

Delivering low-dose CT screening for lung cancer: a pragmatic approach

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Lung cancer kills an estimated 35 000 people in the UK every year. Despite the improvements in treating late-stage disease, lung cancer outcomes have changed little in the last 40 years. Low-dose CT (LDCT) screening for lung cancer reduces lung cancer mortality by 20%–24% and all-cause mortality by 7%.^{1,2} Lung cancer screening (LCS) however remains contentious, particularly how to implement it in an efficient and efficacious way. This contention extends to the potential costs of screening—financial to the National Health Service (NHS), and physical and psychological harms to patients. These concerns are particularly relevant to how we manage both the findings we aim to detect through screening (pulmonary nodules) and those we pick up inadvertently (incidental findings). The SUMMIT Study is the largest CT screening study in Europe and a key endpoint is detailing the feasibility of delivering CT screening across a complete population within the NHS. We present here SUMMIT's approach to nodule and incidental findings management, a pragmatic model that is neither overly burdensome nor unsafe and provides a practical solution to some of the challenges of LDCT LCS.

THE SUMMIT STUDY

The SUMMIT study (ClinicalTrials.gov NCT03934866) is an LCS study recruiting individuals 55–77 years old at high risk of lung and other smoking-related cancers to LDCT screening. Its twin aims are to examine the performance of delivering an LDCT screening service for lung cancer to a high-risk population and to validate a cell-free nucleic acid blood test for detection of multiple cancers. The study began enrolment in April 2019 after the development of protocols for the management of pulmonary nodules and incidental findings that enabled a consistent approach to management across the entirety of the study

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(target recruitment of 25 000). The study aims to deliver a programme of LCS that is pragmatic, evidence-based, and practically deliverable by primary and secondary care, importantly avoiding overzealous investigation of all findings (and therefore potentially increasing harms). Examination of the evidence that medical intervention of incidental findings makes a difference to participants turns out to be sparse, making detailed radiological reporting probably unnecessary. The reader will see here that we provide only limited and highly specific information beyond the presence of lung cancer or pulmonary nodules. It is our hope that this balanced approach will be borne out in the data we collect, bolstering a safe, effective and efficient implementation of LCS. Studies on whether a future health service could manage a more holistic approach, aligning the reporting of incidental findings such as coronary artery calcification (CAC), early emphysema and other findings to a more personalised health intervention with intensive smoking advice, cardiovascular disease (CVD) prevention and the like, are urgently needed.

PULMONARY NODULES: THE EVIDENCE BASE

We use the existing evidence-based British Thoracic Society (BTS) guidelines on the management of pulmonary nodules, with some specific alterations. The BTS guidelines use nodule size and type, along with other criteria such as a nodule malignancy risk score (Brock score) and volume doubling time (VDT), to calculate appropriate follow-up management on a per-nodule basis. The SUMMIT algorithm follows this method closely, but was adapted in several key ways, including accommodation for a 3-year annual screening programme rather than a one-off CT chest; changes in the use of the Brock malignancy score; dispensing with VDT calculations in favour of a growth threshold of $\geq 25\%$ to inform management at 3 months; a minimum size requirement (200 mm^3) before referral to multidisciplinary team (MDT); and 12-month (vs 3-month) follow-up of pure ground glass lesions $\geq 5 \text{ mm}$. The complete SUMMIT Pulmonary Nodule Protocol is available in online supplementary figure S1.

Deviations were made from BTS guidelines either to minimise the burden on secondary care colleagues (eg, where MDT referral is not made until a growing nodule is $\geq 200 \text{ mm}^3$) or where new evidence suggests a safe but more conservative approach (eg, with ground-glass nodules, which often resolve or, if persistent, are unlikely to require immediate intervention). The result, we hope, is a blueprint for managing pulmonary nodules in a safe but measured way, minimising unnecessary stress on patients and providers, while intervening appropriately in those nodules most likely to cause harm.

THE CHALLENGE OF INCIDENTAL FINDINGS

There is considerably less evidence for the appropriate management of incidentally detected non-nodule findings at LCS LDCT, and opinion is split about whether or not to follow up all findings, some or none (see online supplementary table S1). The NELSON trial has publicly stated that following up even potentially clinically relevant radiological incidental findings does not provide any benefit.³ Other LCS professionals advocate that far more findings are reported back and/or investigated further.⁴ Given the heterogeneity of evidence, and our wish to create a low interventional burden approach to screening, the SUMMIT protocol reports back incidental findings only where there is an evidence-based clinical action that can be taken to mitigate or further investigate and treat that finding, leading to patient benefit.

The importance of taking a pragmatic approach is highlighted by the fact that incidental findings may be seen in nearly 100% of participants undergoing lung screening, according to some reports. Identifying and potentially investigating such a high frequency of incidental findings clearly have the potential to constrain lung screening implementation.

Based on the study team's experience delivering the Lung Screen Uptake Trial (LSUT), we had a good understanding of the impact on primary and secondary care colleagues and participants alike when all radiological findings are reported back. The most common incidental findings at LCS are CAC and emphysema, the detection and management of which in the LCS population have been widely discussed but variably applied. CAC is often detected on LDCT and the screening target demographic is at increased risk of CVD due to their smoking histories and ages; because of this, American LCS screening programmes are encouraged to report back CAC to screenees in order

to instigate primary prevention, where appropriate.⁴ In the UK, however, instigation of appropriate management of CVD is based on the calculation of a QRISK2 score. From LSUT data, the vast majority (projected figure >90%) of the SUMMIT population are expected to have a QRISK2 score greater than 10%, the threshold for instigation of primary prevention.⁵ After consultation with cardiology and general practice colleagues, the study team elected to include a prompt in all letters to participants' general practitioners (GPs) recommending assessment via QRISK2 score, an approach which avoids communicating a CAC score, which provides no additional prognostic information nor evidence base for intervention.

Emphysema on CT is another area of contention within the screening and wider lung cancer community. The appearance of emphysema is not currently a criterion for the diagnosis of COPD in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines, unlike spirometric demonstration of airflow limitation and symptomatology. Reporting back the presence and/or severity of emphysema on LDCT will not lead to a diagnosis of COPD; however, the study does report back to GPs prebronchodilator spirometry values and, if the participant does not report a pre-existing diagnosis of COPD but has symptoms and airflow limitation on spirometry (FEV1:FVC <0.7), a recommendation is provided to the GP to investigate the person formally for COPD. There may be good reasons to report back emphysema, or indeed CAC, to participants as a 'teachable moment' to aid smoking cessation, but evidence is still being gathered to support this assertion. Labelling a participant as having emphysema or CAC may also have psychological downsides as well as adverse consequences for health insurance.

The SUMMIT clinical team is cognizant that undiagnosed non-lung cancers may present on an LDCT performed as part of LCS. Again, the appearances that are sometimes consistent with cancer may also represent benign pathology. Currently there is no evidence that screening for thoracic or upper abdominal cancer (other than lung cancer) with CT is beneficial to screenees. But instead of deciding that there is 'neglectable benefit'³ in investigating appearances potentially consistent with non-lung cancers, we have implemented what we think is a sensible, often stepped, approach to further investigation

and management. For example, adrenal nodules identified on LDCT are assessed for size and density, with those of smaller diameter (1–4 cm) or Hounsfield units >10 being rescanned within the study in a year's time to look for stability, and those of larger size instigating immediate referral. This approach is consistent with the American College of Radiology's white paper on abdominal incidental findings and, we believe, strikes a balance between intervening in potentially long-standing and stable appearances, and aiding the diagnosis of otherwise unknown cancers. A similarly pragmatic approach was taken to thyroid nodules and other non-malignant findings (see online supplementary table S1 for more information).

While these protocols may appear complicated, because bespoke reporting proformas and software have been developed for use in SUMMIT, and findings indicated therein are ingested into the software directly, users are automatically presented with the 'correct' management for each scan and are not required to reference these protocols directly themselves. Radiologists may over-ride the management suggested by the software if they feel another management approach is indicated. This means that while the protocols may be detailed, their implementation is user-friendly but flexible where appropriate. Ultimately, the utility of identifying and investigating non-lung-cancer findings in LCS is yet to be determined, and outcome data from SUMMIT may help the wider LCS community understand which findings should be investigated and those that should be ignored.

SUMMIT has used the evidence available in order to develop and implement a consistent approach to findings on LDCT. Compared with breast and cervical cancer screening programmes, LCS is in its relative infancy. We cannot yet be expected to have all the answers on how to deliver it. A pragmatic approach to pulmonary nodules and incidental findings management at LDCT screening will enable us to build a screening programme without causing the collapse of supporting primary and secondary care services, and can be refined in the future, allowing a fledgling service to begin to change lung cancer outcomes now.

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