Implementation of a Lung Cancer Screening Programme in the UK using low-dose Computed Tomography – does the literature support it?

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1. Introduction

In the United Kingdom (UK) there were approximately 46,403 new cases of lung cancer diagnosed in 2014. There were a reported 35,895 deaths directly related to the onset of lung cancer in the UK in 2014. Although there have been some significant improvements in the prognosis of other cancers in recent years, lung cancer is still associated with poor survival due to it being diagnosed predominantly at a later stage. The detection of lung cancer at an earlier stage (I-II) will usually indicate a better prognosis than those diagnosed with late stage lung cancer (III-IV). Primarily lung cancer is more prevalent in smokers; however it is not exclusive to this population group and is similarly prevalent in ex-smokers or those exposed to second hand smoke. [1] Currently there are no approved national screening programmes for lung cancer in the UK. The early diagnosis of lung cancer is difficult as significant symptoms do not present until a patient has progressed into a late stage of the disease. Therefore the early diagnosis of the disease through an approved national screening programme would be associated with early detection and prolonged survival.

Author & Date	Title & Country of Origin
Pedersen et al, 2009. [2]	'The Danish Randomised Lung Cancer CT Screening Trial – Overall Design and Results of the Prevalence Round.' (DLCST) Denmark
Van Klaveren et al, 2009. [3]	'Management of lung nodules detected by Volume CT scanning.' (NELSON) Belgium/ Netherlands
Aberle et al, 2011. [4]	'The National Lung Screening Trial: overview and study design.' (NLST) USA
Becker et al, 2012 [5]	'Randomized study on the early detection of lung cancer with MSCT in Germany: study design and results of the first screening round.' (LUSI) Germany
Field et al, 2016. [6]	'UK Lung cancer RCT pilot screening trial: baseline findings from the screening arm provide evidence for the potential implementation of lung cancer screening.' (UKLS) United Kingdom

Figure 1: Papers selected after application of inclusion and exclusion criteria.

2. Purpose

The aim of this review is to critically evaluate current literature looking at the use of low dose computed tomography (LDCT) in a lung cancer screening programme in the UK. To do this the primary focus of this literature review was to:

1) Critically appraise appropriately selected randomised control trials (RCT) that explore the use of LDCT as a diagnostic tool in a potential lung cancer screening programme.

2) Explore and highlight the potential advantages associated with a lung cancer screening programme; including the potential for less invasive treatments being utilised and the potential reductions in mortality.

3) Address the potential disadvantages to implementing a lung cancer screening programme in the UK.

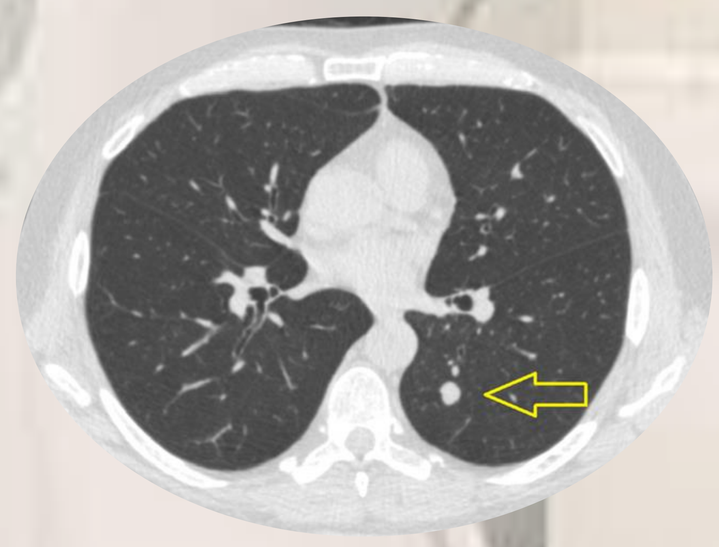

Figure 2: CT slice identifying detection of lung nodule (yellow arrow) derived from Ritchie et al (2016).[7]

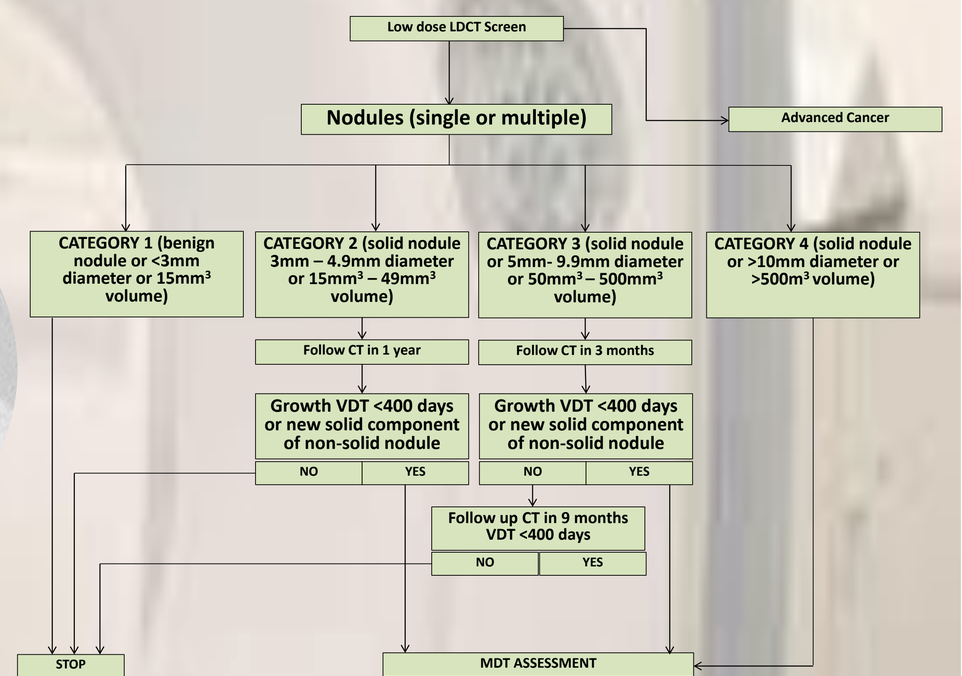

Figure 3: Lung nodule classification, interpretation and pathway derived from the UKLS trial (2016). [6]

3. Method

A literature search was conducted to identify articles which reported on the effect of LDCT in the screening of lung cancer. Papers were selected based on strict inclusion and exclusion criteria. The CASP tool was used to critically appraise and evaluate each paper. Through analysis of the papers further appropriate papers were identified by snowballing. The methods and results of the selected papers were critically reviewed. From this literature search, 5 relevant papers were selected based on the search criteria set in this review. (Fig 1) The critical analysis of these papers yielded consistent themes that enabled discussion for all 5 papers.

3.1. RCT: Method

Each RCT aimed to assess LDCT as a diagnostic tool for potential lung cancer screening programme with an overall endpoint of mortality reduction. The selection of participants followed a similar process throughout each trial; they all utilised a voluntary process, were based on risk stratification models and were all randomised into a screening and control arm. The method of scanning with LDCT was with initial base line scan followed by subsequent scans at varied intervals in each trial. The method of assessment of lung nodules (Fig 2) was also varied in each trial as they were based on trust specific protocols. (Fig 3)

4. Key Findings

- The NLST found an overall 20% reduction in lung cancer mortality using LDCT versus conventional chest x-ray.
- The NELSON found evidence for optimal screening interval time at 2.5 years which reduces the number of missed cancers.
- The analysis of cancerous nodules using volume (mm^3) rather than diameter (mm) increased sensitivity and the detection of early stage (I-II) lung cancer was significantly higher than late stage (III-IV) lung cancer in all the trials.

- The NLST data aside; other trials in this review can only speculate on the long term effects of LDCT screening on mortality.
- LDCT has high sensitivity but it is not specific for malignancy and therefore may result in false positive results.
- Evidence of inter-observer variability in the method of analysis of lung nodules across all trials.
- DLCST, LUSI and UKLS trials had low participant uptake; thus compromising the validity of the results.
- There was not a significant representation of lower socioeconomic groups in all the trials.

5. Conclusion

The implementation of a screening programme has the potential to reduce lung cancer related mortality in the UK. The detection of early stage (I-II) lung cancer is higher than late stage (III-IV) lung cancer due to the high sensitivity of LDCT. This will result in the use of less invasive treatments, thus improving patient QoL. However, lower socio-economic location with high smoking prevalence is associated with poorer uptake in the UKLS suggesting a false representation of the target population for screening. An inconsistent review system across the screening trials is open to observer variability and the potential negative impact of false-positive results and overdiagnosis are also evident. These barriers must be addressed to justify a lung cancer screening programme in the UK.[8, 9]

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6. References **[1]** Cancer Research UK. *Lung Cancer incidence statistics.* 2014. http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/lung-cancer/incidence. **[2]** Pedersen J, Ashraf H, Dirksen A, Toennesen P, Clemensten P, Richter K, et al. The Danish Randomised Lung Cancer CT Screening Trial – Overall Design and Results of the Prevalence Round . *Journal of Thoracic Oncology* 2009; 4(5): 608-614. **[3]** van Klaveren R, Ouderk M, Prokop M, Scholten E, Nackaerts K, et al. Management of lung nodules detected by Volume CT scanning. *The New England Journal of Medicine* 2009; 361(23): 2221-9. **[4]** Aberle D, Berg C, Black W, Church T, Fagerstrom R, Zylak C, et al. The National Lung Screening Trial: overview and study design. *Radiology* 2011; 258(1): 243-253. **[5]** Becker N, Motsch E, Gross M, Eigentopf A, Heussel C, Delorine S, et al. Randomized study on the early detection of lung cancer with MSCT in Germany: study design and results of the first screening round. *Journal of Cancer Research and Clinical Oncology* 2012; 138(9): 1475-1486. **[6]** Field J, Duffy S, Baldwin D, Devaraj A, Rintoul R, et al. UK Lung Cancer RCT Pilot Screening: baseline findings from the screening arm provide evidence for the potential implementation of lung cancer screening. *Thorax* 2016; 71(2): 161-170. **[7]** Ritchie A, Sanghera C, Jacobs C, Zhang W, Mayo J, et al. Computer Vision Tool and Technician as First Reader of Lung Cancer Screening CT Scans. *Journal of Thoracic Oncology* 2016; 11(5): 709-717. **[8]** Roy Castle Lung Cancer Foundation. *MP calls for lung cancer screening.* 2018. https://www.roycastle.org/news/mp-calls-for-lung-cancer-screening **[9]** BBC News: Health. *'my sister died of lung cancer but never smoked'.* 2018. https://www.bbc.co.uk/news/health-43034764

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