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Articles selected and commented on by: **Dr Henry Marshall**, University of Queensland Thoracic Research Centre, Department of Thoracic Medicine, The Prince Charles Hospital, Brisbane

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Screening benefits

Impact of low-dose CT screening on smoking cessation among high-risk participants in the UK Lung Cancer Screening Trial.

Brain, K., et al.

Thorax 2017, 72: 912-918.

http://thorax.bmj.com/content/72/10/912.long

The UK Lung Cancer Screening (UKLS) Pilot Trial randomised 4055 high-risk individuals aged 50-75 years to LDCT or non-screening control. Self-reported smoking status was analysed at baseline, at T1 (2 weeks after baseline scan results or control assignment) and T2 (up to 2 years after recruitment) using adjusted Intention-to-treat (ITT) regression analysis.

RESULTS: 1546 (38%) were baseline smokers (759 intervention, 787 control). Smoking cessation rates were 8% (control n=36/479) versus 14% (intervention n=75/527) at T1 and 21% (control n=79/377) versus 24% (intervention n=115/488) at T2. Adjusted OR of quitting were significantly higher in the screenees than controls at both time-points (T1 aOR 2.38, 95% CI 1.56 to 3.64; T2 aOR 1.60, 95% CI 1.17 to 2.18). Intervention participants who needed additional clinical investigation were more likely to quit in the longer term compared with the control group (aOR 2.29, 95% CI 1.62 to 3.22, p=0.007) and those receiving a negative result (aOR 2.43, 95% CI 1.54 to 3.84, p<0.001).

CONCLUSION: In line with previous reports, lung cancer screening presents a teachable moment for smoking cessation, especially among those with a positive scan result.

Screening harms

Long-term psychosocial outcomes of low-dose CT screening: results of the UK Lung Cancer Screening randomised controlled trial.

Brain, K., K. J. Lifford, et al.

Thorax 2017, 71: 996-1005

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5099188/

UKLS participants completed questionnaires on cancer distress, anxiety, depression and decision satisfaction at baseline (T0), T1 (2 weeks after baseline scan results or control assignment, completed by 84% intervention and 78% control group) and T2 (up to 2 years after recruitment, completed by 82% intervention and 65% control group).

RESULTS: Positive screening results produced temporarily higher cancer distress at T1 (p≤0.001) but not at T2 (p=0.04). Anxiety and depression were higher in the control arm at T2 but the absolute differences were small and not clinically relevant. Cancer distress was higher in women, participants aged ≤65 years, current smokers, those with lung cancer experience and those recruited from the Liverpool area.

CONCLUSION: Similar to prior studies, screening does not appear to have clinically significant long-term psychosocial impacts.

Exposure to low dose computed tomography for lung cancer screening and risk of cancer: Secondary analysis of trial data and risk-benefit analysis.

Rampinelli C, et al.

BMJ 2017;356:j347

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5421449/

COSMOS, a non-randomised, single centre screening trial estimated cumulative radiation exposure and lifetime attributable risk of cancer following 10 years of annual LDCT screening in 5,203 participants aged 50 and older, current or former smokers (≥20 pack years).

RESULTS: 42,228 low dose CT and 635 PET CT scans were undertaken. After 10 years of CT screening, median cumulative effective dose was 9.3 mSv for men and 13.0 mSv for women. Lifetime attributable risk of lung cancer and major cancers ranged from 5.5 to 1.4 per 10,000 men screened, and from 8.1 to 2.6 per 10,000 women screened. In women aged 50-54, the lifetime attributable risk of lung cancer and major cancers was about fourfold and threefold higher than for men aged 65 and older, respectively. The estimated numbers of lung cancer and major cancer cases induced by 10 years of screening were 1.5 and 2.4, respectively, corresponding to an additional risk of induced major cancers of 0.05% (2.4/5203). 259 lung cancers were diagnosed thus one radiation induced major cancer would be expected for every 108 (259/2.4) screen-detected lung cancers.

CONCLUSION: Radiation exposure and cancer risk from low dose CT screening for lung cancer, even if non-negligible, can be considered acceptable in light of the substantial mortality reduction associated with screening.

Biomarkers

Multimodal lung cancer screening using the ITALUNG biomarker panel and low dose computed tomography. Results of the ITALUNG biomarker study.

Carozzi, F. M., et al.

Int J Cancer 2017, 141: 94-101.

http://onlinelibrary.wiley.com/doi/10.1002/ijc.30727/abstract

ITALUNG screening RCT retrospectively enriched a random subset of cancer-free intervention arm participants (n=481) with participants with prevalent or incident screen detected cancer (n=36) and analysed baseline blood and sputum for plasma DNA quantification, loss of heterozygosity and microsatellite instability. The biomarker panel (IBP) was considered positive if at least one of the two biomarkers was positive.

RESULTS: IBP was positive in 17/18 (94%) baseline screen detected lung cancers, 12/18 (66%) incident cancers and 34.9% of participants without lung cancer. Extrapolating across the entire screening arm, screening with IBP followed by LDCT if positive, improved specificity from 71% to 89% compared to LDCT alone, whilst maintaining sensitivity at 90%.

CONCLUSION: pre-screening with a biomarker panel could reduce the burden of LDCT scans.

Nodule detection and risk stratification

Comparing the performance of trained radiographers against experienced radiologists in the UK lung cancer screening (UKLS) trial.

Nair, A., et al.

Br J Radiol 2016, 89: 20160301.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5124804/

Four radiographers, trained in CT nodule detection, and three radiologists were prospectively evaluated. 290 CTs were independently read by 2 radiologists and 2 radiographers. The reference standard comprised all radiologist-identified positive nodules after arbitration of discrepancies (n=599 nodules in 209/290 (72.1%) CT studies). Relative sensitivity and average false positives (FPs) per case were compared for all cases read, as well as for subsets of cases read by each radiographer-radiologist combination (10 combinations).

RESULTS: The relative mean (+/-SD) sensitivity of the four radiographers was 71.6 +/- 8.5% compared with 83.3 +/- 8.1% for the three radiologists. Radiographers were less sensitive and detected more FPs per case than radiologists in 7/10 and 8/10 radiographer-radiologist combinations, respectively (ranges of difference 11.2-33.8% and 0.4-2.6; $p < 0.05$). For nodules ≥100 mm^3 in volume or ≥5 mm in maximum diameter, radiographers were relatively less sensitive in half the radiographer-radiologist combinations (range of difference 16.1-30.6%; $p < 0.05$).

CONCLUSION: Although overall radiographer performance was lower than that of experienced radiologists, some radiographer performances were comparable with that of radiologists especially when considering larger, potentially clinically relevant nodules. Radiographers may be able to fulfil the role of an assistant reader.

The Vancouver Lung Cancer Risk Prediction Model: Assessment by Using a Subset of the National Lung Screening Trial Cohort.

White, C. S., et al.

Radiology 2017, 283: 264-272.

http://pubs.rsna.org/doi/10.1148/radiol.2016152627

The Authors applied the PanCan nodule risk calculator (full model) to a NLST nodule subset of 116/270 (43%) individuals with a proven malignancy and 2703/6779 (39.9%) individuals without proven malignancy, yielding 4315 benign and 116 malignant nodules.

RESULTS: The NLST and Vancouver data sets differed in that the former included fewer nodules per study, fewer nonsolid nodules, and more nodule spiculation and emphysema. A composite risk score threshold of 10% was determined to be optimal, demonstrating sensitivity, specificity, positive predictive value, and negative predictive value of 85.3%, 93.9%, 27.4%, and 99.6%, respectively. The receiver operating characteristic curve demonstrated an area under the curve of 0.963 (95% CI: 0.945, 0.974).

CONCLUSION: the risk calculator had a high discriminant value, which supports the method to distinguish between benign and malignant nodules.

Incidental findings

Extrapulmonary Findings and Malignancies in Participants Screened With Chest CT in the National Lung Screening Trial.

Nguyen, X. V., et al.

J Am Coll Radiol 2017, 14: 324-330.

http://linkinghub.elsevier.com/retrieve/pii/S1546144016310092

CT scans from 17,309 NLST participants were retrospectively analyzed for clinically significant extrapulmonary findings, coded as "minor" or "potentially significant." Extrapulmonary malignancies diagnosed during screening were identified from medical records.

RESULTS: Extrapulmonary findings were noted in 58.7% of CT-screened participants, and 19.6% had findings coded as potentially significant. Potentially significant abnormalities were mostly cardiovascular (8.5%), followed by renal (2.4%), hepatobiliary (2.1%), adrenal (1.2%), and thyroid (0.6%). Sixty-seven participants (0.39%) had primary extrathoracic cancers diagnosed during screening. (0.26% (n = 45) kidney, 0.08% (n = 14) thyroid, and 0.05% (n = 8) liver cancers).

CONCLUSION: One in five patients screened with CT for lung cancer have extrapulmonary findings potentially requiring further evaluation. Extrapulmonary malignancies diagnosed during screening are uncommon. Indiscriminate workups of incidental findings could place a significant burden on the health care system with little benefit.

Screening interval

Low-dose computed tomography for lung cancer screening: comparison of performance between annual and biennial screen.

Sverzellati, N., et al.

Eur Radiol 2017, 26: 3821-3829

https://dx.doi.org/10.1007/s00330-016-4228-3

The MILD trial compared annual (LDCT1) or biennial (LDCT2) screening over median follow-up 7.3 years.

RESULTS: 1152 LDCT1 and 1151 LDCT2 participants underwent a total of 6893 and 4715 LDCT scans, respectively. The overall recall rate was higher in LDCT2 arm (6.97 %) than in LDCT1 arm (5.81 %) (p = 0.01), which was counterbalanced by the overall lower number of LDCT2 scans. No difference was observed for the overall LC detection rate (0.56 % in both arms). The two LDCT arms had similar specificity (99.2 % in both arms), sensitivity (73.5 %, in LDCT2 vs. 68.5 % in LDCT1, p = 0.62), PPV (42.4 %, in LDCT2, vs. 40.6 %, in LDCT1, p = 0.83) and NPV (99.8 %, in LDCT2 vs. 99.7 %, in LDCT1, p = 0.71).

CONCLUSION: Biennial screen may save about one third of LDCT scans with similar performance compared to annual screening.

Final screening round of the NELSON lung cancer screening trial: the effect of a 2.5-year screening interval.

Yousaf-Khan, U., et al.

Thorax 2017, 72: 48-56.

http://thorax.bmj.com/content/72/1/48.long

The Dutch-Belgian Lung Cancer Screening RCT (NELSON) screened 7915 participants using increasing interscan intervals: at baseline, after 1 year, 2 years and 2.5 years.

RESULTS: In the final round (round 4), 46 cancers were screen-detected and there were 28 interval cancers between the third and fourth screenings. Compared with the second round screening (1-year interval), a higher proportion of stage IIIb/IV cancers (17.3% vs 6.8%, p=0.02) and higher proportions of squamous-cell, bronchoalveolar and small-cell carcinomas (p=0.001) were detected in round 4. Compared with a 2-year interval, the 2.5-year interval showed a higher non-significant stage distribution (stage IIIb/IV 17.3% vs 5.2%, p=0.10). Additionally, more interval cancers manifested in the 2.5-year interval than in the intervals of previous rounds (28 vs 5 and 28 vs 19).

CONCLUSION: A 2.5-year interval reduced the effect of screening: the interval cancer rate and proportion of advanced disease stage was higher compared with the 1-year and 2-year intervals in the previous rounds.

Screenee selection/ risk stratification

Risk stratification based on screening history: the NELSON lung cancer screening study.

Yousaf-Khan, U., et al.

Thorax 2017, 72: 819-824.

http://thorax.bmj.com/content/72/9/819.long

The NELSON RCT investigated if prior screening results and lung cancer risk predicted screening result in the final (4^{th}) screening round. CT screening took place at baseline, and after 1, 2 and 2.5 years. Scan results could be negative, indeterminate or positive.

RESULTS: Based on results of the first three rounds, three subgroups were identified: (1) exclusively negative results (n=3856; 73.0%); (2) ≥1 indeterminate result, but never a positive result (n=1342; 25.5%); and (3) ≥1 positive result (n=81; 1.5%). Group 1 had the highest probability for having a negative scan result in round 4 (97.2% vs 94.8% and 90.1%, respectively, p<0.001), and the lowest risk for detecting lung cancer in round 4 (0.6% vs 1.6%, p=0.001). In multivariate analysis, 'Smoked pack-years' and 'screening history' significantly predicted the fourth round test result. The third round results implied that the risk for detecting lung cancer (after an interval of 2.5 years) was 0.6% for those with negative results compared with 3.7% of those with indeterminate results.

CONCLUSION: Previous CT lung cancer screening results provide an opportunity for further risk stratification of those who undergo lung cancer screening.

Identifying high risk individuals for targeted lung cancer screening: Independent validation of the PLCOm2012 risk prediction tool.

Weber M, et al.

***Int J Cancer* 2017;141:242-253**.

http://onlinelibrary.wiley.com/doi/10.1002/ijc.30673/abstract

Optimising the balance of benefits and harms Lung cancer screening via selection of a high risk population is critical. The authors aimed to validate the predictive performance of the PLCOm2012 logistic regression model in a cohort of 95,882 ever-smokers aged ≥45 years in the Australian 45 and Up Study.

RESULTS: 1,035 lung cancer diagnoses were identified. PLCOm2012 had good discrimination (area under the receiver-operating-characteristic-curve; AUC 0.80, 95%CI 0.78-0.81) and excellent calibration (mean and 90th percentiles of absolute risk difference between observed and predicted outcomes: 0.006 and 0.016, respectively). Sensitivity (69.4%, 95%CI, 65.6-73.0%) of the PLCOm2012 criteria in the 55-74 year age group for predicting lung cancers was greater than that using NLST eligibility criteria (≥30 pack-years smoking and ≤15 years quit; 57.3%, 53.3-61.3%; p < 0.0001), but specificity was lower (72.0%, 71.7-72.4% versus 75.2%, 74.8-75.6%, respectively; p < 0.0001).

CONCLUSION: Targeting high risk people for lung cancer screening using PLCOm2012 might improve the balance of benefits versus harms, and cost-effectiveness of lung cancer screening.

Participant selection for lung cancer screening by risk modelling (the pan-canadian early detection of lung cancer [PanCan] study): A single-arm, prospective study.

Tammemagi MC, et al.

***Lancet Oncol* 2017**

https://doi.org/10.1016/S1470-2045(17)30597-1

The Pan-Canadian Early Detection of Lung Cancer (PanCan) study prospectively assessed the efficacy of the PanCan lung cancer risk prediction model, a precursor to the validated PLCOm2012 model, to select candidates for LDCT lung cancer screening in eight centres across Canada. Participants were aged 50-75 years, ever-smokers, without history of lung cancer. Participants had ≥2% 6-year estimated risk of lung cancer and were screened at baseline (T0), and at 1 (T1) and 4 (T4) years post-baseline.

RESULTS: 2537 participants were followed for a median of 5.5 years (IQR 3.2-6.1). 172 lung cancers were diagnosed in 164 individuals (cumulative incidence 0.065 [95% CI 0.055-0.075], incidence rate 138.1 per 10,000 person-years [117.8-160.9]). There were ten interval lung cancers (6% of lung cancers and 6% of individuals with cancer): one diagnosed between T0 and T1, and nine between T1 and T4. Cumulative incidence was significantly higher than that observed in NLST (4.0%; p<0.0001). Compared with 593 (57%) of 1040 lung cancers observed in NLST, 133 (77%) of 172 lung cancers in the PanCan Study were early stage (I or II; p<0.0001).

CONCLUSION: The PanCan model was effective in identifying individuals who were subsequently diagnosed with early, potentially curable, lung cancer. The incidence of cancers detected and the proportion of early stage cancers in the screened population was higher than observed in previous studies. This approach should be considered for adoption in lung cancer screening programmes.

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Articles selected and commented on by Dr Henry Marshall, University of Queensland Thoracic Research Centre, Department of Thoracic Medicine, The Prince Charles Hospital, Brisbane

Editor in chief: Dr David CL Lam, Department of Medicine, University of Hong Kong, Hong Kong, China

Compiled by Dr Christel Norman, Respirology Editorial Office, Perth, Australia