

The continuum of screening and early detection, awareness and faster diagnosis of lung cancer

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The principal reason lung cancer outcomes are poor is that most patients are diagnosed with what, with current technologies, is incurable disease. Despite unprecedented recent advances in the understanding of the biology, oncogenesis and immunology of cancer, and the subsequent development of innovative systemic therapies for lung cancer, the long-term prognosis for patients beyond stages I and II remains poor. The cost of the new agents, largely indicated for people with advanced disease and good performance status (PS), is such that the International Agency for Research on Cancer recently said that 'No country can afford to treat its way out of the cancer problem'.¹ In any case, many patients with advanced disease are ineligible because of poor performance status.

Although lung cancer survival rates have been improving in England since 2006,² the latest data from the Concord study still rate the UK behind many other nations.³ Later diagnosis is likely a major factor explaining the consistent observation that the proportion of patients that have early stage disease at the time of diagnosis in the UK is less than in many comparator countries.⁴ In a recent study comparing older patients with non-small cell lung cancer (NSCLC) in England with those in the USA, 15% were diagnosed at stage I in England compared with 25% in the USA.⁵

To address these issues, we need to consider ways in which we can detect lung cancer at an earlier stage to increase the

curative treatment rate, and where cancer is detected at a later stage, provide rapid work-up to minimise deterioration in fitness to maximise the impact of systemic therapy. Essentially this means: screening of people at relatively high risk of lung cancer; using public and professional awareness campaigns to promote the earlier referral of patients with symptoms suspicious of a diagnosis of lung cancer; and rapid and accurate diagnosis of those being referred to secondary care.

The evidence base for lung cancer screening with low-dose CT has been building, recently having been collated in a European position statement,⁶ and many countries are now implementing screening programmes in one form or another. The position of the UK National Screening Committee⁷ is currently that 'Systematic population screening programme (is) not recommended' and is awaiting the European NELSON trial⁸ to report. In the meantime, as evidenced by a CRUK-sponsored event in April 2018,⁹ clinical pressure within the UK is growing and a number of pilot programmes have emerged, implementing 'high-risk case finding' initiatives using some form of 'Lung Health Check' approach. Such programmes in Manchester and Liverpool have already reported 2%–3% detection rates with both high rates of stage I lung cancer and high curative treatment rates.^{10,11} Such an approach has now been endorsed by NHS England and further pilots are planned.

Most patients with early stage lung cancer are either asymptomatic or have vague and non-specific symptoms, which make early recognition by both patients and primary care clinicians difficult. However, there is evidence that there are potential missed opportunities in primary care in the 3–6 months before diagnosis.¹² As a result, a number of programmes have been developed to increase awareness of the symptoms and the potential benefits of early diagnosis of lung cancer. The first of these was in the Doncaster area¹³ where persistent cough was chosen as the alert symptom. This innovative study was limited by relatively small numbers, but prompted a number of regional campaigns

under the banner of the National Awareness and Early Diagnosis Initiative (NAEDI).¹⁴ The most successful of these is reported in *Thorax*¹⁵ where a combined approach to public and primary care awareness of persistent cough as a warning symptom, combined with 'walk-in' chest X-ray facilities in more deprived areas of Leeds is described. Community-ordered chest X-rays almost doubled and a significant stage shift towards earlier stage lung cancer was shown, with an 8.8 percentage point increase in the proportion of patients diagnosed with stage I/II lung cancer (26.5% pre-campaign vs 35.3% during campaign) and a 9.3% reduction in the absolute number of patients diagnosed with stage III/IV disease. Over the period of the intervention, the proportion of patients undergoing treatment with curative intent increased from 16.8% to 30.6%, the 1-year survival rate rose from 30.3% to 39.1% and the proportion of patients diagnosed as part of an emergency presentation fell from 37.1% to 29.1%. The authors are rightly cautious because the temporal comparison means that a causal link between the campaign and stage-shift cannot be proven and other factors (particularly the emergence of SABR as a therapeutic option over the period of the study), could explain some of the findings. However, it seems unlikely, given that all of the findings are consistent with earlier diagnosis, that the intervention was not the main cause of improvement in outcomes that now approach those in other comparable countries.⁵

Over a similar period, the national programmes of promoting public awareness in cancer, the 'Be Clear On Cancer' campaigns, were introduced, beginning with a regional and then three national campaigns advertising 'cough for 3 weeks or more' as an alert symptom for lung cancer.¹⁶ The evaluation of these campaigns showed a doubling of 2ww referrals between 2011 and 2015, with the rate of rise faster after the first campaigns and a statistically significant shift towards earlier stage disease after all the national campaigns.^{16,17} As with the authors of the Leeds study referred to above, it was accepted that proving a causal relationship was not possible, but it was concluded that there was evidence of a 'whole system response', starting with increased public recognition of the messages to increases in attendance at general practitioner (GP) practices, then increases in urgent suspected cancer referrals from GPs to secondary care. There was evidence of an increased number of cases, more use of diagnostic tests, a shift to earlier stage disease, better PS at the time of

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diagnosis and increased numbers of patients undergoing surgery. There was no evidence of a statistically significant improvement in 1-year survival directly related to the campaigns.

'Rapid Diagnosis' is a relatively new term but has long been supported by the cancer waiting times targets in the UK and more recently by the more challenging targets set by the Independent Cancer Taskforce.¹⁸ The UK Government is now promoting the implementation of a 'National Optimal Lung Cancer Pathway',¹⁹ one aim of which is to reduce the interval from referral to decision to treat to a maximum of 28 days. While the relationship between this interval and survival in cancer is complex,²⁰ there is little doubt that a matter of weeks' delay in treatment can be significantly detrimental to survival. Even within the six sub-stages from stage 1a to 2b in the new 8th UICC classification of tumour stage in NSCLC, the prognosis for 5-year survival varies from 92% to 46%.²¹ We know that the doubling time of some NSCLC tumours can be as short as 1–2 months²² and in one recent study, 5-year survival was found to be significantly worse in patients where surgery was delayed beyond 38 days and progressively worsened as time to surgery increased.²³ O'Rourke and colleagues demonstrated that, while waiting for radical radiotherapy in Scotland, 21% of their patients progressed to the point where only palliative treatment was feasible.²⁴ Apart from a stage shift over a typical period of waiting for diagnosis and treatment, patients of borderline fitness can deteriorate from being fit for treatment with curative intent at the time of referral to being fit only for palliative treatments by the time treatment can be started. The only randomised trial of the impact of a rapid diagnostic pathway compared with 'standard' care is the Lung-BOOST trial²⁵ in which the median interval between referral and diagnosis was reduced by 15 days and the median survival increased by 191 days. Also, for those patients who have advanced disease, PS can deteriorate rapidly, making systemic treatment less effective or impossible. Delays in diagnosis and treatment also distress patients and carers, providing another important reason to achieve rapid diagnosis.

Screening, early diagnosis and rapid diagnosis represent interventions in a continuum of the progress of people with lung cancer. In all of these, earlier is better, but one intervention alone is not enough as only a minority of patients will benefit. Integrating these initiatives by identifying people and populations at risk may be a key to their more effective use. Public and

professional awareness programmes highlighting both the risk profile of patients and the value of early diagnosis need to continue and to be constantly evaluated and improved; screening or 'high-risk case-finding programmes should be implemented now, and every healthcare provider should be working towards the universal implementation of a rapid diagnostic pathway. The work of the Leeds group¹⁵ demonstrates one way of making significant inroads into reducing the impact of this commonly fatal disease but clearly more needs to be done.

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