Commentary

Delays in diagnosis and treatment of lung cancer: Lessons from US healthcare settings

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Most cancer disparities research has traditionally focused on two key outcomes, access to appropriate treatment and survival. While continuing research on these two measures remains critical, they do not encompass important aspects of patient-centred care such as the timeliness of diagnosis and treatment [1]. Prolonged time intervals between symptom onset and treatment initiation increase the risk of poorer clinical outcomes and are associated with worse patient experience of subsequent cancer care [2,3]. Studies examining inequalities in the timeliness of diagnosis and treatment are therefore particularly welcome.

In this Journal, Nadpara et al. examined intervals to lung cancer diagnosis, treatment, and associations between timely treatment on mortality [4]. They used linked data from the Surveillance Epidemiology and End Results (SEER)-Medicare database on nearly 50,000 US patients who were diagnosed with lung cancer during 2002–2007 and were 65 years of age or older. The authors estimated the time of symptom onset based on the date of Medicare consultation claims with ICD-9 codes denoting symptoms of lung cancer and then combined it with information in the patients' SEER records about the approximate timing of diagnosis. The latter source also provided information about the timing and nature of treatment, and survival.

The investigators report a median diagnostic interval (between first symptomatic presentation and diagnosis) of about 180 days; further, more than one in four patients experienced diagnostic intervals exceeding 300 days [4]. Relatedly, a median diagnostic interval of 113 days (with an upper quartile value of 249 days) was reported by a recent English primary care records study of lung cancer patients diagnosed during 2007–2010 and aged over 40 [5]. These alarmingly long diagnostic intervals observed on both sides of the Atlantic reflect the symptom signature of lung cancer which is dominated by symptoms of low predictive value, making lung cancer one of the 'harder-to-suspect' malignancies [6]. For example, possible lung cancer symptoms such as persistent cough and dyspnoea have low specificity and are difficult to distinguish from manifestations of chronic pulmonary disease in smokers. Conversely, haemoptysis, a classic 'red flag' symptom with relatively high predictive value, only occurs in a minority of patients [7]. Tellingly, the proportion of patients with haemoptysis in the reviewed study was so small that count data had to be suppressed for information governance purposes [4].

Nadpara and colleagues also describe disparities in diagnostic intervals by age and sex. Older patients had longer median diagnostic intervals (e.g., 213 vs 146 days for 80+ and 65–69 year olds, respectively), and this was also seen in women (209 vs 162 days in men) [4]. Concordant patterns of variation have been described previously, but the age and sex inequalities in diagnostic timeliness reported by this US study are particularly large [5]. The observed steep age gradients may in part reflect greater diagnostic challenges in patients with a higher burden of comorbidity. Nevertheless future research to elucidate possible responsible mechanisms is a relative priority.

Unusually for studies in this field, the investigators examined variation in delays to both diagnosis and treatment. Perhaps unsurprisingly, intervals from diagnosis to treatment were substantially shorter than intervals from symptom onset to diagnosis, with median intervals from diagnosis to treatment initiation of 27 and 18 days for patients with non-small cell and small cell lung cancer, respectively [4]. Reassuringly, and in spite of their sizeable influence on timeliness of diagnosis, patient characteristics such as age, sex and comorbidity status had little influence on the timeliness of treatment initiation. Concordantly, evidence from England indicates that performance status, stage at diagnosis, and lung cancer type have much greater effects on treatment timeliness than socio-demographic factors [8].

The findings regarding delays from diagnosis to treatment amplify recent relevant evidence for patients with lung and other common cancers [9–13]. In addition to causing concern for patients and their carers, post-diagnostic delays signal system-level inefficiencies in cancer care. Increasingly, functional imaging PET–CT investigations and biomarker profiling tests (e.g. to ascertain tumour EGFR status) are being used to guide decisions on optimal treatment for patients with lung cancer. Unfortunately, these novel diagnostic technologies that can 'personalise' management options could substantially increase intervals from diagnosis to treatment [14,15]. These considerations present challenges for health policy planners and decision makers and identify the need for streamlining and integrating care pathways and services for cancer patients after diagnosis. Doing so can help to improve both treatment timeliness and healthcare system efficiency.

Defining treatment timeliness can be difficult. Nadpara et al. operationally defined untimely treatment as receipt of surgery, radiotherapy, or chemotherapy after 8, 7, and 6 weeks, respectively, based on guidelines from the British Thoracic Society and the RAND Corporation. While these externally validated standards can be used to 'benchmark' practice, defining timeliness as a binary outcome has limitations, given the continuous nature of this measure and that many patients experience particularly long delays. As the authors also remark, guideline-based definitions of timeliness vary in the length of periods of time within which care is judged as 'timely', while previous data-driven approaches have used 95th centile cut-offs to define untimely treatment [11]. Development of further methodological consensus is needed in this area. Considering the precise types of chemotherapy, radiotherapy or surgery, and palliative or curative treatment intent in future studies will be useful.

The study identified lung cancer type and stage at diagnosis as strong independent predictors of timely diagnosis and treatment: patients with small cell lung cancer or advanced stage at diagnosis were more likely to have shorter pre-diagnostic intervals and to start treatment promptly [4]. Further, patients with shorter intervals to treatment had poorer survival. These findings concord with the 'waiting time paradox' (or 'sicker–quicker') hypothesis, where patients with most severe symptoms experience the shortest delays in diagnosis or treatment and have worse survival [2,8].

Epidemiological studies using administrative data can describe patterns of variation in diagnostic and treatment processes and outcomes precisely, but cannot identify the exact causes of such variations. Diagnostic delays are often generated by multiple pre-diagnostic consultations, which occur in at least a third of all patients subsequently diagnosed with lung cancer [16]. In other instances, clinically appropriate investigations may not be ordered or, if ordered, they may be a source of additional delays [17,18]. Further, small proportions of patients may have expressed preferences for delayed investigations or decline referral [19]. The obviously diverse nature of 'missed opportunities' for suspecting lung cancer makes clinical audit studies that are based on case-record reviews a necessary supplement to epidemiological studies in order to identify targets for improvement interventions [20,21]. Similar approaches are needed to study mechanisms leading to potentially avoidable delays from diagnosis to treatment.

The commented study poignantly demonstrates that the fundamental challenges in promptly diagnosing and treating patients with cancer transcend healthcare systems worldwide. In recent years, major research initiatives hosted within the International Cancer Benchmarking Partnership have helped to unearth a wealth of comparative evidence on cancer outcomes and their determinants in countries with broadly similar healthcare systems (Australia, Canada, Denmark, Norway, Sweden, and the UK) [22]. Including data from patients treated by US population-based healthcare providers in future international cancer outcomes research consortia can provide additional insights into the causes of diagnostic and treatment delays, accelerating the pace of discovery and elucidating effective solutions to these universal problems.

Acknowledgement

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