Minimising diagnostic delay in lung cancer

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Lung cancer outcomes have improved only marginally over the last 40 years and remain dismally poor in comparison to most other cancers: only 17.7% of women and 12.9% of men in the UK survive after diagnosis for 5 years or longer.[1] This is despite significant investments, with notable recent improvements in diagnostic and staging tools, treatment options and the organisation of teams responsible for streamlined delivery of these. Poor survival is largely attributable to low rates of radically treatable disease at diagnosis. Given that survival rates do vary significantly both within and between countries,[2 3] they should be amenable to improvement. How best to do this? Options might include increasing public awareness, improving identification and investigation of putative lung cancer symptoms in primary care, streamlining of secondary care service pathways and screening. All of these have been investigated and they are all of importance.

The finding of a 20% mortality reduction in the National Lung Screening Trial in the USA[4] has prompted great interest in low-dose CT (LDCT) screening in high-risk groups. This should be tempered, however, for a number of reasons: only 27% of patients developing lung cancer in the USA would meet the NLST entry criteria, and it is unknown what proportion even of these would attend a screening programme outside a clinical trial; symptomatic presentation particularly of highly malignant forms including small cell lung cancers occurs between screening rounds; screening tends to identify cases of indolent disease ('overdiagnosis', estimated to have occurred in up to 18%of the cases in the NLST) as well as cancers with lethal potential ;[5] LDCT screening programmes are very costly and only become reasonably cost effective when combined with smoking cessation programmes;[6] knowledge regarding appropriate entry criteria, screening protocols and optimal management of lung nodules is still evolving. For all these reasons, it is unlikely that LDCT screening alone will have a major effect on lung cancer mortality in the near future. Recent results from the Nelson trial, presented at the World Conference on Lung Cancer, indicate for the first time that there is a mortality benefit in European patients using LDCT and employing volumetric nodule analysis. There was a 26% (95% CI 9% to 41%) reduction in lung cancer deaths at 10 years of study follow-up in men and a likely significant and even larger reduction in lung cancer mortality in the women.[7]

Following the patient consulting the primary care practitioner with symptoms, the next hurdle to timely diagnosis is recognition of lung cancer as a possible cause, ideally before the disease has become incurable. The average diagnostic interval was found to be over 3 months from presentation among patients with lung cancer in the North of England and was particularly long for patients with early stage disease (average 168 days).[8] Tørring and colleagues found increasing mortality with longer diagnostic intervals among the approximately 40% of the patients who presented in primary care with symptoms suggestive of any of five common cancers (including lung cancer).[9] They also identified the initially counter-intuitive association of high mortality with short diagnostic intervals, explainable by the 'sick-quick' phenomenon, whereby patients with advanced disease are easy to identify yet their outcome is inevitably poor. Challenges faced by the primary care practitioner include the frequent absence of a sensitive presentation signature (eg, haemoptysis, occurring in only 22% of their cases) with many patients presenting multiple, non-specific symptoms.[8] In response to the difficulties of timely identification of lung cancer in primary care, a number of risk prediction tools have been developed. While several show real promise, so far none has been externally validated nor have their clinical or cost-effectiveness been demonstrated.[10]

One of the longest intervals in the patient journey from symptom onset to diagnosis appears to be the delay in presenting symptoms.[11] One study reported a median time between onset of symptoms and consultation of 99 days (IQR 31–381).[12] It is probable that reducing this delay may result in improvement in stage at diagnosis, especially given the exponential growth pattern of most lung cancers. This delay is particularly striking given the median life expectancy from presentation being less than 180 days.[13] Holmberg *et al* showed that most of the excess mortality in English patients in comparison to Norwegian and Swedish patients occurred early in follow-up and postulated that this reflected poorer access to healthcare/population awareness.[3] Forbes and colleagues found that UK patients seemed to have less awareness that the risk of cancer increases with age and reported more reluctance to seek medical attention amid concern about wasting the doctor's time.[14] An early study by Athey *et al* evaluated the effects of a public awareness campaign in conjunction with brief intervention training in general practices in Doncaster, UK. Primary care chest X-ray referral rates increased by 20% in the targeted practices, associated with a 27% increase in lung cancer diagnoses.[15] Recently, Kennedy and colleagues reported on the impact of an early diagnosis campaign in Leeds, UK, that also focused both on public awareness and primary care.[16] They found that community-ordered chest X-ray rates increased by an impressive 81% compared with before the campaign. This was associated with a significant stage shift towards earlier stage lung cancer: the proportion of patients diagnosed with stage I/II lung cancer increased from 26.5% precampaign to 35.3% during the campaign. Importantly, there was also a fall in the absolute number of patients diagnosed with advanced disease. An evaluation of the UK Department of Health's 'Be Clear on Cancer' campaign, conducted in the English Midlands, found an improvement in public awareness and an increase in the presentation of lung cancer symptoms, and an in the number of cancers detected, and a significant stage shift to earlier stage at diagnosis.[17] There is also evidence that patients presenting with an isolated cough, with or without haemoptysis, have earlier stage disease, higher radical treatment rates and achieve markedly improved survival compared with patients with other or multiple symptoms.[13] In contrast to these findings, Ades and colleagues using case-control methodology failed to show any relationship between lung cancer symptoms recorded in primary care and disease stage, concluding that there is little prospect of improving outcomes by earlier detection of symptomatic disease.[18] It is possible that this study lacked adequate power to detect any relationship, given that it included only 247 patients with lung cancer.

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Rather than community-wide interventions, it is possible specifically to target high-risk groups to concentrate efforts on early diagnosis, generally based on smoking history. Smith and colleagues developed and refined a theory-based, complex intervention designed to overcome some of the barriers to presentation of lung cancer symptoms[19] and undertook the randomised controlled CHEST Trial to evaluate its effects in patients at high risk of lung cancer in Scotland.[20] They found a significant, 15% increase in all consultations, and a non-significant 19% increase in consultations for new chest symptoms in the intervention group, with a trend towards a reduction in presentation delay.

The paper by Emery and colleagues in this edition of the journal[21] reports extension and further evaluation of this approach in an Australian population at high risk of lung cancer, the 'CHEST Australia Trial'. While maintaining the core elements of the CHEST trial, they modified the self-help manual and employed more intensive efforts to engage patients: some form of monthly prompts to monitor current symptoms were tailored to individual preferences, including SMS and email reminders, postcards, phone calls and fridge magnets. They found a statistically and clinically significant 40% relative increase in respiratory consultations in the intervention group compared with controls and this was achieved with no overall increase in consultation rates. No harmful effects were identified, with no increase in cancer worry, Hospital Anxiety and Depression Scale (HADS) scores or quality of life scores. Disappointingly, there was only a non-significant trend to earlier respiratory presentations with a reduction of 14 days and patients still taking an average of 2 months to consult and there was no increase in the number of chest X-rays obtained in the intervention group. As the authors identify, in further studies additional effort to emphasise the importance of the GP in responding to the symptoms being presented may be very important. An economic assessment assumed that the cost of this intervention might be a substantial A$42 500 (about £23 000) for each lung cancer case detected.

Starting treatment earlier in the natural history of lung cancer should be possible, should result in outcome benefits and delays do seem to be modifiable at several stages of the patient journey. It is good to see interventions being developed and tested in randomised trials to improve access to care, a phase of the journey that contributes substantially to delays in treatment, particularly in the UK. Larger-scale evaluation of CHEST trial-type interventions will be required to establish to what extent they can materially improve lung cancer outcomes and at acceptable cost.

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