, the majority of the screens in UKLS were former smokers, whereas they were current smokers in ITALUNG. Twelve-month LDCT were obtained in

**Table 1** Screens risk profile and results of LDCT in pilot UKLS and ITALUNG RCT

| | Pilot UKLS | ITALUNG |
|---|---|---|
| Age (years) of selected subjects | 50–75 | 55–69 |
| Eligibility criteria | 5-year lung cancer risk of ≥5%, based on the Liverpool Lung Project v2 risk prediction model | Smokers or former smokers of ≥20 pack/years |
| Sample size | | |
| Control arm | 2027 | 1593 |
| Screened arm | 2028 | 1613 |
| *Screeens' characteristics* | | |
| Mean age at randomisation (years SD) | 67 (4.1) | 61 (4.2) |
| Gender (male/female ratio) | 1529/499 (3.06) | 1035/578 (1.79) |
| Current smokers | 777 (38.3%) | 1060 (65.7%) |
| Ex-smokers | 1249 (61.6%) | 553 (34.3%) |
| Never smokers | 2 (0.1%) | 0 |
| *Smoking duration* | | |
| 10–19 years* | 117 (5.8%) | 1 (0.06%) |
| 20+ years* | 1895 (93.4%) | 1612 (99.94%) |
| Unknown* | 14 (0.7%) | 0 |
| % Asbestos exposed | 763 (36%) | 93 (6.6%)† |
| % With history of respiratory disease‡ | 1056 (52.1%) | 494 (35.1%)† |
| % With history of blood cancer§ | 26 (1.28%) | Not eligible |
| % With history of solid tumour¶ | 378 (18.6%) | Not eligible |
| % With family history of lung cancer | 498 (24.6%) | 237 (16.8%)† |
| % With family history of other cancer (not lung)** | 1026 (50.6%) | 640 (45.5%)† |
| Baseline LDCT completed | 1994 (98.3%) | 1406 (87.2%) |
| LDCT detected primary lung cancers | 42/1994 (2.1%) | 25/1406 (1.7%)†† |
| At baseline scan | 34/1994 (1.7%) | 21/1406 (1.4%) |
| Adenocarcinoma | 25/42 (59.5%) | 13/25 (52.0%) |
| Stage I lung cancer | 28/42 (66.7%) | 14/25 (56.0%) |
| Stage I or II lung cancer | 36/42 (85.7%) | 17/25 (68.0%) |
| Surgical resection | 35/42 (83.3%) | 17/25 (68.0%) |
| Subjects undergoing 12-month scan LDCT | 1015/1994 (50.9%)‡‡ | 1356 (96.4%) |
| Overall category 3 and 4 nodules§§ | 536/1994 (26.8%) | 426/1406 (30.2%) |
| Of these, subjects found to have lung cancer | 42/536 (7.8%) | 25/426 (5.8%) |
| Surgical resection for benign disease | 4/39 (10.3%) | 1/21 (4.7%)¶¶ |

*All smoking (cigarettes, cigars, pipes) duration figures refer to current and ex-smokers combined.
†Information available in 1406 subjects undergoing baseline LDCT.
‡Asthma, bronchitis, TB, pneumonia, COPD or emphysema.
§Leukaemia or lymphoma, including Hodgkin's.
¶Cancers of brain, head and neck, oesophagus, breast, colon or 'other'.
††Data of ITALUNG refer to baseline and first annual repeat LDCT screening rounds.
‡‡Due to evidence at baseline of nodules >3 mm diameter.
**Cancers of brain, head and neck, oesophagus, breast, colon or 'other'.
§§Category 3 nodules correspond to: solid nodules with 5–9.9 mm diameter; part-solid nodules with non-solid component >5 mm diameter and solid component of 3–9.9 mm diameter; non-solid nodules ≥5 mm diameter.
Category 4 nodules correspond to: solid nodules ≥10 mm diameter; part-solid nodules with solid component ≥10 mm diameter.
¶¶One case of atypical adenomatous hyperplasia reclassified as adenocarcinoma in 2015.

50.9% of UKLS and 96.4% of ITALUNG screens. However, the rate of intervention for benign lesions was lower in ITALUNG (4.7% vs 10.3%).

In conclusion, the UKLS recruitment strategy increases the yield of screen-detected lung cancer compared with ITALUNG, but the gain is mild (19%). This supports the view that incorporation of additional risk factors of lung cancers as pulmonary emphysema[6] and serum biomarkers[7 8] in selection criteria of eligible subjects for LDCT screening might increase such a yield. Moreover, above data demonstrate feasibility of comparison of risk factors in subjects recruited in RCTs of lung cancer screening that is required before pooling and joint analysis of lung cancer mortality data.[9]

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**Contributors** MM devised the paper and wrote the paper draft, ALP reviewed the recruitment data and critically discussed the paper. LC critically discussed the risk factors data. FC critically reviewed the manuscript. FF critically discussed the radiological data. GP reviewed radiological data. EP critically revised the paper.

**Competing interests** None declared.

**Ethics approval** Local Ethic Committees of Florence, Pistoia and Pisa Hospitals (approval number 29–30 of 30 September 2003; number 23 of 27 October 2003; and number 00028543 of 13 May 2004.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data sharing statement** The authors intend to share the data from the ITALUNG study concerning recruitment, risk factors of eligible subjects and results of LDCT screening.

**To cite** Mascalchi M, Lopes Pegna A, Carrozzi L, *et al*. *Thorax* 2016;**71**:950–951.

Received 28 January 2016
Accepted 25 April 2016
Published Online First 23 May 2016

*Thorax* 2016;**71**:950–951.
doi:10.1136/thoraxjnl-2016-208409

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