



Improving lung cancer diagnosis: the evolving role of patients and care providers

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Lung cancer remains the leading cause of cancer mortality worldwide, comprising 12% of all new cancer cases and 19% of cancer deaths globally (1). Even with recent advances in treatment, the survival rate for lung cancer remains low and can vary even among developed countries (2-4). Lung cancer stage at time of diagnosis remains a critical prognostic factor, and delays in diagnosis may explain the outcome disparities that are seen across nations (4). Most lung cancer patients are symptomatic at the time of diagnosis, usually presenting with advanced stage disease and multiple symptoms with cough as the most common (5-7). Patients are often unequipped to recognize the seriousness of their symptoms and need for medical attention (8-10). In addition, they often require multiple visits to their primary care provider prior to investigation, diagnosis or referral for their lung cancer (9). The International Cancer Benchmarking Partnership (ICBP) suggested that delays in diagnosis may be contributing to poorer outcomes, for example in the U.K. (11). One approach to accelerate diagnosis is through symptom awareness campaigns, aiming to increase awareness of cancer and also facilitating diagnosis (12,13). A community-based lung cancer symptom awareness intervention in the Doncaster area of England demonstrated a 20% increase in primary care referrals for chest X-ray and a 27% increase in lung cancer diagnosis, supporting awareness and early recognition initiatives that may facilitate lung cancer diagnosis (12).

A recent study by Kennedy *et al.* developed a public awareness campaign in Leeds (UK) and assessed lung cancer outcomes for 3 years prior [2008–2010] to implementation

and during the 5 years over which the campaign took place [2011–2015] (14). The early diagnosis campaign included: (I) distribution of a primary care health professional educational package including a national clinical guideline for chest X-ray referral; (II) initiation of a marketing communications campaign initially targeting underserved areas with high lung cancer incidence and later expanded to the entire city; (III) delivery of key messages about early symptom recognition to local target populations by community health educators; and (IV) establishment of a self-request chest X-ray service for patients fulfilling certain symptom criteria. The results of the study showed that annual community referrals for chest X-rays increased by 80.8% between 2008–2010 and 2013–2015, with a dramatic increase in the number of community-ordered X-rays following general practitioner educational events and a national TV advertising campaign. In addition, there was a significant stage-shift towards diagnosis of earlier stage lung cancer—the proportion of patients diagnosed with stage I/II lung cancer increased by 8.8% during the campaign along with a 9.3% reduction in the absolute number of patients diagnosed with stage III/IV disease in Leeds Teaching Hospitals. There was an increase in the proportion of patients receiving radical or curative lung cancer therapy, and a decline in the proportion referred for supportive care alone. A significant reduction was also seen in the proportion of patients diagnosed via emergency room presentation (from 36.0% to 28.8%) and intra-hospital referral, with a corresponding increase in those diagnosed after clinic referral or through follow-up of pulmonary nodules. While lung

cancer mortality improved throughout the UK over this time period, the study reported greater reduction in mortality in Leeds than in the UK and Wales during that time period. While the proportion and number of advanced lung cancer diagnoses decreased in Leeds, they appeared to increase or at least remain stable over time nationally.

Because of the study's design, a direct causal link between the intervention and decreased mortality cannot be confirmed. However, the temporal relationship between the intervention, increased use of chest X-rays, stage shift and meaningfully improved outcomes is highly suggestive that the intervention was effective.

Key limitations for the study include the potential impact of overdiagnosis and lead time bias. The absolute decrease in late stage diagnoses in the report appears to offset the increase in early stage diagnoses, suggesting minimal if any risk of overdiagnosis with the awareness intervention. Lead time bias may result in improved survival outcomes, and cannot be ruled out as an important factor in the study's results. But in contrast to more indolent cancers such as early stage prostate cancer, we know that most patients with symptomatic lung cancer die from their disease within a few years. Lung cancer screening with computed tomography in high risk populations without symptoms leads to significantly decreased lung cancer mortality and even all-cause mortality in one randomized trial (15,16). The study from Kennedy *et al.* focuses on those with chronic cough, a recognized symptom of lung cancer but also other diseases, for which chest X-ray is an important component of the diagnostic work-up (17). It has been estimated that 29% of all symptoms attributable to lung cancer occur more than 6 months before diagnosis, thus a significant proportion of patients could be diagnosed earlier and potentially even receive curative treatment if there were greater awareness of concerning symptoms (18).

Early recognition and prompt diagnosis in those with key lung cancer symptoms like persistent cough, hemoptysis, chest pain and weight loss is essential to avoid missed opportunities for both curative and life-prolonging therapies in lung cancer. The population targeted by Kennedy *et al.* with their educational intervention is distinct from those eligible for screening trials, and represents an opportunity to further improve outcomes in this disease.

Two systematic reviews have found that patient delay in presentation is largely a result of the lack of awareness of the seriousness of symptoms or their relation to cancer (19,20). Healthcare practitioners may further contribute to the delays through clinical misdiagnosis, application and interpretation

of tests. A Swedish study reported a median delay of 21 days from onset of first symptom to patient presentation to a general practitioner, an additional 33 days for referral to specialist, and another 9 days for diagnosis for a median of 110 days from onset of first symptom to diagnosis (9). The median time from first symptom to treatment was 189 days, and is very similar to a Canadian study where the time from initial symptoms to treatment was 138 days (21). For patients with atypical symptoms, such as bone and joint pain or fatigue, the time to referral is over three-fold longer than those with typical symptoms like cough (median 104 *vs.* 29 days) (22). Two tertiary hospitals found that 38% of lung cancer cases had missed opportunities for earlier diagnosis, with a substantially increased time to diagnosis compared to patients without missed opportunities (132 *vs.* 19 days) (23). Preventable delays arose from failure to follow up on documented abnormal imaging results, failure to complete key diagnostic procedures in a timely manner, and poor patient adherence. The use of rapid diagnostic programs has been highly successful in multiple countries to shorten time to treatment initiation in addition to improving both patient experience and rate of radical treatments (24). The combination of reducing time to presentation through increasing knowledge among patients and care providers and simplifying the diagnostic process through improving ease of access may help to optimize diagnosis and care delivery and improve patient outcomes and satisfaction (21,25).

While additional studies may help us further quantify the impact of symptom awareness interventions on earlier diagnosis and outcomes, the question is no longer whether or not we should pursue symptom awareness campaigns in the symptomatic population. The real question to be answered is why haven't we already implemented symptom awareness campaigns as a standard? What are we waiting for? As nations struggle to implement lung cancer CT screening in asymptomatic individuals, surely we can move faster to implement symptom-based awareness campaigns to promote earlier diagnosis and better outcomes in those with symptoms through guideline-based care.

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