How long is too long? A scoping review of health system delays in lung cancer

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Delays to lung cancer care occur, especially in secondary care; variation in timeframe guidelines needs addressing http://ow.ly/hZt730kvKAb

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ABSTRACT Earlier access to lung cancer specialist (LCS) care improves survival, highlighting the need for streamlined patient referral. International guidelines recommend 14-day maximum time intervals from general practitioner (GP) referral to first LCS appointment ("GP–LCS interval"), and diagnosis to treatment ("treatment interval"). We compared time intervals in lung cancer care against timeframe benchmarks, and explored barriers and facilitators to timely care.

We conducted a scoping review of literature from MEDLINE, Embase, Scopus and hand searches. Primary end-points were GP–LCS and treatment intervals. Performance against guidelines and factors responsible for delays were explored. We used descriptive statistics and nonparametric Wilcoxon rank sum tests to compare intervals in studies reporting fast-track interventions.

Of 1343 identified studies, 128 full-text articles were eligible. Only 33 (26%) studies reported GP–LCS intervals, with an overall median of 7 days and distributions largely meeting guidelines. Overall, 52 (41%) studies reported treatment intervals, with a median of 27 days, and distributions of times falling short of guidelines. There was no effect of fast-track interventions on reducing time intervals. Lack of symptoms and multiple procedures or specialist visits were suggested causes for delay.

Although most patients with lung cancer see a specialist within a reasonable timeframe, treatment commencement is often delayed. There is regional variation in establishing timeliness of care.

Introduction

Lung cancer is the leading cause of cancer death in men and women worldwide [1]. The majority of patients present in advanced stages, with a 5-year survival of 3–7% [2, 3]. Therapeutic advances can improve poor survival rates. It is, therefore, important patients with suspected lung cancer receive timely diagnosis and treatment, but there is marked heterogeneity in referral practice leading to avoidable delays [4].

To standardise patterns of cancer care and improve clinical outcomes, guidelines for optimal timing of diagnosis and treatment of lung cancer have been implemented in some countries. Examples include the

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British National Health Service (NHS) "Two-week wait" system introduced in 2000 for urgent general practitioner (GP) referral to first lung cancer specialist (LCS) appointment [5, 6]; with treatment recommended to commence within 31 days of date of clinical decision to treat and 62 days from date of GP referral [6]. Standards from the USA recommend that patients should not wait >10 days for specialist review [7] and treatment be initiated within 42 days of a nonsmall cell lung cancer (NSCLC) diagnosis [8]. In Australia, recent guidelines recommend timeframes of 14 days from initial GP referral to first LCS appointment, and from diagnosis to first cancer-specific treatment [9, 10].

Limited data exist regarding concordance of cancer care with guidelines, due to inconsistent definitions of patient timelines to diagnosis and treatment [11, 12]. To rectify this, Olesen *et al.* [13] validated a schema for defining key time intervals in the pathway to diagnosis and treatment for cancer, specifying division between "patient related" delays and "health system related" delays. Patient related delays in lung cancer care have been examined extensively previously [11, 14–16] and are challenging to quantify accurately if we are to improve service delivery [17]. However, health system related delays are yet to be comprehensively reviewed and analysed alongside standards of care.

We aimed to 1) synthesise health system related waiting times to milestones of lung cancer care using standardised definitions; 2) benchmark measures of performance against relevant guidelines for timeframes; 3) supplement quantitative findings with barriers to timely care described in the literature; and 4) explore the impact of facilitators such as fast-track referral systems on waiting times.

Methods

We adapted operational definitions from the Aarhus consensus statement to extract data about time intervals in the route from first clinical presentation until start of treatment for lung cancer [13, 18]. Figure 1 describes these time intervals, together with the origin and year of corresponding published timeframe guidelines.

Our primary end-points were the GP–LCS interval and treatment interval. Secondary end-points were other time intervals detailed in figure 1, or any time interval beyond first clinical presentation defined by studies.

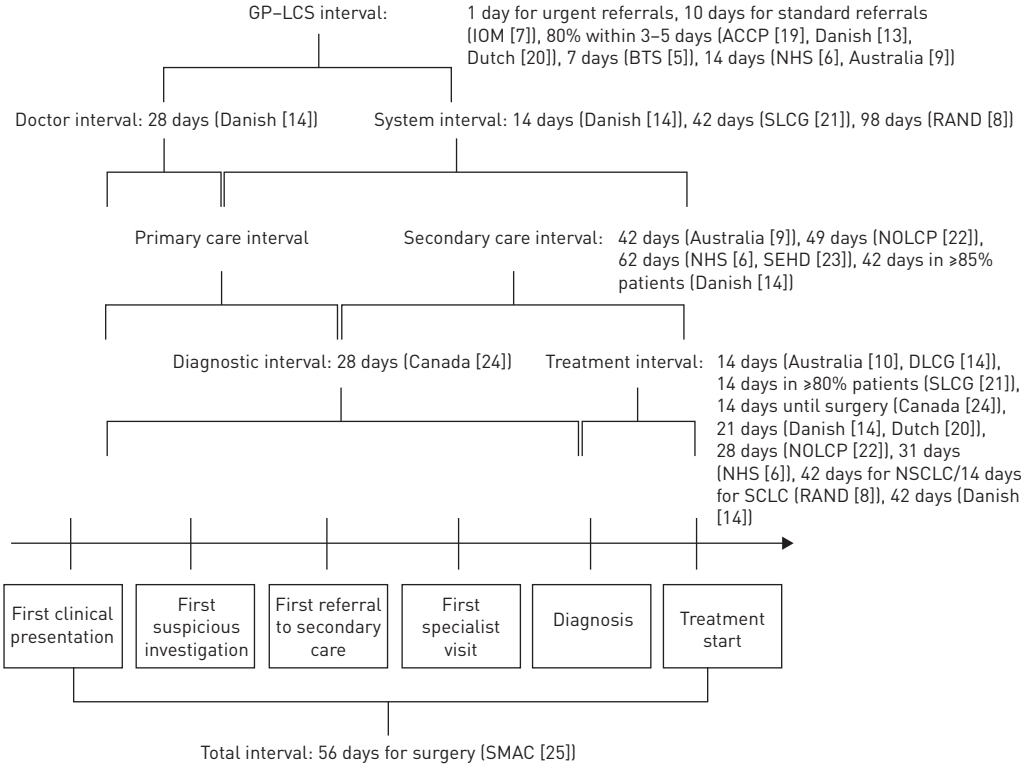

FIGURE 1 Time intervals and corresponding published guidelines in lung cancer care. GP: general practitioner; LCS: lung cancer specialist; IOM: Institute of Medicine; ACCP: American College of Chest Physicians; BTS: British Thoracic Society; NHS: National Health Service; SLCG: Swedish Lung Cancer Group; RAND: Research and Development; NOLCP: National Optimal Lung Cancer Pathway; SEHD: Scottish Executive Health Department; DLCG: Danish Lung Cancer Group; NSCLC: nonsmall cell lung cancer; SCLC: small cell lung cancer; SMAC: Standing Medical Advisory Committee.

We excluded studies about symptom onset within the patient interval, given bias associated with variable prediagnostic symptom recognition [11, 26–29].

We conducted a scoping review to aggregate research on the range and nature of time intervals in international lung cancer literature [30]. A scoping review was performed in preference to a systematic review for three reasons: there is a wide and complex variety of study designs in this area; 2) there is a scarcity of randomised controlled trials; 3) traditional scoping review methodology allows capture of all clinically relevant health system milestones to cancer care relevant to our research aims, while allowing scope to detect activity of other reported time intervals.

We based our scoping review on Arksey and O'Malley's [31] six-stage methodological framework, further clarified by Levac *et al.* [30].

Research questions

Our primary research question was "what are the waiting times spent by patients in healthcare to obtain a diagnosis and treatment for lung cancer, and are they acceptable?" Our secondary question was "what are the factors identified in the literature that expedite or delay lung cancer care?"

Search strategy and selection criteria

Published studies were identified from electronic literature databases including MEDLINE (1946 onwards), Embase (1974 onwards), Scopus (any year), editorials, cancer institute publications, government websites, publications from cancer councils/foundations and hand searches of grey literature or references of key articles. We contacted authors to request full-text articles where necessary. The literature search included Medical Subject Headings (MeSH) headings and related text and keyword searches in a manner that combined terms related to lung cancer, primary and secondary healthcare, referral patterns and time intervals (online supplementary appendix 1).

Study selection

One author (AM) performed a search of electronic literature databases in January 2016 and a final update in August 2017. Two authors (AM and SN) independently reviewed and screened abstracts for study inclusion using the following eligibility criteria. 1) Describes any/all of the time durations or intervals from patient's first clinical presentation or first suspicious clinical presentation, to diagnosis and treatment of adults with NSCLC and/or small cell lung cancer (SCLC); 2) original human studies; 3) full-text articles available in English.

Exclusion criteria

Articles with the only primary end-point defined as patient interval (defined as first symptom to first clinical presentation [13]), articles focused on guideline development, screening, public health awareness campaigns and accuracy of diagnostic methods.

Chart data

A framework for standardised data extraction was developed. Relevant data were extracted independently by two authors (AM and SN) into a data extraction chart (online supplementary appendix 2) and included study bibliometrics and design, outcome measures of interest, time intervals (adapting standardised definitions with permission from Olesen *et al.* [13]), suggested factors responsible for delays and relevant involvement of local guidelines or fast-track systems.

Synthesis plan

Numerical summaries for each of the seven time intervals were collated to answer our primary research question. Time intervals, geographical region, sample size and proportion of cases where time intervals met relevant timeframe guidelines were tabulated. Where only mean time intervals were reported, these values were extracted for comparative purposes only. All inferential analyses were conducted on medians due to positive skew of time distributions. Timeframes for unpaired samples in cohort studies were analysed separately for uniformity of comparison.

A coding system was developed to classify authors' suggested reasons for delays in lung cancer care using the following categories: patient, primary care, secondary care, diagnostics and other. This system was used to capture specifics of patient, provider and system barriers to timely care and to summarise frequency.

To study the effect of fast-track intervention systems on primary end-points, we used nonparametric Wilcoxon rank sum tests to compare groups of median time intervals stratified by a categorical variable (fast-track system *versus* no fast-track system).

Consultation

As recommended by Levac *et al.* [30], medical specialists with clinical experience in lung cancer management (PB, JV and SK) were consulted for higher levels of content expertise and to standardise the abstract screening process, discuss preliminary findings and validate direction of potential research output.

Results

The study search and selection process is outlined in the PRISMA (preferred reporting items for systematic reviews and meta-analyses) flow diagram [32] in figure 2. After abstract screening and exclusion of 29 full-text articles that did not meet eligibility criteria, a total of 128 articles were included for data extraction (online supplementary appendix 2). Of these, 24 (19%) were prospective in design and 25 (20%) were cohort studies.

Included studies were conducted between 1980 and 2015 in 23 different countries, including 36 (28%) from the UK, 35 (27%) from Europe excluding UK, 21 (16%) from USA and 19 (15%) from Canada. The average sample size was 1962, with means of pooled means as follows: age 66.6 years (reported in 76 study samples), 66.6% male (100 samples), 74.2% with NSCLC (62 samples), 19.8% with SCLC (34 samples) and 26.9% having stage IV disease (34 samples).

A thematic analysis is presented below.

Time intervals and adherence to guidelines

A total of 33 (26%) studies reported on GP–LCS intervals, which ranged from 0 to 33 days. The median and mean of pooled GP–LCS intervals was 7 and 8 days, respectively.

Overall, 52 (41%) studies reported treatment intervals, which ranged from 6 to 80 days, with a pooled median and mean of 27 days and 28 days, respectively. The treatment interval end-point in the majority of studies was any treatment modality (n=30, 58%); some studies specifically reported initial treatment to surgery (n=13, 25%), radiotherapy (n=4, 8%), chemotherapy (n=2, 4%) and either chemotherapy or radiation (n=2, 4%).

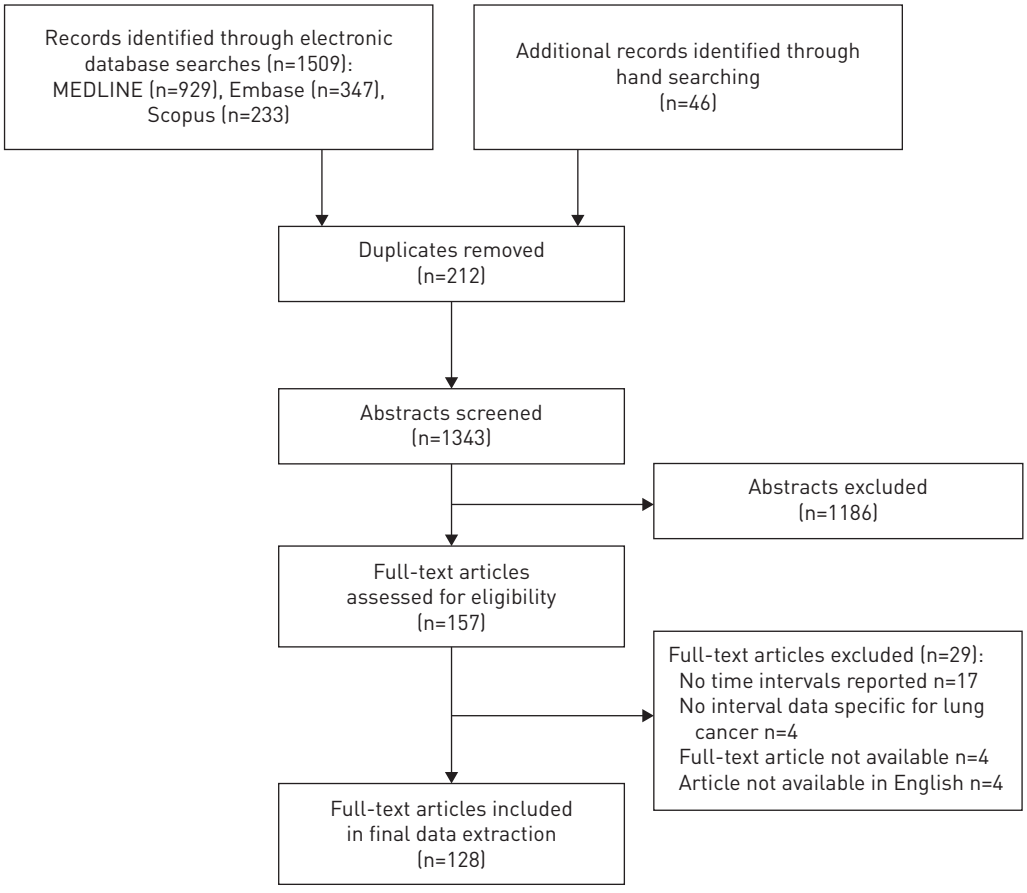

FIGURE 2 PRISMA (preferred reporting items for systematic reviews and meta-analyses) flow diagram.

Online supplementary appendix 3 summarises the frequency of median time intervals in all studies, categorised by geographical region and, where available, relevant local guidelines. As one purpose of this scoping review was to assess other frequently reported time intervals, we present a summary of reported time intervals from first LCS visit to both date of diagnosis and to treatment start.

Apart from diagnostic and treatment intervals, the median of the median times for all other time intervals met corresponding guidelines. However, maximum times exceeded guidelines for all intervals.

Figure 3 displays the distribution of GP–LCS and treatment intervals by region and total study sample size, referenced against corresponding established guidelines from Europe [5, 6, 20, 21, 33] and Australia [5, 10]. In studies where only mean time intervals were reported, these are charted for comparison. There is demonstrable variation in maximum recommended wait times, affecting interpretation of whether GP–LCS or treatment intervals fell within target timeframes.

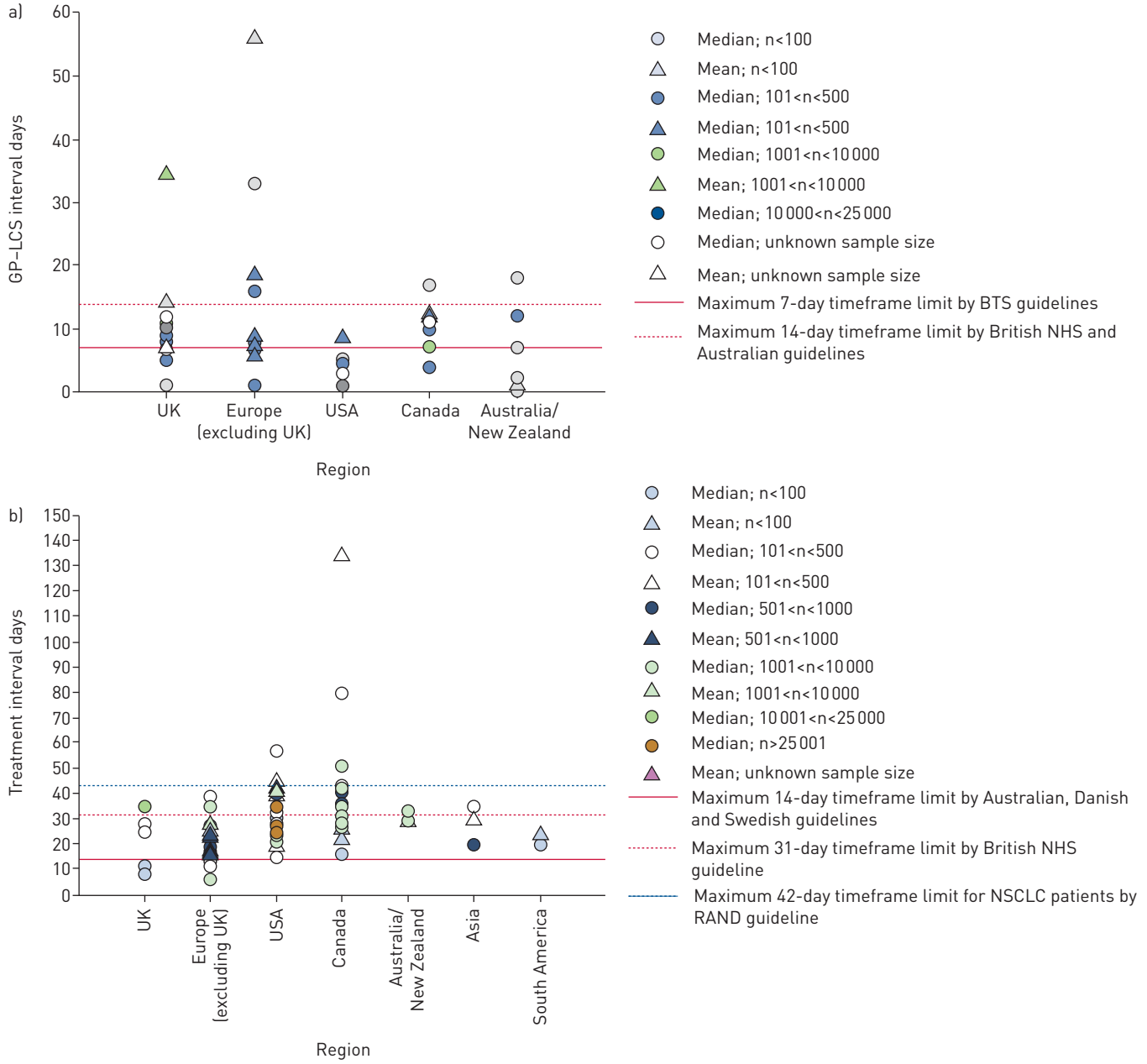

FIGURE 3 Comparison of primary end-points against guidelines. a) Distribution of general practitioner (GP)–lung cancer specialist (LCS) intervals (time from first GP referral until first LCS visit) by study region; b) distribution of treatment intervals (time from confirmed diagnosis to treatment start) by study region. Shape of datapoint signifies mean or median study sample size (n), colour of datapoint signifies sample size category. BTS: British Thoracic Society; NHS: National Health Service; NSCLC: nonsmall cell lung cancer; RAND: Research and Development.

Only 24 (19%) out of 128 studies reported both a time interval and adherence to established guidelines for primary end-points. Online supplementary appendix 4 provides details of eight studies reporting percentage adherence to guidelines for GP–LCS intervals and 16 studies for treatment intervals in online supplementary appendix 5. There was wide variation in adherence to guidelines. While median GP–LCS intervals largely met guideline limits, the percentage of patient timeframes exceeding limits was >50% in five studies (online supplementary appendix 4). Median treatment intervals frequently exceeded limits, with >50% adherence in only six studies (online supplementary appendix 5). Based on Swedish guidelines, where it is recommended that 80% of patients have acceptable treatment intervals [21, 33], all 16 studies fell short of meeting standards of care.

Effect of fast-track intervention systems

In total, 24 (19%) out of 128 studies explored the effect of a fast-track intervention system on lung cancer care (table 1). Of these, only eight (33%) were prospective in design.

Seven studies of interventions designed to impact GP–LCS interval were described. Interventions ranged from the British NHS "2-week wait" system for urgent referral of suspected cancer [45, 48–51, 55], to streamlined outpatient referral triage and staging systems [34, 42]. A further seven studies described interventions affecting the treatment interval, ranging from systems described above to nurse-led coordination programmes [39], quality improvement methods [54] and specialised thoracic oncology clinics [57].

Six studies demonstrated statistically significant reductions in various time intervals falling within both primary and secondary care jurisdictions. However, Lewis *et al.* [55] evaluated waiting times before and after introduction of the 2-week wait system and concluded that not only did the system fail to reduce waiting times, but the median GP–LCS interval significantly increased from 7 to 9 days, despite an escalation in urgent referrals. Devbhandari *et al.* [50] found that delays in secondary care intervals persisted despite urgent referrals *via* the 2-week wait system, specifying a negative initial bronchoscopy as a barrier.

Overall, there was no evidence of a significant difference in the groups of median GP–LCS intervals or treatment intervals from studies using a fast-track system *versus* those not using a fast-track system (p=0.33 and p=0.88, respectively). Nonparametric testing for other commonly described time intervals revealed evidence of shorter times from first suspicious image to diagnosis in intervention groups compared with controls, but numbers of studies were small (p-value=0.05; mean 4 days in three studies *versus* mean 8 days in seven studies, respectively). No significant differences between the groups were observed for the secondary care interval and the interval from first LCS visit to diagnosis (p=0.52 and p=0.76 respectively).

Factors contributing to delays in care

A total of 78 factors responsible for reported delays to lung cancer care were identified on 745 occasions (online supplementary appendices 6 and 7). The five most frequent factors by patient, primary care, secondary care, diagnostics, and other categories are presented in figure 4, together with the total number of occasions per category. Patient factors were the most common category quoted related to any delay (n=250, 34%). The most common patient factors were lack of clinical symptoms (n=53, 21%) and presentation with early-stage disease (n=35, 14%), in contrast with lower educational levels or socioeconomic position (n=1, 0.4% and n=5, 2%, respectively). For primary care, the most common factor was a low index of suspicion (28 out of 104, 27%) that did not prompt referral for further diagnostic testing or to secondary care. In secondary care, obtaining access to definitive diagnostic procedures and results caused delays in 78% (106 out of 136) of cases. Other causes of delays were waiting for multiple specialist consultations (50 out of 178, 28%) and lack of rapid multidisciplinary team assessment (26 out of 77, 34%). Finally, treatment delays to surgical resection (27 out of 178, 15%) and radiation therapy (14 out of 178, 8%) were documented.

Discussion

This scoping review demonstrates several findings with respect to primary end-points, explanations for delays and reveals gaps in knowledge.

- Patients' GP–LCS intervals ranged from 0 to 33 days (33 studies). The median of the pooled medians (7 days) and distribution of times generally met recommended timeframe guidelines, with >50% adherence in the majority of studies.
- Treatment intervals ranged from 6 to 80 days (52 studies), with a median of 27 days, failing to comply with most guideline timeframes and only six studies reporting >50% adherence. Multiple well powered,

TABLE 1 Impact of fast-track intervention systems on time intervals

First author, year [ref.]	Study design, intervention and setting	Sample size without intervention/ control group (group C) n	Sample size with intervention (group I) n	GP–LCS interval days	Treatment interval days	Other intervals from figure 1 days	New intervals described days	Author conclusions	Statistical significance
Brocken, 2011 [34]	Retrospective study comparing delays in a RODP (including PET-CT) for suspected lung cancer patients with delays described in literature and guideline recommendations (the Netherlands, 1999–2009)		280	Median (IQR) 7 (5–9) days n=236	Median (IQR) for group I 19 (6.5–27) days n=215	Median (IQR) primary care interval 18 (6–46) days; median (IQR) secondary care interval 36 (26–46) days	Median (IQR) interval from LCS to diagnosis ("diagnostic delay") 2 (1–17.5) days	The RODP including PET-CT resulted in timely care, with strongest effect on diagnostic and secondary care intervals	N/T
Prades, 2011 [35]	Mixed–methods study including prospective data analysing a cancer fast-track programme's impact on reducing the time that elapsed between clinical suspicion of breast, colorectal and lung cancer and treatment start (Spain, 2006–2009)		3481 (for year 2009)			Mean total interval 36.7 days		Approximately half of all new patients with breast, lung or colorectal cancer were diagnosed *via* the fast track programme, although the cancer detection rate declined across the period	N/T
Murphy, 2015 [36]	Prospective cluster randomised trial assessing use of electronic health record-based trigger algorithms to identify patients at risk of diagnostic delays (USA, 2015)	Unknown (total sample 19)	Unknown (total sample 19)				Median interval from scan to diagnosis 65 days in group I *versus* 93 days in group C (p=0.59)	No statistical difference was observed in the time to diagnostic evaluation between the intervention and control groups	Nonsignificant
Leiro-Fernandez, 2014 [37]	Prospective analysis of effectiveness of an email alert system to a pulmonologist attached to a lung cancer rapid diagnostic unit (Spain, 2008–2010)		47				Median (IQR) interval from scan to diagnosis 13 (7.3–30) days	This strategy for radiological suspicion of lung cancer improves diagnostic efficacy and the communication between GPs, radiologists and pulmonologists	N/T
Iachina, 2017 [38]	Retrospective cohort study evaluating effect of hospital transfers on the delay in diagnosis and treatment using 2009 national fast track cancer care pathways initiative (Denmark, 2008–2012) and data from the		11 273		Mean±SD for group I 16.9 ±10.64 days	Mean±SD secondary care interval 38.4 ±15.42 days		Transfer between hospitals during the care pathway might cause delay from diagnosis to treatment as well as in the total time from referral to treatment in patients with NSCLC	N/T

Continued

TABLE 1 Continued

First author, year [ref.]	Study design, intervention and setting	Sample size without intervention/ control group (group C) n	Sample size with intervention (group I) n	GP–LCS interval days	Treatment interval days	Other intervals from figure 1 days	New intervals described days	Author conclusions	Statistical significance
Alsamarai, 2013 [39]	Danish Lung Cancer Registry Retrospective cohort study analysing effect of the CCCP at a Veterans Affairs hospital (USA, 2005–2010)	163	189		Median (range) 28 (0–265) days; mean 40 days for total sample n=352 Mean for n=163 *versus* n=189: 46 days *versus* 43 days (p=0.6)	Mean system interval in group C *versus* group I 126 days *versus* 101 days (p=0.015)	Mean interval from scan to diagnosis in group C 76 days *versus* group I 53 days (p=0.016)	A centralised, hospital-based CCCP can significantly reduce times to diagnosis of cancers that are early stage/ incidentally found and reduce system interval by 25 days	Significant reduction for system and scan to diagnosis intervals; not for treatment interval
Cattaneo, 2015 [40]	Report on effect of RACLAP in one medical centre RACLAP includes rapid thoracic nurse consultation, navigation and triage referral system (USA, 2010)		121				Median interval from scan to diagnosis 16 days	RACLAP provided rapid and evidence-based evaluation and management of patients resulting in a short time to diagnosis	N/T
Murray, 2003 [41]	Multisite prospective randomised pilot study to test feasibility of two-step rapid diagnostic system (Royal Marsden Hospital) compared to conventional diagnostic workup in three local district hospital chest clinics (UK, 1998–2001)	45	43			Median total interval in group C *versus* group I 49 days *versus* 21 days (p=0.0025)		There are several advantages to investigations and diagnosis in the intervention arm, particularly in time to treatment initiation, patient satisfaction and rate of radical treatments	Significant reduction in total interval
Lo, 2007 [42]	Retrospective cohort study of waiting times pre- and post-implementation of TTT programme: streamlined referral system from GPs to LCS (Canada, 2004–2005)	52	430	Median for group C 17 days *versus* group I 4 days			Median times from scan to diagnosis in group C *versus* group I 39 *versus* 6; "suspicion" to LCS referral in group C *versus* group I 20 *versus* 6; LCS visit to CT in group C *versus* group I 52 *versus* 3; "suspicion" to diagnosis in group	TTT programme was effective in shortening the time from suspicion of lung cancer to diagnosis and reduced time intervals at each step in the process	N/T

Continued

TABLE 1 Continued

First author, year [ref.]	Study design, intervention and setting	Sample size without intervention/ control group (group C) n	Sample size with intervention (group I) n	GP–LCS interval days	Treatment interval days	Other intervals from figure 1 days	New intervals described days	Author conclusions	Statistical significance
							C *versus* group I 128 *versus* 20 Median time from LCS to diagnosis in resected patients *versus* nonresected patients 70 days *versus* 8 days (p<0.001) Median time from LCS to resection in resected patients 104 days		
Dransfield, 2006 [43]	Retrospective cohort study of timeliness for patients referred to specialised lung mass clinic (USA, 1999–2003)		31 (resected), 125 (nonresected)					Since the inception of the lung mass clinic, the resection rate at Birmingham VA Medical Center has improved	Significant reduction only for LCS to diagnosis
Laroche, 1995 [44]	Prospective review of a new quick access "two-stop" multidisciplinary investigation service at Papworth Hospital (UK, 1995)		209				Median (range) time from LCS to surgical resection 35 (7–81) days	The two-stop investigation service led to higher rates of histological confirmation, routine CT scanning and review of every patient with confirmed lung cancer by a thoracic surgeon. This resulted in a substantial increase in the successful surgical resection rate	N/T
Spurgeon, 2000 [45]	Retrospective tracking cohort study assessing impact of TWW system (UK, 1997–1998)	Unknown (total sample 767)	Unknown (total sample 767)	Median (IQR) before and after 12 (7–22) days *versus* 7 (3–13) days, respectively		Median (IQR) secondary care interval in group C *versus* group I 47 (28–77) days *versus* 39 (21–61) days, respectively		Waiting times for urgent appointments were significantly less than the waiting times for nonurgent appointments for all 10 types of cancer	N/T
Jiwa, 2004 [46]	Retrospective review of impact of urgent (TWW or marked "urgent") system (UK, 1990)	Unknown (total sample 6)	Unknown (total sample 6)			Mean primary care interval 40 days; mean diagnostic interval 95 days	Mean time from GP referral to diagnosis 55 days	Patients referred as "urgent" were diagnosed soonest	Nonsignificant
Neal, 2014 [47]	Retrospective cohort study of diagnostic intervals between two cancer cohorts, defined before and after the implementation of the 2005 NICE referral guidelines for suspected cancer and by	1816	2851			Median (IQR) diagnostic interval in group C *versus* group I 114 (48–238) days *versus*		Fast-track referrals may prioritise those with advanced disease in lung cancer, who are more likely to have "red flag" symptoms	Nonsignificant

Continued

TABLE 1 Continued

First author, year [ref.]	Study design, intervention and setting	Sample size without intervention/ control group (group C) n	Sample size with intervention (group I) n	GP–LCS interval days	Treatment interval days	Other intervals from figure 1 days	New intervals described days	Author conclusions	Statistical significance
	NICE-qualifying presenting symptoms (UK, 2001–2008)					112 (45–251) days (p=0.47)			
Neal, 2007 [48]	Retrospective cohort study comparing outcomes of cancer patients referred through the urgent TWW referral guidance with those who were not (UK, 2000–2001)	313	96	Median (IQR) for group C 10 (4–17) days *versus* group I 10 (6–13) days, respectively			Median LCS to diagnosis in group C *versus* group I 15 (4–28) days *versus* 18 (8–36) days, respectively	Urgent guideline referrals had later-stage diagnosis compared with patients diagnosed through other routes. There was some evidence for differences in outcomes for lung cancer between urgent guideline referrals (and all referrals marked as urgent) and those diagnosed through other routes	Nonsignificant
Forrest, 2015 [49]	Retrospective data linkage study investigating factors impacting timely care in the setting of NHS Cancer Plan diagnostic pathways, including the TWW system	Unknown (total sample 28 733)	Unknown (total sample 28 733)	Median (IQR) 10 (6–17) days (n=14 507)	Median (IQR) 35 (21–55) days (n=14 692)	Median (IQR) secondary care interval 56 (39–79) days	Median (IQR) time from GP referral to diagnosis 13 (7–24) days and from LCS to diagnosis 0 (0–0) days	No detail of proportion of urgent referrals, but 70% of patients referred by GP saw a LCS within target interval of 14 days and 61% within secondary care target interval of 62 days	N/T
Devbhandari, 2008 [50]	Prospective tracking cohort study of how bronchoscopy results affected waiting times to lung cancer treatment in patients referred by standard (*via* urgent GP TWW referral) and nonstandard referral pathways (UK, 2003–2005)	149	193	Median for group C 1 day	Range of medians in group C 8–12 days	Range of median secondary care intervals 45–75 days	Range of median times from LCS to diagnosis 33–57 days	Delays persist despite TWW fast-track system due to hospital barriers Treatment, secondary care and LCS diagnosis intervals significantly longer for bronchoscopy-negative groups	
Bowen, 2002 [51]	Prospective pilot study evaluating time between occurrence of symptoms and presentation to GP for patients presenting with lung cancer to two NHS trusts with "rapid access clinics" (UK, 2002)		37				Median (range) interval from first GP visit to first LCS visit 56 (0–175+) days	There were delays in assessment and referral in primary care	N/T
Hunnibell, 2012 [52]	Prospective tracking cohort study to investigate timeliness of lung cancer care before and after creation of a CT-VAHCS nurse navigator position (USA, 2007–2010)	57	66			Median system interval in group C *versus* group I 40 and 45 days	Median scan to LCS group C *versus* group I 13 and 10 days, respectively	CT-VAHCS created and modified several processes to improve timeliness and quality of cancer care as soon as a patient's imaging suggested a new diagnosis of malignancy. The cancer care coordinator	N/T

Continued

TABLE 1 Continued

First author, year [ref.]	Study design, intervention and setting	Sample size without intervention/ control group (group C) n	Sample size with intervention (group I) n	GP–LCS interval days	Treatment interval days	Other intervals from figure 1 days	New intervals described days	Author conclusions	Statistical significance
								effected a measurable improvement in timeliness	
Lal, 2011 [53]	Retrospective comparative cohort study of patients referred by GPs to lung cancer clinics for investigation of suspicious imaging before and after introduction of fast-track CT pathway (UK, 2006–2007)	124	86			Median secondary care interval in group C *versus* group I 55 and 49 days, respectively (p=0.095)	Median referral to decision to treat l in group C *versus* group I 42 and 35 days, respectively (p<0.05)	Fast-tracking outpatients with suspicious chest radiographs straight to CT results in more effective use of clinic appointments, reduced diagnostic delay and more rapid treatment decision times	Significant reduction only for interval from referral to diagnosis
Aasebo, 2012 [54]	Retrospective cohort study of workup times for patients with lung cancer using the "Lean" quality improvement process (using mechanisms to identify and sustain high-value encounters and eliminate obstacles) to improve patient flow (Norway, 2006–2009)	40	33		Median time to surgery/ chemo/ XRT=26.5/6/ 5.5 days, respectively Median/mean time to surgery for intervention group 15/ 17 days (n=14)		Median scan to diagnosis in group C *versus* group I 64 *versus* 16 days, respectively Median time from chest radiography to CT in group C *versus* group I 10 *versus* 5.5 days, respectively	It is feasible to improve patient flow for patients with lung cancer by employing the Lean method as a pathway instrument	N/T
Lewis, 2005 [55]	Retrospective comparative cohort study examining the impact of TWW referral pathway for lung cancer over three different time periods, presented here as three separate samples: 1) 1999–2000; 2) 2000–2001; and 3) 2001–2002 (UK, 1999–2002)	Sample (1) n=286	Sample (2) n=352 Sample (3) n=404	Median (range): 1) 7 (0–124) days 2) 8 (0–101) days 3) 9 (0–98) days (p=0.0009 for (1) *versus* (3))		Median (range) secondary care interval: 1) 37 (2–228) days; 2) 41 (2–307) days; 3) 42 (0–239) days (p<0.04 for (1) *versus* (2) *versus* (3))	Median (range) GP referral to diagnosis: 1) 26 (0–228) days; 2) 33 (2–307) days; 3) 27 (0–300) days (p<0.00001 for (1) *versus* (2); p=0.0003 for (2) *versus* (3)) Median (range) LCS to diagnosis: 1) 15 (0–219) days; 2) 21 (0–294) days; 3) 15 (0–300) days (p<0.00001 for (1) *versus* (2) *versus* (3))	The TWW system failed to reduce waiting times for lung cancer in this study due to urgent referral routes used outside the TWW scheme and a large increase (42%) in referrals. Patients referred outside the TWW appear to be disadvantaged	Significant increase in all waiting times
Larsen, 2013 [56]	Retrospective population-based study of	Vejle n=387; other n=3131	Vejle n=388; other n=2612			Median (IQR) secondary care		Urgent referral systems had a positive effect on secondary	Significant reduction in

Continued

TABLE 1 Continued

First author, year [ref.]	Study design, intervention and setting	Sample size without intervention/ control group (group C) n	Sample size with intervention (group I) n	GP–LCS interval days	Treatment interval days	Other intervals from figure 1 days	New intervals described days	Author conclusions	Statistical significance
	changes in secondary care intervals in two hospital groups (Vejle *versus* other) after 2008 introduction of urgent referral scheme for cancer (Denmark, 2007–2009)					interval in group C *versus* group I for Vejle 31 (20–41) days *versus* 29 (23–65) days (p=0.39) Median (IQR) secondary care interval in group C *versus* group I for other 37 (21–64) days *versus* 33 (16–53) days (p=0.008)		care intervals, although location-specific factors played a role	secondary care interval
Riedel, 2006 [57]	Retrospective sequential single-institution (Veterans Affairs) cohort study evaluating the impact of a MTOC (USA 1999–2003) pre- and post-implementation	101	244		Median before (n=89) *versus* after (n=205) 23 *versus* 21 days, respectively (p=0.38)	Median diagnostic interval in group C *versus* group I 47 (n=89) *versus* 45 days (n=201), respectively (p=0.12)	Median GP visit to LCS visit interval in group C *versus* group I 22 (n=90) *versus* 25 days (n=162), respectively (p=0.01) Median LCS to diagnosis interval in group C *versus* group I 14 (n= 90) *versus* 12 days (n=166), respectively (p=0.97) Median LCS to surgery interval in group C *versus* group I 40 (n=30) *versus* 50 days (n=56), respectively (p=0.21)	Retrospective comparison with attendant confounders failed to reveal benefit of a MTOC as an intervention for timely lung cancer care	Significant reduction only for interval from first GP to first LCS visit

Group C: control group: group I: intervention group; GP: general practitioner; LCS: lung cancer specialist; RODP: rapid outpatient diagnostic programme; PET-CT: positron emission tomography-computed tomography; IQR: interquartile range; N/T: not tested; NSCLC: nonsmall cell lung cancer; CCCP: cancer care coordination programme; RACLAP: rapid access chest and lung assessment programme; TTT: time to treat; TWW: 2-week wait; NICE: National Institute for Health and Clinical Excellence; NHS: National Health Service; CT-VAHCS: Connecticut Veterans Affairs Healthcare System; XRT: radiation therapy; MTOC: multidisciplinary thoracic oncology clinic.

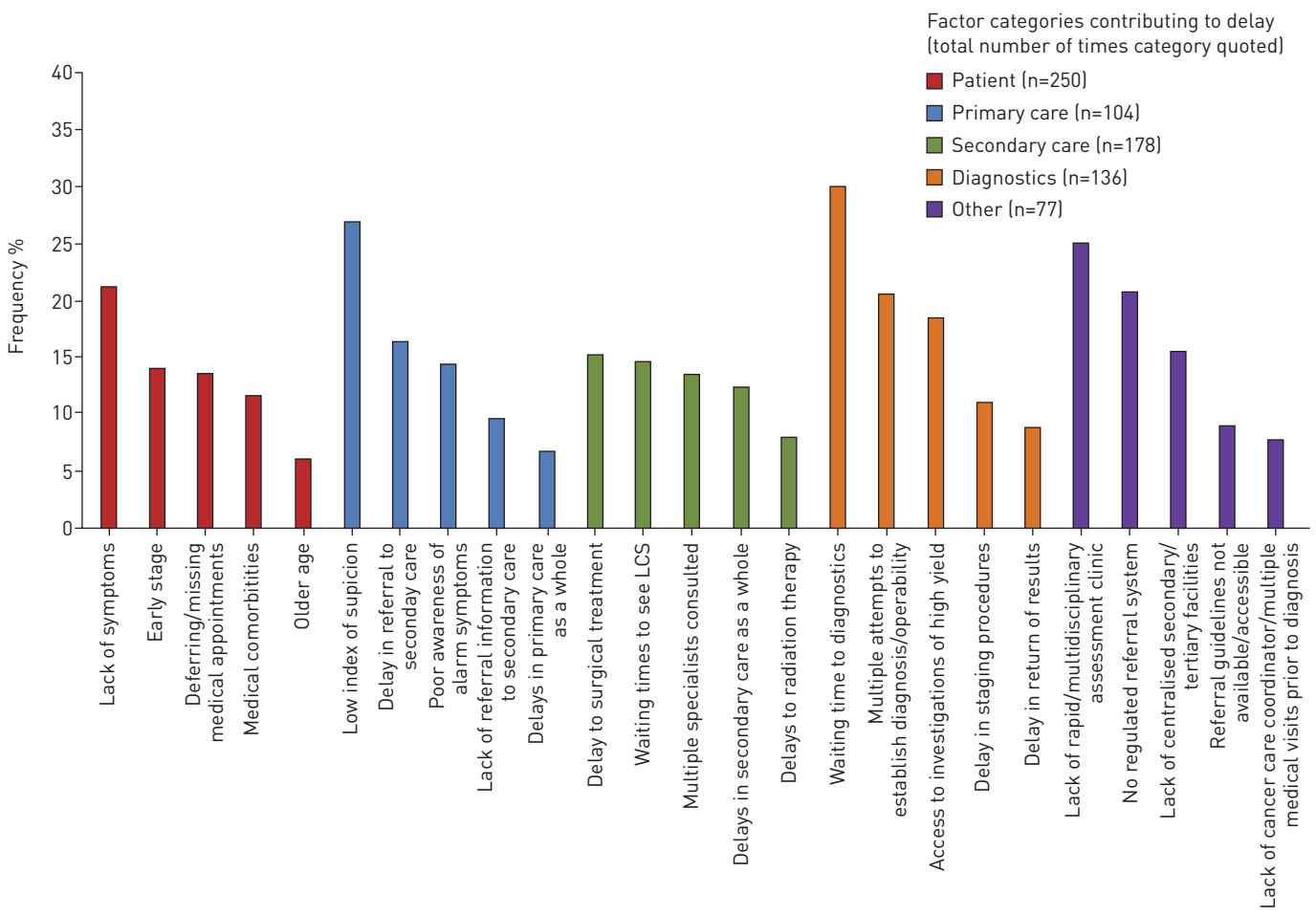

FIGURE 4 Frequency of factors contributing to delays to lung cancer care (total number of times category quoted). LCS: lung cancer specialist.

international studies demonstrate that some countries did not appear to meet guideline recommendations.

- There was limited evidence of an effect of fast-track systems on median waiting times. Time from suspicious scan to diagnosis improved in a limited number of studies.
- Delays were commonly attributed to patient factors and poor coordination of medical services to obtain a diagnosis and cancer-specific treatment at the secondary care level.
- Maximum waits exceeded guideline limits for all time intervals. It is difficult to establish "timeliness" due to regional variation in maximum recommended waiting times.

Taken together, this review systematically gauges measurement of health system delays to lung cancer care for targeted service improvement.

Comparison with previous literature

Previous reviews on timeliness of lung cancer care have examined similar time intervals, but have been more limited and focused on patient-related delays [11, 12, 15, 16]. In their systematic review, Olsson *et al.* [16] reported the range of GP–LCS intervals as 1–12 days for 10 studies and a range of treatment intervals as 12.5–52 days for 11 studies published from 1995 onwards. All studies were from North America or Europe, benchmarked against British guidelines. A recent scoping review by Jacobsen *et al.* [12] assessed how wait times to lung cancer care were measured in 65 studies from 2007 onwards, including nine studies reporting GP–LCS intervals and 27 reporting treatment intervals. The unweighted median treatment interval was 22 days, similar to our findings, but with narrower ranges of median values [6–18, 20–34, 39, 41–43, 45, 48–51, 53–55, 57–59] and 15–63% patients estimated to exceed the UK benchmark of 31 days [6, 12].

Our findings are consistent with previous literature, demonstrating that fast-track systems or guidelines do not necessarily facilitate timely cancer care. A 2011 systematic review found limited evidence to suggest interventions in primary care reduced delays in referral of cancer patients to secondary care [58], but the study did not report time intervals or include lung cancer patients, and excluded the 2-week wait system.

Jacobsen *et al.* [12] evaluated 14 studies examining screening or referral interventions, but not all studies tested for or found statistical significance. We report details of 24 studies, including six where interventions resulted in significantly shorter processing times within primary and secondary care [39, 41, 43, 53]. Guidelines may lack efficacy if adherence is low. In their survey of 2795 GPs, Nicholson *et al.* [59] reported wide international variation (24–82%) in adherence to lung cancer guidelines, with UK GP adherence significantly lower than that of other geographical regions. Authors acknowledge that lack of available guidelines may have contributed to very low rates of proposed definitive action.

Our findings regarding factors responsible for delay in lung cancer care are similar to that seen in the extant literature [11, 16, 49]. Lack of overt symptoms in patients with early stage lung cancer [11] and recognition of subtle symptoms of lung cancer [60] are commonly implicated barriers to timely care. Establishing when first clinical suspicion of lung cancer occurs is challenging [61], and this was reflected in review of the literature and, indeed, our inclusion criteria. Although we found low educational level to be a patient delay factor in our study, Forrest *et al.*'s [49] systematic review found no evidence of socioeconomic inequalities in treatment, diagnostic or referral intervals for lung cancer. Studies in their review did not include the primary care interval. Multiple visits to GPs prior to being referred to a LCS have previously been suggested as a cause of delay [12], but our findings also implicate delays in secondary care due to multiple visits to specialists and iterative diagnostic patterns.

Clinical implications

There are extensive clinical implications for timely health system performance in lung cancer care. Delayed confirmation of cancer diagnosis increases patient anxiety and distress [62]. Missed opportunities for following-up radiologically detected suspicious lesions are linked to increased hazard of death due to increments in tumour growth [63, 64] and underutilisation of definitive therapy [65, 66]. Impact on survival has been extensively explored in the literature, with mixed results [12, 15, 16]. Danish studies report increased mortality with longer diagnostic intervals [67] and improved survival rates following implementation of timeframe targets [14]. This contrasts with Forrest *et al.*'s [49] findings that patients treated within guideline targets had lower likelihood of 2-year survival, attesting to the "sicker quicker" hypothesis that management is expedited for symptomatic patients with advanced lung cancer [68].

It is important to have consistent definitions of optimal waiting times to lung cancer care. Clinical interpretation of timeliness will differ if examining by higher median, range or maximum patient waiting times or by heterogeneous quality metrics. In our study, GP–LCS intervals from more studies met British NHS and Australian rather than British Thoracic Society (BTS) guidelines. Conversely, treatment intervals from multiple, well-powered studies did not meet Australian, Danish or Swedish guidelines, but were acceptable by British standards. More recently, the 2017 National Optimal Lung Cancer Pathway was developed by the UK Lung Clinical Expert Group to 1) account for variation in pathways that invariably occurs for patients with suspected or confirmed lung cancer and 2) clearly indicate the corresponding maximum waiting time for each element of the pathway [22]. Standardised measurement of time intervals and outcome measures will allow more robust analysis in health services research.

Our findings expose further gaps in the availability and nature of timeframe guidelines. A number of regions lack guidelines, requiring attention given geographical variation in lung cancer epidemiology and survival [38, 69]. In addition, guidelines lose utility if they are too broad or arbitrary. As suggested by Saint-Jacques *et al.* [66], unpacking time intervals and examining them under "high resolution" will "identify bottlenecks in care delivery". Additionally, guideline content should be designed at high resolution to target delays, such as the treatment modality-specific BTS [5] and Canadian [70, 71] guidelines for radical management of lung cancer.

Examination of diagnostic and treatment intervals at high resolution by our methodology reveals inadequacies in healthcare, despite acceptable GP–LCS intervals. This may be due to two mechanisms. Demonstrable efforts to accelerate transition through primary care will uncover insufficiencies in later stages, namely secondary care. Secondly, and more importantly, by investigating pathways subsequent to clinical presentation, inappropriate health system delays can be mitigated. Heightened physician recognition of risk factors for lung cancer will justify a lower threshold for targeted specialist referral. Once the need becomes evident, a specialist network supported by health infrastructure should be able to be navigated efficiently. Waitlist management will ensure access to high value clinical encounters. While multidisciplinary assessment is optimal, new patient referrals need to be filtered to prevent overinvestigation. Judicious choice of first diagnostic test modality and investigations of comparable standard are optimal. Centralised access to surgical and radiation therapy services is a particular priority in earlier stages of lung cancer. In advanced lung cancer, coordinated recruitment of anatomical pathology services is essential to determine if patients would benefit from a targeted therapy.

Appraisal of methods

Limitations of this scoping review include lack of quality assessment of studies; this is usual for scoping review methodology [30, 31]. We used validated definitions of time intervals to guide our literature search, but acknowledge gaps in results may be due to incongruent definitions rather than lack of available data. Establishing when the "clock starts" for a patient with lung cancer is difficult; our inclusion criteria aimed to capture literature covering first patient clinical presentation and/or first clinical presentation thought to be suspicious for lung cancer. To this end, we encompassed all clinically relevant, health system milestones to cancer care within our methodology, while allowing scope to detect activity of other reported time intervals. In addition, we chose primary end-points that are more "measurable" and are targeted by a number of guideline bodies. Robust quantitative synthesis of all interval data is limited due to the heterogeneity of reported outcome measures. For example, "date of diagnosis" was not always specified in studies, and may refer to date of first positive biopsy result or date of last additional diagnostic test, impacting determination of treatment intervals. We specified sample size where relevant and use reasonable statistical assumptions to take evaluation of fast-track systems in cancer care one step further. We benchmarked distribution of time intervals against established timeframe guidelines but acknowledge that one region's guidelines may not apply to other health systems. However, our presentation of waiting time distributions is transferable and relevant to any healthcare system. While we summarised adherence to guidelines in studies that also reported corresponding time intervals, it is important to note that adherence is reported in the literature in other forms without necessarily quantifying times, such as percentage uptake of rapid referral systems [72–74]. However, this too may be an unreliable measure of optimal care, given higher urgent referral rates do not equate to higher conversion or detection rates of cancer [74]. These points emphasise the gap in consistent methodology in descriptive health services research into timeliness of cancer care. Given the exponential advances in lung cancer management in the past 20 years or so, we acknowledge that studies performed before these advances may report time intervals pertaining to outdated management options. Finally, we did not stratify waiting times by cancer stage, treatment modality or histopathology, but conveyed influence of these factors in our coding system and presentation. We extracted factors identified from multivariable logistic regression performed in studies where available, as well as in authors' conclusions. This enabled capture of both statistically and clinically significant determinants of delay.

Conclusion

In leveraging information on breadth and acceptability of waiting times to diagnosis and treatment of lung cancer, this scoping review offers practical strategies for effective patient transition through the health system. Although patient factors continue to be implicated as barriers to timely care, our findings expose specific bottlenecks within the health system for remedy. Cohesive time interval definitions and benchmarks for treatment will provide definitive quality metrics to inform cancer service provision.

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