The Practitioner
1868-2022 Supporting general practitioners for more than 150 years

# Early diagnosis the main driver to improving outcomes in lung cancer

Thu A, O'Dowd EL, Baldwin DR. Early diagnosis the main driver to improving outcomes in lung cancer. *Practitioner* November/December 2022;266(1863):11-15

**Abstract**

**Earlier diagnosis of lung cancer improves outcomes for two main reasons. First, the disease stage may be earlier allowing more chance of curative-intent treatment. Second, patients may be fitter at presentation. Functional status is one of the most important independent predictors of survival. Although lung cancer is caused by smoking in 80-85% of cases, around 6,000 patients per year do not have smoking-attributable lung cancer and 3,500 patients have never smoked. These patients are often diagnosed late, so it is important to refer patients who have persistent symptoms either for chest X-ray, or when symptoms persist and no alternative diagnosis is found, refer for consideration of CT. NHS England has started a phased implementation of screening with low radiation dose CT in areas with a high incidence and mortality from lung cancer, the Targeted Lung Health Check programme. More than 1,200 cancers have been detected and 76% are stage I/II. For those with early stage disease, unwilling or unable to undergo surgery, curative-intent radiotherapy such as stereotactic ablative body radiotherapy is widely available. Advances in stereotactic radiosurgery mean many patients with brain metastases can still be treated with curative intent. Smoking cessation advice and therapy should be integral to the management of lung cancer, whether suspected or confirmed and when screening. Smoking cessation improves outcomes for all stages of lung cancer.**

Dr Akari Thu
MB BS MRCP
Specialist Registrar,
Nottingham University Hospitals NHS Trust,
Nottingham, UK

Dr Emma L O'Dowd
MBBS(Hons) MRCP PhD
Consultant Respiratory Physician,
Honorary Associate Professor,
Nottingham University Hospitals NHS Trust,
Nottingham, UK

Professor David R Baldwin
MD FRCP
Consultant Respiratory Physician,
Honorary Professor of Medicine,
Nottingham University Hospitals NHS Trust,
and University of Nottingham,
Nottingham, UK

Practitioner
Medical Publishing Ltd

# Early diagnosis the main driver to improving outcomes in lung cancer

**AUTHORS**
**Dr Akari Thu**
MB BS MRCP
Specialist Registrar, Nottingham University Hospitals NHS Trust, Nottingham, UK

**Dr Emma L O'Dowd**
MBBS(Hons) MRCP PhD
Consultant Respiratory Physician, Honorary Associate Professor, Nottingham University Hospitals NHS Trust, Nottingham, UK

**Professor David R Baldwin**
MD FRCP
Consultant Respiratory Physician, Honorary Professor of Medicine, Nottingham University Hospitals NHS Trust, and University of Nottingham, Nottingham, UK

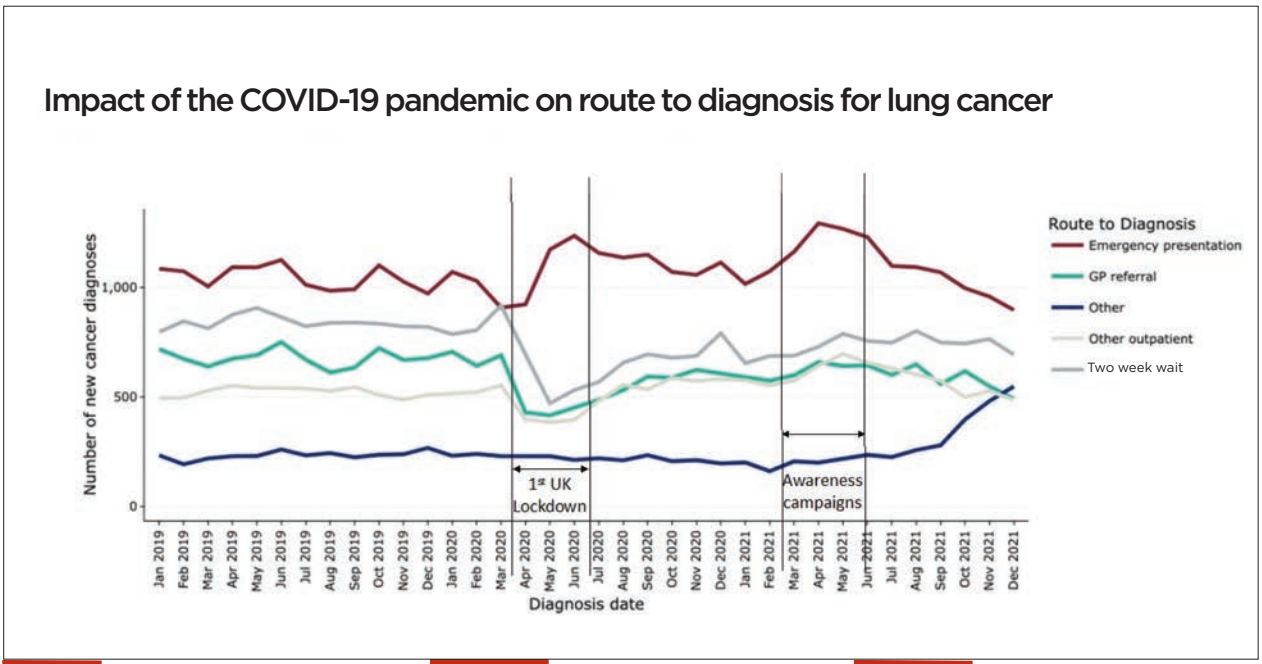



**FIGURE 1**
Impact of the COVID-19 pandemic on route to diagnosis for lung cancer[4]

## How can early diagnosis be improved?

**EARLY DIAGNOSIS OF LUNG CANCER IS FUNDAMENTAL TO IMPROVING OUTCOMES IN A CANCER THAT KILLS** more people than breast and bowel cancer combined in the UK. In 2017-2019, there were 34,771 deaths from lung cancer compared with 11,500 from breast cancer and 17,707 from bowel cancer.[1]

Progress was being made over the past 15 years with the International Cancer Benchmarking Partnership showing a doubling of five-year survival from 7.2% in 1995-1999 to 14.7% in 2010-14.[2,3] With improved systemic anti-cancer treatment (SACT) and screening starting this looked set to improve further until the COVID-19 pandemic. The pandemic served to show just how important early diagnosis is in what is often a rapidly lethal cancer.

Immediately following the first lockdown, where patients with a cough were encouraged to stay at home, the incidence of diagnosed lung cancer fell by up to 30% as shown by the rapid cancer dataset.[4]

Furthermore, there was no compensatory increase in diagnoses later in the year and in fact incidence rates took more than a year to get back to expected levels. Secondary care services were maintained for cancer patients, so the root cause was the lack of patients presenting and subsequent referral.

Of those that did present, a stage shift towards later disease was seen and survival was reduced to levels seen 15 years ago. The National Lung Cancer Audit reported a reduction in curative treatment rates for patients with non-small cell lung cancer with good performance status and at stage I/II from 81% in 2019 to 73% in 2020 and surgical resection rates fell in 2020 from 20% to 15% which is similar to the rate ten years ago.[5] Thus, the impact of the COVID-19 pandemic illustrates that early diagnosis is the principal driver of the improvements we had seen.

## What are the criteria for urgent referral in suspected cases?

## What are the management options?

### AUGMENTING EARLY DIAGNOSIS

Earlier diagnosis of lung cancer improves outcomes for two main reasons. First, patients may be at an earlier stage allowing more chance of curative-intent treatment. Second, patients may be fitter at presentation. Functional status, as measured by WHO performance status, is one of the most important independent predictors of survival.[6] When first seen in secondary care clinics, it is common for patients to report a decline in their fitness in the past few weeks. Today SACT is more effective, and indeed only recommended, for patients with adequate performance status (WHO 0, 1 and 2) for some SACT.

The focus should therefore be on restoration of early diagnosis which is a significant challenge. Early diagnosis of clinical presentation is achieved through patients seeking advice early, easy access to healthcare assessment and prompt investigation and diagnosis.

Awareness campaigns for lung cancer were piloted in 2012 and »

rolled out after showing a significant increase in referrals and curative surgery.[7] Research from Leeds has shown that these, and GP educational events, are associated with a greater number of chest X-rays (CXR) being performed and a better stage distribution of diagnosed lung cancer.[8] However, recent 'route to diagnosis' data show that awareness campaigns have resulted in minimal increase in referrals from primary care and instead more diagnoses through the emergency route (see figure 1, p11).[4]

Restoring easy access for patients is essential and GPs should be familiar with the NICE referral guidelines for suspected cancer (see table 1, below).[9] One proposal that is being piloted, in several sites in England and one in Wales, is a 'lung cancer concern hotline'. Awareness campaigns are linked to a hotline that allows patients to be risk assessed according to symptoms, age and smoking status and triaged into observation, CXR or CT. This has the potential to bring diagnosis forward considerably and results from pilots are awaited.

The model varies but one pilot in Nottingham targets patients at specific primary care practices with information about the symptoms of lung cancer and a number to call if these symptoms are present. Trained administration staff ask a series of questions which may then trigger a referral to respiratory medicine consultants who decide if a CT is appropriate. This model allows the risk assessment algorithm to be tested and changed according to the outcomes.

Although lung cancer is caused by smoking in 80-85% of cases, this leaves around 6,000 patients per year who do not have smoking-attributable lung cancer and 3,500 who have never smoked. These patients are often diagnosed late, so it is important to refer patients who have persistent symptoms either for CXR, or when symptoms persist and no alternative diagnosis is found, refer for consideration of CT.

**Table 1**

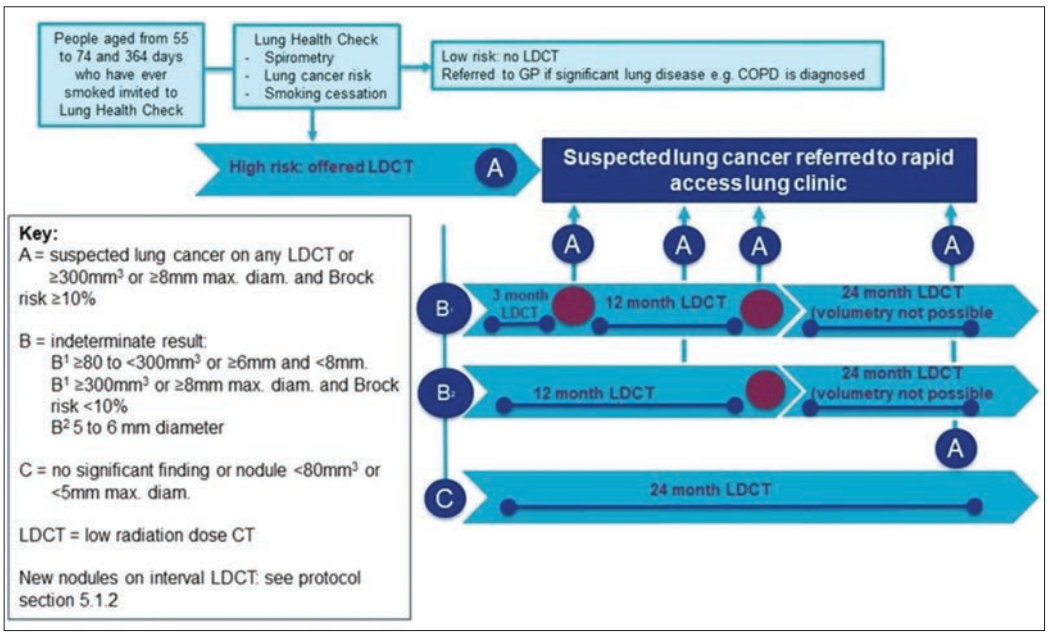
**NICE (NG12) referral and investigation criteria for suspected lung cancer[9]**

**Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for lung cancer if they:**
- Have chest X-ray findings that suggest lung cancer or
- Are aged 40 and over with unexplained haemoptysis

**Offer an urgent chest X-ray (to be done within 2 weeks) to assess for lung cancer in people aged 40 and over if they have 2 or more of the following unexplained symptoms, or if they have ever smoked and have 1 or more of the following unexplained symptoms:**
- Cough
- Fatigue
- Shortness of breath
- Chest pain
- Weight loss
- Appetite loss

**Consider an urgent chest X-ray (to be done within 2 weeks) to assess for lung cancer in people aged 40 and over with any of the following:**
- Persistent or recurrent chest infection
- Finger clubbing
- Supraclavicular lymphadenopathy or persistent cervical lymphadenopathy
- Chest signs consistent with lung cancer
- Thrombocytosis

**FIGURE 2**
Summary of the Targeted Lung Health Check[17]




## LUNG CANCER SCREENING

Screening is another way to achieve early diagnosis. This aims to detect lung cancer at a much earlier stage so that more curative-intent treatment can be given, and mortality reduced.

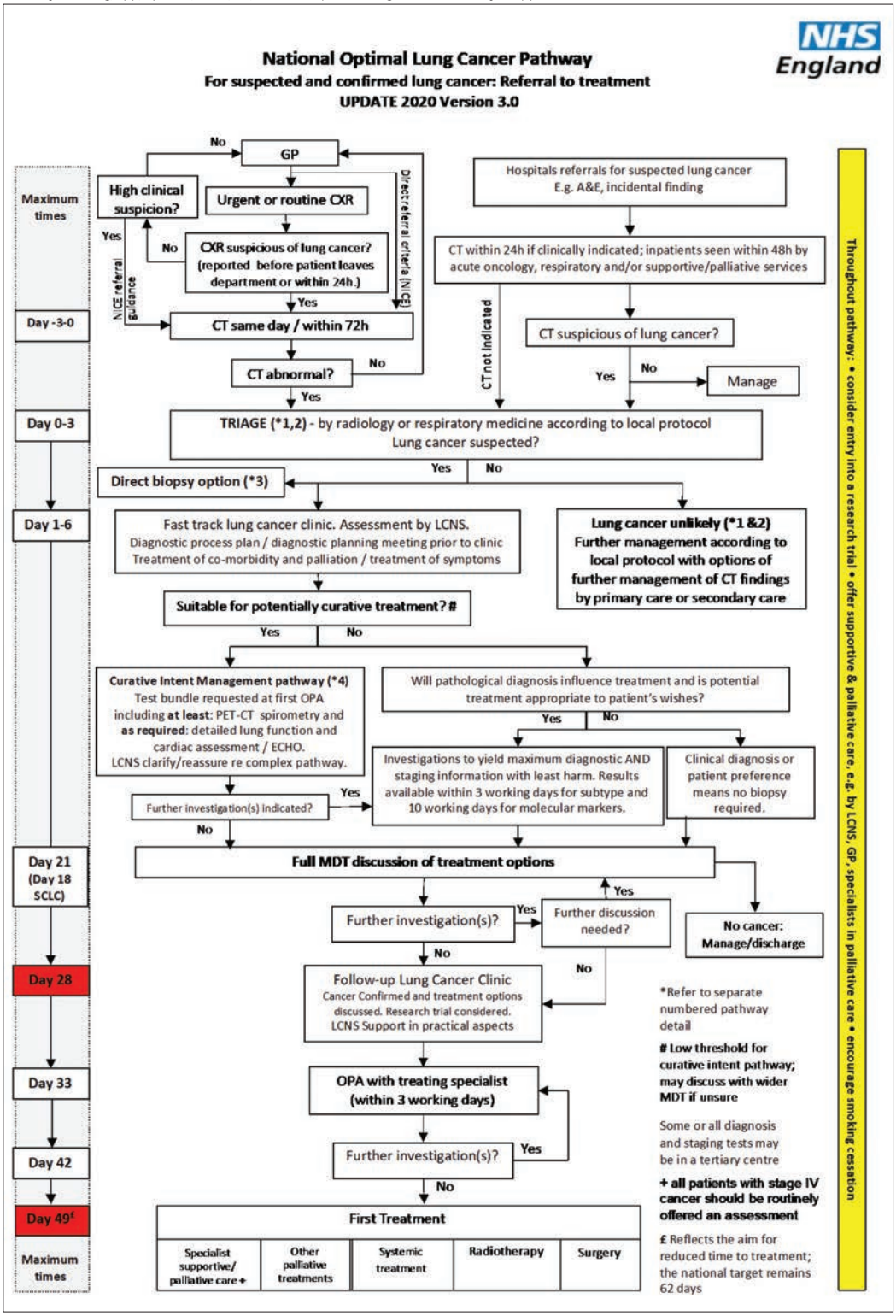
Given the fact that 65% of people with lung cancer present with stage III or IV disease, when five-year survival is 13% and 3% respectively, screening with CT, which reduces stage III and IV to around 20% would be expected to reduce mortality substantially because five-year survival in stage I and II is 57% and 34% respectively.[10] However, screening detects very early stage disease in about 65% of those found to have lung cancer when the five-year survival is 90% for stage IA1 and 80% for stage IA2.[11,12] Two large randomised controlled trials have confirmed this and meta-analyses that include other smaller trials have shown not only a reduction in lung cancer mortality but also a 3% reduction in all-cause mortality, something not seen in either breast or bowel cancer screening trials.[13-15]

The strength of the evidence prompted NHS England to start a phased implementation of screening with low radiation dose CT (LDCT) in areas with a high incidence and

mortality from lung cancer, the Targeted Lung Health Check programme (TLHC) (see figure 2, p12). More than 1,200 cancers have been detected and 76% are stage I/II.

In October 2022, after an exhaustive assessment of the clinical and cost effectiveness of LDCT screening, the UK National Screening Committee recommended that LDCT be offered to people aged 55 to 74 determined to be at high risk of lung cancer, with the TLHC as a feasible starting point.[16] This means that the four UK countries should begin implementation once the recommendation is approved by ministers.

**FIGURE 3**
National Optimal Lung Cancer Pathway for suspected and confirmed lung cancer. NHS England 2020
www.roycastle.org/app/uploads/2020/09/National-Optimal-Lung-Cancer-Pathway-3.0.pptx




The protocol and quality assurance standard were updated and published on 7 November 2022.[17] Participants who have ever smoked and who are aged 55 to 74 are identified from primary care records. They are then contacted via letter and subsequently invited to either a telephone or face to face risk assessment. If they meet a risk threshold for either of two multivariable mathematical models, and are fit enough for curative treatment, they are invited to a lung health check. This involves a further assessment and smoking cessation advice and therapy (for current and recently quit smokers), followed by LDCT. In some cases, cardiovascular risk assessment and spirometry are offered. Further LDCT are scheduled two years later for those with clear scans and at 3 months and 12 months for those with pulmonary nodules (see figure 2, p12).

People with suspected lung cancer are referred directly to secondary care. The referral rate is around 4% and cancer detection rate 1.7% at baseline and around 1% on the second round of screening.

A potentially big challenge for primary care is the need for action on incidental findings. These are often relatively minor abnormalities that could need follow-up or treatment. However, robust guidelines that minimise referrals to primary care are in place and further quality assurance measures are being developed. Some incidental findings are urgent and should be dealt with by secondary care.

The TLHC is being rolled out to every Cancer Alliance and there are now more than 40 sites; scanners may be mobile or fixed site depending on access.

## RAPID DIAGNOSIS AND STAGING

Once referred to secondary care patients follow the national optimal lung cancer pathway (NOLCP) which accelerates the pathway to treatment by using early CT, bundled downstream investigations and prompt treatment, with the aim that patients start treatment a maximum of 49 days from referral (see figure 3, left).

In reality, constraints on capacity »

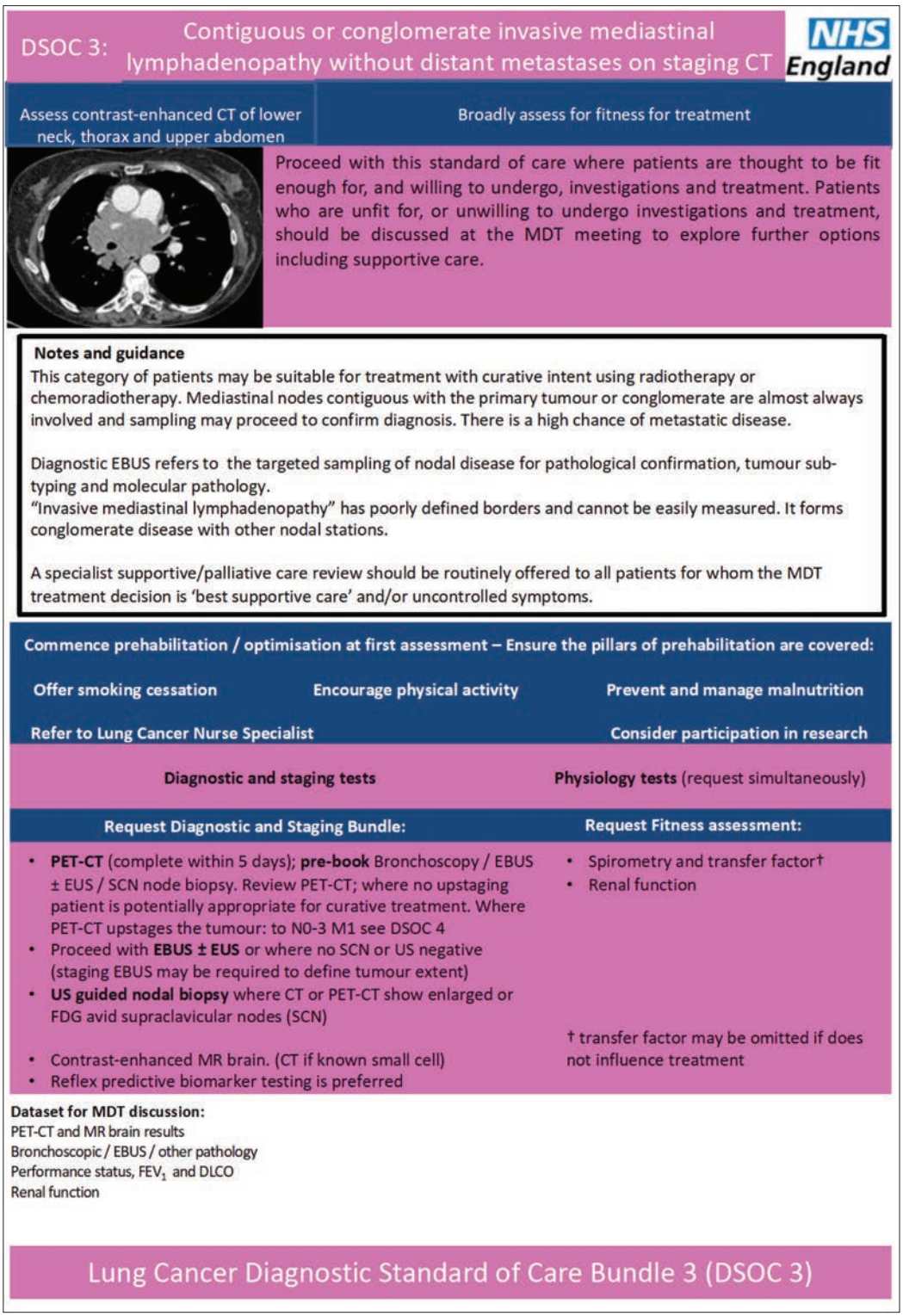
mean most NHS trusts are unable to achieve all elements of the pathway but preliminary data from the National Cancer Programme team suggest that the 28-day to definitive diagnosis target is being achieved in around 80% of cases for lung cancer.

The latest version of the NOLCP includes guidance on diagnosis and staging according to initial CT appearances; an example is provided in figure 4, below. Note the prominent place of PET-CT for any curative-intent treatment, with brain imaging recommended in the 2019 NICE lung cancer guideline (CT head in stage II and MRI head in stage III lung cancer).[18]

Rapid diagnosis is important. A randomised controlled trial showed that a 15 day reduction in time to diagnosis resulted in a nearly 200 day difference in median survival.[19]

Most other studies looking at time to diagnosis and survival are observational and biased by the 'sicker-quicker' effect, where patients with advanced disease and deteriorating status are both easier to diagnose and accelerated through the pathway, but then have a short survival.[20]

**FIGURE 4**
Example of a Diagnostic Standard of Care for locally advanced disease. NHS England 2020
www.roycastle.org/app/uploads/2020/09/National-Optimal-Lung-Cancer-Pathway-3.0.pptx




## TREATMENT

Treatment for lung cancer has advanced considerably, with most surgery now being video assisted (keyhole), including increasing use of robotic assistance. Surgical mortality is half that of ten years ago. The 90-day mortality for all patients treated with surgery is now 3.1% compared with 5.9% a decade ago.[21]

For those with early stage disease unwilling or unable to undergo surgery, curative-intent radiotherapy such as stereotactic ablative body radiotherapy is widely available.

The early detection of brain metastases is also important, as advances in stereotactic radiosurgery mean many patients can still be treated with curative intent.

Chemo-radiotherapy is given with curative intent in locally advanced disease (depicted in figure 4, DSOC 3, left), where the entire tumour volume can be encompassed by a radiotherapy field.

SACT is now very different from five years ago, with the widespread use of immunotherapy and many new treatments targeted at specific mutations.[22] This means that patients can expect longer survival, often of years, rather than the 'months rather than years' that was previously explained to patients at diagnosis. Thus, the conversation with patients has changed because of treatment advances.

However, patients must be fit enough to benefit from the treatment, which comes back to earlier diagnosis. Treatment for small cell lung cancer, about 11% of all patients, is fast tracked and now includes immunotherapy. Palliative treatments remain largely

## key points

SELECTED BY

**Dr Jez Thompson**
Former GP, Leeds, UK

**Earlier diagnosis of lung cancer improves outcomes for** two main reasons. First, the disease stage may be earlier allowing more chance of curative-intent treatment. Second, patients may be fitter at presentation. Functional status, as measured by WHO performance status, is one of the most important independent predictors of survival. Patients often report a decline in fitness when seen in secondary care and today systemic anti-cancer treatment (SACT) is more effective, and only recommended, for patients with adequate performance status (WHO 0, 1 and 2) for some SACT.

**Although lung cancer is caused by smoking in 80-85%** of cases, around 6,000 patients per year do not have smoking-attributable lung cancer and 3,500 patients have never smoked. These patients are often diagnosed late, so it is important to refer patients who have persistent symptoms either for CXR, or when symptoms persist and no alternative diagnosis is found, refer for consideration of CT.

**Screening aims to detect lung cancer at a much earlier** stage so that more curative-intent treatment can be given, and mortality reduced. As 65% of people with lung cancer present with stage III or IV disease, when five-year survival is 13% and 3% respectively, screening with CT, which reduces stage III and IV to around 20%, would be expected to reduce mortality substantially. Two large RCTs have confirmed this. NHS England has started a phased implementation of screening with low radiation dose CT in areas with a high incidence and mortality from lung cancer, the Targeted Lung Health Check programme. More than 1,200 cancers have been detected and 76% are stage I/II.

**Once referred to secondary care patients follow the national** optimal lung cancer pathway which accelerates the pathway to treatment by using early CT, bundled downstream investigations and prompt treatment, with the aim that patients start treatment a maximum of 49 days from referral.

**Most surgery is now video assisted (keyhole), with** increasing use of robotic assistance. For those with early stage disease, unwilling or unable to undergo surgery, curative-intent radiotherapy such as stereotactic ablative body radiotherapy is widely available. Advances in stereotactic radiosurgery mean many patients with brain metastases can still be treated with curative intent. Chemo-radiotherapy is given with curative intent in locally advanced disease. SACT now includes widespread use of immunotherapy and many new treatments targeted at specific mutations. This means that patients can expect longer survival, often years rather than months.

**Smoking cessation advice and treatment should be** integral to the management of lung cancer, whether suspected or confirmed and when screening. Smoking cessation improves outcomes for all stages of lung cancer. The most effective interventions employ pharmacotherapy and counselling with follow-up. Smoking cessation rates are higher in the context of screening for lung cancer.

unchanged and specialist enhanced supportive care is recommended for all patients with stage IV lung cancer.

## SMOKING CESSATION

Smoking cessation advice and treatment should be seen as integral to the management of lung cancer, whether suspected or confirmed and when screening. Evidence suggests that smoking cessation improves outcomes for all stages of lung cancer, particularly when surgically treated.[23]

The most effective interventions employ pharmacotherapy and counselling support with follow-up. Smoking cessation rates are higher in the context of screening for lung cancer.[24,25]

Lung cancer is the leading cause of cancer deaths by some margin in both men and women. Early diagnosis is central to improving outcomes by enabling patients to access the markedly improved treatment now available for all stages.

Prompt recognition and referral is essential, supported by rapid secondary care pathways. Screening will be a challenge to implement but will reduce mortality among those eligible.

**Competing interests**
Professor David Baldwin has received speaker honoraria from AstraZeneca, Roche and MSD. The other authors have no competing interests.

## REFERENCES

**1** Cancer Research UK. www.cancerresearchuk.org/health-professional/cancer-statistics/mortality/common-cancers-compared#heading-Zero
**2** Araghi M, Fidler-Benaoudia M, Arnold M et al. International differences in lung cancer survival by sex, histological type and stage at diagnosis: an ICBP SURVMARK-2 Study. *Thorax* 2022;77:378-90
**3** Arnold M, Rutherford MJ, Bardot A et al. Progress in cancer survival, mortality, and incidence in seven high-income countries 1995-2014 (ICBP SURVMARK-2): a population-based study. *Lancet Oncol* 2019;20(11): 1493-1505
**4** National Cancer Registration and Analysis Service: Rapid Cancer Regisry Dataset. 2022 www.ncin.org.uk/collecting_and_using_data/rcrd [Last accessed 26 Nov 2022]
**5** Royal College of Physicians. National Lung Cancer Audit Report 2022 [Last accessed 26 Nov 2022]
**6** Rich AL, Tata LJ, Free CM et al. How do patient and hospital features influence outcomes in small-cell lung cancer in England? *Br J Cancer* 2011;105:746-52
**7** National Cancer Registration and Analysis Service. Be Clear on Cancer evaluation results. 2022 www.ncin.org.uk/cancer_type_and_topic_specific_work/topic_specific_work/be_clear_on_cancer/.) [Last accessed 26 Nov 2022]
**8** Kennedy MPT, Cheyne L, Darby M et al. Lung cancer stage-shift following a symptom awareness campaign. *Thorax* 2018;73:1128-36
**9** National Institute for Health and Care Excellence. NG12. Suspected cancer: recognition and referral. NICE. London. 2015 Updated 2021 www.nice.org.uk/guidance/ng12
**10** Cancer Research UK. www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/lung-cancer/survival#heading-Three
**11** Remi-Porta R, Bolejack V, Crowley J et al. The IASLC Lung Cancer Staging Project: proposals for the revisions of the T descriptors in the forthcoming eighth edition of the TNM classification for lung cancer. *J Thorac Oncol* 2015;10(7):990-1003
**12** Field JK, Duffy SW, Baldwin DR et al. UK Lung Cancer RCT Pilot Screening Trial: baseline findings from the screening arm provide evidence for the potential implementation of lung cancer screening. *Thorax* 2016;71(2):161-70
**13** Field JK, Vulkan D, Davies MPA et al. Lung cancer mortality reduction by LDCT screening: UKLS randomised trial results and international meta-analysis. *Lancet Reg Health Eur* 2021;10:100179
**14** National Lung Screening Trial Research Team, Aberle DR, Adams AM, Berg CD et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med* 2011;365:395-409
**15** de Koning HJ, van der Aalst CM, de Jong PA et al. Reduced lung-cancer mortality with volume CT screening in a randomized trial. *N Engl J Med* 2020;382:503-13
**16** UK National Screening Committee. Adult screening programme; Lung cancer. 2022 https://view-health-screening-recommendations.service.gov.uk/lung-cancer/ [Last accessed 26 Nov 2022]
**17** NHS England National Cancer Programme. Targeted screening for lung cancer with low radiation dose computed tomography. Standard protocol prepared for the Targeted Lung Health Checks Programme. 2022 www.england.nhs.uk/publication/targeted-screening-for-lung-cancer
**18** National Institute for Health and Care Excellence. NG122. Lung cancer: diagnosis and management. NICE. London. 2019 Updated 2022 www.nice.org.uk/guidance/ng122
**19** Navani N, Nankivell M, Lawrence DR et al. Lung cancer diagnosis and staging with endobronchial ultrasound-guided transbronchial needle aspiration compared with conventional approaches: an open-label, pragmatic, randomised controlled trial. *Lancet Respir Med* 2015;3:282-89
**20** Hall H, Tocock A, Burdett S et al. Association between time-to-treatment and outcomes in non-small cell lung cancer: a systematic review. *Thorax* 2022; 77(8):762-68
**21** Morgan H, Baldwin D, Hubbard R et al. Ninety-day mortality following lung cancer surgery: outcomes from the English National Clinical Outcomes Audit. *Thorax* 2022;77:724-26
**22** National Institute for Health and Care Excellence. Treatment pathways for lung cancer. 2022 www.nice.org.uk/guidance/ng122/resources
**23** Gemine RE, Ghosal R, Collier G et al. Longitudinal study to assess impact of smoking at diagnosis and quitting on 1-year survival for people with non-small cell lung cancer. *Lung Cancer* 2019;129:1-7
**24** Buttery SC, Williams P, Mweseli R et al. Immediate smoking cessation support versus usual care in smokers attending a targeted lung health check: the QuLIT trial. *BMJ Open Respir Res* 2022;9
**25** Brain K, Carter B, Lifford KJ et al. Impact of low-dose CT screening on smoking cessation among high-risk participants in the UK Lung Cancer Screening Trial. *Thorax* 2017;72:912-18

**We welcome your feedback**

If you wish to comment on this article or have a question for the authors, write to: **editor@thepractitioner.co.uk**