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Title:

Achieving earlier diagnosis of symptomatic lung cancer

Authors:
The Roy Castle Lung Cancer Foundation working group on symptomatic diagnosis

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Why focus on symptomatic lung cancer?

Lung cancer is the largest cause of cancer death, with 1.8 million deaths worldwide per year.[1] Despite important improvements in treatment, outcomes remain poor compared with other common cancers. In England and Wales one year survival is only 48%.[2] Stage of cancer and performance status (PS) are the strongest independent predictors of survival. The adjusted hazard ratio for death was 4.39 for PS 4 (the most impaired PS category) compared to PS 0 (the least impaired category) and 4.58 for stage IV compared with IA-IB in the English National Lung Cancer Audit.[3] Unfortunately, almost half of lung cancer patients are diagnosed with stage IV disease in England[4] and 47% of patients present at PS 2-4[5] when they are not eligible for most systemic treatments. Furthermore, systemic treatments are more effective in fitter patients. Achieving diagnosis of lung cancer in earlier stages of the disease is therefore crucial to improving survival.

Targeted screening using low dose computed tomography (LDCT) is an important way to reduce lung cancer mortality, and implementing national programmes across the United Kingdom following the recommendation of the National Screening Committee is vital. However the majority of patients will present via the symptomatic route. More than half of lung cancers arise in people who would not meet the eligibility criteria for screening[6] and of those eligible, only around a half choose to participate.[7]

Evidence suggests there is an opportunity to bring forward the diagnosis in people with symptoms and given that many patients deteriorate prior to diagnosis, this could have important impacts on treatment eligibility and efficacy. The median symptom lead time to diagnosis of lung cancer is three months[8] and 33% of those with lung cancer who attend general practice before diagnosis have three or more consultations prior to referral.[9] An Australian study has shown that in retrospect, numbers of blood tests are increased in those with lung cancer six months prior to diagnosis and that these patients frequently have abnormal inflammatory markers and full blood counts.[10] Similarly, a Danish population cohort study has demonstrated that 93% of those with lung cancer consult with their GP in the year prior to diagnosis and that those subsequently diagnosed with lung cancer have more frequent contacts with their GP and increased activity such as investigations and antibiotic prescriptions, than comparator patients who do not have lung cancer. [11] However, most patients who present with possible lung cancer symptoms do not receive imaging with chest x-ray (CXR) within two weeks as recommended by guidelines.[12] Along with the summary recommendations presented in this analysis paper, a comprehensive version of this review is available (Supplement).

Promoting awareness of lung cancer symptoms and help-seeking

Concern about not wishing to take up doctors' time has been identified as a barrier to symptomatic presentation, particularly in the UK. Patients most affected by such concerns also estimate that they would wait longer before consulting with a GP (odds ratio of anticipated interval ≥ 4 weeks 2.50, 95% CI 2.27 to 2.75).[13] Therefore, in addition to raising awareness of symptoms, efforts are required to address three aspects of behaviour change important to earlier presentation - motivation, capability and opportunity.[14] A validation-endorsement-motivation-action framework has been proposed to help patients who are deterred from presenting to health services by fear that medical professionals will dismiss their symptoms as not worthy of concern or investigation.[15]

Campaigns should feature the recognisable branding of the health service prominently to convey a sense of official endorsement and to assure patients that their health service encourages them to seek help for symptoms. Inclusive approaches are required to maximise reach to those with less fluency in English, who have lower levels of health literacy and/or learning disabilities. Focusing on a positive message that early presentation improves the chances of effective treatment is important to confront nihilism about the disease and to motivate patients to present.

Messaging should also communicate that lung cancer also occurs in those who have never smoked, and thus encourage prompt presentation for persistent symptoms.[16] To maintain their profile and public engagement, awareness campaigns should be funded as a long-term commitment, with continuous evaluation to enable content to be refined and updated. Campaigns have tended to focus on the most common symptoms (cough) and there is some evidence this has achieved greater public recognition of this symptom. The expert group highlighted the need to strike a balance between communicating a clear message, for example focusing on cough, whilst not neglecting the range of symptoms which could represent lung cancer. A campaign using a range of media, with links to further information across or even the capacity to check cancer symptoms, for example on the NHS app, may be warranted. Messaging should also address factors that influence capability to seek help such as how to request assessment. It is important to recognise that many patients currently struggle to arrange general practice appointments. Similarly, the adoption of triaging systems and the increased use of remote consultations may add barriers to prompt diagnosis since face-to-face discussion and examination may now be less readily available in many practices.

Supporting early investigation for possible lung cancer in primary care

CXR in diagnosis of symptomatic lung cancer

Guidelines worldwide recommend CXR as the first line test for the majority of lung cancer presentations.[17] CXRs are less costly and can be reported in around a fifth of the time taken for a CT scan.[18] Therefore, CXR is suitable as a high volume investigation for large numbers of patients at relatively low levels of risk, with English GPs requesting 2.1 million CXRs in 2022-2023, compared to less than 100,000 abdominal or chest CTs.[19] However, the sensitivity of CXR for lung cancer in symptomatic patients in primary care is approximately 80%. Therefore, both the use and interpretation of negative results requires consideration of both pre-test probability of lung cancer, persistence of symptomatology and patient concern. For example, patients with haemoptysis have a risk of having lung cancer of 3% even after a negative CXR and may warrant CT as the first line test.[20]

Research on rates of referral for cancer and disease outcomes in the UK has demonstrated a reduced risk of death from lung cancer in patients from GP practices in the highest tertile for referrals on the urgent suspected cancer pathway compared to the lowest tertile (HR 0.95, 95% CI 0.94-0.97).[21] Variation in the use of CXR may be a crucial underlying cause of differences in referral rates for suspected cancer. UK GPs appear to be less likely to arrange investigation for symptomatic patients, compared to their peers in similar health systems. A vignette study has suggested that UK GPs were less likely to arrange cancer investigation including CXR.[22] There is scope for interventions targeted at primary care providers who use CXR infrequently to encourage greater testing of symptomatic patients.[23] In particular, we recommended that existing information on annual numbers of CXRs performed per practice should be provided to practices alongside other cancer metrics such as urgent suspected cancer referral rates.

Improving access through patient-initiated investigation and referral

Given present difficulties patients face in accessing primary care in several healthcare systems, widespread adoption of services which enable patients to arrange investigation without a GP consultation warrants urgent consideration. Self-request CXR services have been established in English regions including Leeds and Greater Manchester. Patients who fulfil symptom criteria, based on those specified by the National Institute for Health and Care Excellence, are enabled to access radiology services directly, with the report of their x-ray sent to their GP. Patients are advised that because the test does not identify all lung cancers and because symptoms may be caused by other serious problems that they should still consult with their GP if these persist. Patients also need to be informed that haemoptysis requires assessment regardless of CXR findings.[20] The prevalence of lung cancer amongst patients investigated via self-referral and those who have CXR arranged in the

conventional way by GP are similar and these services have been targeted effectively at deprived population groups, with higher levels of uptake from these communities.[20] An alternative approach, currently under evaluation in some areas including Nottingham, is for patients with symptoms to access a lung cancer concern telephone hotline which applies a risk stratification algorithm to determine the imaging modality (either CXR or CT) along with 'safety-netting' advice for lower risk patients who are investigated with CXR only.

Direct access to CT from general practice

Despite high degrees of concordance between guidelines worldwide, the extent to which GPs in different healthcare systems request CT is highly variable. The low levels of investigation with CT from general practice in the UK[24] compared to other high-income countries may reflect greater capacity constraints in delivering CT and uncertainty about the indications.

Since 2022, policy in the English NHS has been that GPs should have direct access to urgent CT for circumstances in which lung cancer is suspected but criteria for urgent cancer referral are not met. Barriers to this include radiology capacity, implementing pathways locally, and supporting GPs with guidance on modality of imaging according to risk. Without appropriate and clear guidance on risk stratification, this could lead to a detrimental impact on CT capacity with a suboptimal return in earlier diagnosis. Thus, the primary imaging modality should be determined according to risk stratification based on basic patient characteristics, such as age, smoking status and symptoms along with modelling of likely impact on capacity to ensure services are not overwhelmed. In the absence of such evidence, it remains very challenging for GPs who have access to direct access CT to decide for which patients should be investigated using direct access CT, either as a first line test instead of CXR, or following an unremarkable CXR if symptoms persist. Formulation of clear guidance, informed by consideration of radiology capacity, should be prioritised to support GPs to decide when to use direct access CT. Even where robust evidence is not currently available there may be a role for consensus-based guidelines formulated by a multi-disciplinary group.

Mitigating risk of diagnostic delay resulting from lung cancer not identified on chest x-ray

Patients who are deemed to have a high pre-test probability of cancer or other serious illness warrant planned follow-up with a clinician who is aware of the degree of concern, to ensure appropriate further management is in place, including immediate referral for CT. For those with lower risk, alternative strategies are required to ensure the possibility of lung cancer is not overlooked. The development of automated trigger-based interventions or other monitoring systems should be prioritised to reduce risk of diagnostic delay resulting from failure to reassess patients who have

symptoms which persist or evolve. Pro-active safety-netting interventions, implemented at a system level rather than on individual clinician initiative could have a role in encouraging patients to re-present if symptoms have persisted or worsened. Such measures could include an automated text message following an interval after CXR investigation prompting patients to re-consult if symptoms have persisted. It is also important that general practices have robust systems in place to ensure that planned repeat imaging or assessment occurs for those who have had abnormal imaging for which repeat imaging after an interval (e.g. 6-8 weeks) is recommended.

Expediting lung cancer diagnosis in people who have never smoked

Worldwide over 10% of those diagnosed with lung cancer have never smoked,[20] a proportion which will increase as smoking rates decline. People who have never smoked experience barriers to investigation. A qualitative study of lung cancer patients' experiences found that smoking history was instrumental to how individuals perceived and responded to early symptoms of lung cancer, resulting in risk of diagnostic delay for those without a smoking history.[25] GPs should be encouraged to have a low threshold to use CXR in patients who have never smoked but who have persistent symptoms. Interventions to achieve this include improving GP awareness which should include information regarding the extremely low radiation dose from a CXR.

Conclusion

Substantial progress has been made in lung cancer care over the last two decades, but much more improvement is required in achieving earlier diagnosis of symptomatic lung cancer. Early identification of lung cancer in symptomatic people before they become unfit for treatment is now even more important because of the marked improvement in outcomes seen with modern treatment. To achieve this, the expert group recommend enhancing messaging to increase awareness of symptoms and motivate and empower people to act should symptoms arise. Health systems need to be ready to provide improved access to services, timely imaging with an appropriate modality along with safety netting for those with normal initial imaging receive further assessment should symptoms persist or worsen. A summary of recommendations is presented in box 1.

Promoting symptom awareness and help-seeking

- Campaigns should be endorsed by health authorities and assure patients that help seeking is encouraged.
- Messaging needs to be clear and designed reach people who have never smoked, as well as those who have.
- Awareness campaigns should be funded as a long-term commitment, with continuous evaluation and regular refinement and updating of content.

Facilitating prompt investigation for possible symptoms of lung cancer

- Provide accessible data on imaging utilisation (e.g. annual number of CXRs requested by general practices) to identify services where patients may benefit from increased opportunistic investigation
- Facilitate access to investigation through patient-initiated pathways (e.g. self-request CXR or lung cancer hotline)
- Formulate clear guidance for GPs on when to use direct access to CT using expert consensus where robust evidence is not available

Mitigating diagnostic delays in those at low risk and who have had negative initial investigation

- Promote consideration of imaging for those at low risk (including never smokers) who have symptoms, particularly if persistent and/or patient/clinician concern
- Provide guidance for GPs, through expert consensus if insufficient evidence available, on patients for whom CT should be considered following a negative CXR
- Support GPs to provide specific ‘safety-netting’ advice to encourage patients to re-present if symptoms persist or evolve

Box 1: Summary of recommendations to improve symptomatic diagnosis of lung cancer

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Author Contributions

The paper was authored by Stephen H. Bradley (stephen.bradley@sheffield.ac.uk), David Baldwin, Bobby Sudhir Kumar Bhartia, Georgia B Black, Matthew EJ Callister, Karen Clayton, Sinan R Eccles, Matthew Evison, Jesme Fox, Willie Hamilton, Judit Konya, Richard W. Lee, Samuel W D Merriel, Neal Navani, Ben Noble, Samantha L Quaife, Amelia Randle, Janette Rawlinson Michael Richards, Nick Woznitza and Emma O'Dowd.

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Competing interests

JF is the medical director of the Roy Castle Lung Cancer Foundation

SWD is Associate Editor and Editorial Board member of the *British Journal of General Practice.*MR reports that he is chair of the UK National Screening Committee and is an advisor to NHS England on diagnostic services.

NW is a member of the College of Radiographers AI and Diagnostic Imaging advisory groups, the Royal College of Radiologists group for validation standards for thoracic AI and College of Radiographers & Royal College of Radiologists CXR reporting standards joint working group

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