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Title

Do ethnic patients report longer lung cancer intervals than Anglo-Australian patients? - Findings from a prospective, observational cohort study

Abstract

Introduction: Lung cancer patients from ethnic minorities have poorer outcomes than their Caucasian counterparts. We compared lung cancer intervals between culturally and linguistically diverse (CALD) and Anglo-Australian patients to identify ethnic disparities.

Material and methods: This was a prospective, observational cohort study comprising a patient survey and reviews of patients' hospital and general practice records. Across three states, 577 (407 Anglo-Australian and 170 CALD) patients were recruited and their hospital records reviewed. The survey was returned by 189 (135 Anglo-Australian and 54 CALD) patients and a review was completed by general practitioners (GPs) of 99 (76 Anglo-Australian and 23 CALD) patients. Survival and Cox regression analyses were conducted.

Results: CALD patients had longer hospital diagnostic interval (median 30 days, 95% CI 26 – 34) than Anglo-Australian patients (median 17, 95% CI 14 – 20), p = .005, hazard ratio (HR) = 1.32 (95% CI 1.09 - 1.60). This difference persisted after relevant factors were taken into consideration, adjusted HR = 1.~~46~~ 26 (95% CI 1.~~17~~ 03 - 1.~~83~~54, p =.~~001~~022). CALD patients also reported longer pre-hospital intervals, however, these differences were not statistically significant.

Discussion: Target interventions need to be developed to address ethnic disparity in hospital diagnostic interval.

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Key words

Lung cancer, ethnicity, diagnostic intervals, cancer pathway, immigrants

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Introduction

Lung cancer is the leading cause of cancer mortality, estimated in 2018 to be responsible for 1.76 million (or 18.4% of the total) cancer deaths worldwide (Ferlay et al., 2019). One reason for this high mortality rate is that lung cancer is often diagnosed at a late stage when curative treatment is an unlikely option (Walters et al., 2013). Therefore, early diagnosis and treatment is a key focus for reducing lung cancer mortality and improving patient outcomes (Walters et al., 2013). It is important to analyse intervals along the lung cancer pathway to identify where delays are ocurring so as to better focus the development of interventions that can address these delays and achieve more timely diagnosis and appropriate treatment (Walter, Webster, Scott, & Emery, 2012; Weller et al., 2012).

Patients from ethnic minority backgrounds are a vulnerable group of patients with lung cancer. Compared to Caucasians, they are often diagnosed at more advanced stages, have poorer survival rates, and are less likely to receive timely and appropriate treatment (Lin et al., 2014; Richards et al., 2017; Varlotto et al., 2018). They also face additional barriers to accessing healthcare, such as holding more fatalistic beliefs towards cancer and its treatment, language barriers, unfamilarity with the healthcare system (Licqurish et al., 2017; Lin et al., 2014).

Relatively few studies have examined intervals along the lung cancer diagnostic and treatment pathways amongst ethnic minority patients. Jacobsen et al's (2017) scoping review on lung cancer diagnostic intervals identified only six studies reporting on ethnic minority patients. All of these studies were conducted in the United States (US) and only examined hospital intervals. Of them, five reported longer intervals among ethnic minority patients than Caucasian patients (Jacobsen et al., 2017). Another study conducted in Australia found that of patients with lung cancer, those born overseas had a 5-day longer interval from referral to diagnosis than Australian-born patients (Evans et al., 2016).

Given the great differences in healthcare systems and the composition and history of the ethnic communities between the US and other multicultural countries such as Australia, there is a need for further studies on ethnic disparity in the lung cancer intervals in countries outside the US. In addition,

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even though the pre-hospital intervals account for a significant proportion of the lung cancer diagnostic pathway (Jacobsen et al., 2017), to our knowledge, no study has examined intervals prior to hospital involvement amongst ethnic minority patients.

The LEAD project (Lung cancer diagnostic and treatment pathways: a comparison between culturally and linguistically diverse [CALD] and Anglo-Australian patients) was designed to address these limitations through comparing intervals along the lung cancer diagnostic and treatment pathways between CALD and Anglo-Australian patients. Australia is one of the most culturally diverse countries in the world (Pison, 2019). More than a quarter (29%) of Australia's population were born overseas and over 200 languages are spoken in Australian homes (Australian Bureau of Statistics, 2017). Based on earlier studies, we hypothesised that CALD patients would report longer intervals along the lung cancer pathway than Anglo-Australian patients. We also hypothesised that the differences in the intervals would persist after the impact of other relevant factors, such as age and stage of lung cancer at the time of diagnosis, was taken into consideration.

Methods

Study design and participants

LEAD was a prospective, observational cohort study using a mixed-method approach *(blinded for reviewers)*. Here we report on the quantitative sub-study, which comprised a case-note analysis of patients' hospital records, a patient survey, and a record review by the patients' general practitioners (GPs). The study was conducted in five study sites across three states in Australia: three Integrated Cancer Services in Melbourne, Victoria; one public hospital in Sydney, New South Wales; and, one public hospital in Brisbane, Queensland. These health services provide coverage for all the metropolitan regions of Melbourne, Sydney and Brisbane, which account for 49% of Australian population (Australian Bureau of Statistics, 2017), and have significant numbers of patients with lung cancer and CALD patients.

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The patient eligibility criteria were: (1) having a new diagnosis of primary lung cancer within the previous month or during the recruitment phase (May 2017 to July 2018), and (2) being either Anglo-Australian or CALD. We used prospective recruitment and also included patients diagnosed within the previous month to minimise the risk of recall bias and participant attrition due to death.

Anglo-Australian patients were defined as those born in Australia and four other major English-speaking countries (Canada, New Zealand, the United Kingdom, and the US). CALD patients were defined as those born overseas and from one of five ethnic groups: Arabic, Chinese, Greek, Italian, and Vietnamese. These are the most common ethnic groups for overseas-born people in Australia (Australian Bureau of Statistics, 2017). Patients who were pregnant or aged under 18 years were excluded because lung cancer is uncommon among these two groups and those patients tend to have a different diagnostic pathway to the general lung cancer population (Mitrou, Petrakis, Fotopoulos, Zarkavelis, & Pavlidis, 2016; Yu et al., 2010).

As outlined in our protocol paper *(blinded for reviewers)*, we aimed to recruit 724 patients (362 per group) (assuming a 50% patient survey completion rate and a 80% GP review completion rate, based on previous studies, e.g., Emery et al., 2013) in order to achieve a final sample of 290 participants (145 per group). This sample size provides 90% power for a log-rank test with a two-sided alpha of 0.05 to detect a difference in median intervals of 60 versus 88 days (assuming an exponential distribution of survival times). A 28 day difference in median intervals was judged clinically important based on previous studies that indicate tumour size increases by about 20% every 28 days (Henschke et al., 2012; Torring, Frydenberg, Hansen, Olesen, & Vedsted, 2013).

We obtained ethics approval for a multiple-site study from Monash Health Human Research Ethics Committee (HREC/16/MonH/311) and research governance approval from all participating sites.

Procedure

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The study coordinators at each site identified eligible patients from the list of new cases presented at their respective lung cancer multidisciplinary team (MDT) meetings. Additional recruitment sources, such as the bronchoscopy lists, were also used in some study sites. The site coordinators went through these lists regularly throughout the recruitment phase. The recruitment target for the Anglo-Australia group was reached at some sites before the recruitment period finished. For these sites, Anglo-Australian participants were recruited at a slower speed (i.e., one of every two or three patients was recruited into the study depending on how fast the site reaching the recruitment target) once the recruitment target was reached.

After an eligible patient was identified, the site coordinators conducted a case-note analysis of the patients' hospital medical records using an audit tool developed based on those previously used by the research team *(blinded for reviewers)*. This tool collected data relevant to the lung cancer diagnostic and pre-treatment treatment pathway (e.g., dates of referral, dates of diagnosis, and the nature and stage of lung cancer at the time of diagnosis) and the patients' demographic background (e.g. age, gender, and country of birth). Waiver of consent was used for this component and identifiable patient information was removed in the case-note analysis.

The site coordinators sent an invitation letter to the patient, together with the patient survey and a reply-paid envelope. Two weeks after the initial invitation, the patients who had not already returned the survey received a reminder phone call, as well as a reminder letter. For CALD patients who did not speak English, we sent the invitation letter and the survey in English and in their preferred languages, and the reminder phone call was made to the contact person listed in their medical records instead of the patients themselves.

The patient survey comprised the Cancer Symptom Interval Measure (C-SIM) instrument (J Emery et al., 2013) plus questions on patients' socio-demographic characteristics (e.g. education level), clinical history (e.g. smoking history), and health literacy. Implied consent was used for this component. In addition, we asked for patients' written consent for the research team to access their hospital and general practice medical records in the patient survey. For those who provided written consent, we then

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contacted their GP and also conducted data linkage between their survey data and their case-note analysis data. This was achieved by site coordinator providing patients' case-note ID upon receipt of written consent forms from the research team.

For those who returned the survey but did not provide written consent, we had their case-note and survey data, but these data were saved separately and were not linked. For those who did not return survey, we only had their case-note data which were de-identified.

We contacted the GPs of the patients who had provided written consent in the patient survey by mail to invite them to complete a review of the patients' general practice medical records. The invitation letter was sent together with a GP review proforma, the patient's written consent, and a reply-paid envelope. A reminder letter was sent two weeks later and a reminder phone call was made to the GP practice. To increase GPs' interest in completing the review, a certificate of participation was offered to GPs who completed the review. This certificate could be used by the GPs to self-report to relevant medical colleges for Continuing Professional Development points.

The GP review proforma was posted with patients' survey IDs only, so there was no identifiable patient information on the review proforma when returned, whereas the survey ID enabled data linkage between the patient survey and the GP review. The review proforma was based on an earlier one used by the research team (J Emery et al., 2013) and captured key data on presentations to general practice and investigations conducted by GPs prior to referrals.

Outcomes

The primary outcomes were nine intervals along the lung cancer diagnostic and pre-treatment pathway (see Figure 1). These intervals were developed based on the Model of Pathways to Treatment (Scott, Walter, Webster, Sutton, & Emery, 2013; Walter et al., 2012) and the Aarhus Statement (Weller et al., 2012), which provide internationally accepted theoretical and methodological guidance in cancer early diagnosis research. In situations where there was uncertainty about specific dates, we used the mid-

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point rule proposed by Allgar and Neal (2005). However, unlike Allgar and Neal (2005) who did not include intervals greater than one year, we included these intervals to maximum the number of participants in analyses, but coded them as 366 days as the intervals were unlikely to be accurate in number of days. Negative intervals sometimes arose because the lung cancer diagnostic and treatment pathways might not always occur in a linear fashion (Walter et al., 2012; Weller et al., 2012). These intervals were converted to 0 before entering the analyses.

Statistical analyses

Data from the patient surveys and the GP reviews were entered centrally into separate databases using SPSS Version 25. Data from the case-note analysis were entered locally by the site coordinators into an online database using Research Electronic Data Capture (REDCap) (Harris et al., 2009) and then downloaded into the SPSS. As noted above, for participants who provided written consent in the patient survey, their case-note analysis, patient survey and GP review data were linked. For participants who did not provide this consent, their case-note analysis data were de-identified and were not linked to their survey data (for those who returned the survey without written consent).

Differences between CALD and Anglo-Australian groups in socio-demographic variables were compared using Pearson's chi-squared tests for categorical variables (e.g. smoking status), t-tests for continuous variables that are normally distributed (e.g. health literacy measures), and Mann-Whitney U test for continuous variables that are not normally distributed (e.g., age). The distribution of intervals was characterised using the Kaplan–Meier method, and the log-rank test was used to compare the intervals between CALD and Anglo-Australian groups. Each interval reflects the time elapsed from a starting point (e.g. noticing symptoms) until an event occurs (e.g. presenting symptoms to GPs). Proportional Hazards (PH) regression was used estimate the ratio of the hazards in the two participant groups. A hazard ratio (HR) > 1 indicates a longer interval in the CALD group, and a HR < 1 a shorter interval in the CALD group.

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PH regression was also used to examine the sensitivity of results to adjustment for selected covariates. The covariates investigated included: (1) patient demographic factors (e.g., age and gender), (2) disease and symptom factors (e.g., nature ~~and stage~~ of lung cancer, and whether or not the patient reported particular lung cancer symptoms), (3) investigation related factors (e.g., referral source, and whether or not the patient was discussed at a lung MDT meeting). The relevance of these covariates for each interval was established by evaluating each covariate individually in a series of univariable PH models (see Supplemental Table 1 for covariates examined for each time interval). Covariates from these PH models that were significant at < 0.05 were selected for inclusion in the multivariable models and the assumptions for PH regression were checked and confirmed.

Role of the funding source

The funder of this study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

A total of 577 patients were recruited into the study, of whom 189 (33%) returned the survey, 156/189 (83%) patients provided written consent, and the GPs of 99 (63%) patients returned the review (see Figure 2). There was no difference between CALD and Anglo-Australian patients in the survey response rate ($p = .74$), the consent rate ($p = .81$), and the GP review return rate ($p = .07$), respectively. There was also no difference between the two groups in the availability of key data in the case-note analysis, the patient survey and the GP review (see Supplemental Table 2).

As can be seen in Tables 1 and 2, compared to Anglo-Australian patients, CALD patients were older, less likely to be single or divorced, and less likely to be a current or former smoker. There was, however,

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no difference in other variables, such as socio-economic status and health literacy, or the types and stages lung cancer at the time of diagnosis.

In the comparisons of the intervals between ethnic groups, a difference was found in the hospital diagnostic interval with the estimate HR of 1.32 (95% CI: 1.09-1.60, p = .005), reflecting a longer interval for the CALD group (median of 30 days; 95% CI: 26 to 44 days) compared to the Anglo-Australian group (median 17 days; 95% CI 14 to 20, log-rank p =. 003) (see Figure 3). This effect remained statistically significant even after taking into account the nine comparisons of intervals performed (using the Bonferroni method where the p-value for an individual test amongst the set of nine performed must fall below the critical value of 0.05/9 = 0.0056 to be declared statistically significant). Among the remaining intervals, there was a statistically insignificant trend towards longer intervals amongst CALD patients for: 1) total diagnostic and treatment interval; 2) total diagnostic interval; 3) help-seeking interval; 4) GP diagnostic interval, and 5) hospital care interval (see Figure 3).

The univariable PH regression analyses for the hospital diagnostic interval identified the following covariates for inclusion in the multivariable PH model: age, state of residence, ~~the stage of lung cancer,~~ the type of specialists seen at the first appointment, whether the patient had computed tomography (CT) scan or fine needle aspiration (FNA) biopsy completed, whether the patients were discussed at the MDT, and the source of diagnosis (see Table 3). After adjustment of covariates of interest, the HR for CALD patients was 1.~~46~~ 26 (95% CI: 1.~~17~~ 03 to 1.~~83~~54, p=.~~001~~022).

Discussion

Guided by the Model of Pathways to Treatment (Scott et al., 2013; Walter et al., 2012) and the Aarhus Statement (Weller et al., 2012), we measured and compared the lung cancer diagnostic and pre-treatment pathways between CALD and Anglo-Australian patients through nine intervals. We found that CALD patients experienced a longer hosptial diagnostic interval than Anglo-Australian patients (HR = 1.32, p = .005).

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The difference in medians between groups was 30 days (95% CI 26 – 34) vs 17 days (95% CI 14 – 20). The effect persisted after adjustment for other relevant factors, such as the age and ~~the stage of lung cancer~~ the source of diagnosis, adjusted HR = 1.~~46~~26, *p* =.~~001~~022. These results are consistent with those from earlier studies (Evans et al., 2016; Jacobsen et al., 2017) and provide further evidence of a longer hospital diagnostic interval among patients with lung cancer from ethnic minorities.

The size of the difference between groups in median hospital diagnostic interval is unlikely to lead to significant differences in clinical outcomes, because tumour size is only thought to increase by 20% every 28 days (Henschke et al., 2012; Torring et al., 2013). This suggestion is supported by our finding that there was no difference in the stages of lung cancer at the time of diagnosis between CALD and Anglo-Australian patients.

In spite of this, the 13-day difference may still have negative consequences on outcomes, such as poorer psychological wellbeing and quality of life, among patients with lung cancer from ethnic minorities and their families. There is clear evidence that waiting for a cancer diagnosis is a distressing time for patients and families and that they have high levels of anxiety and depression and low levels of health-related quality of life during this time (Brocken, Prins, Dekhuijzen, & van der Heijden, 2012; Moseholm et al., 2016; Wiljer et al., 2012). In addition, studies have found that ethnic minority cancer patients have worse psychological outcomes and quality of life than locally-born patients (Sze et al., 2015).

There are a number of factors that might explain the ethnic disparity that we observed in the study, including different beliefs towards cancer and its treatment, language barriers and unfamilarity with the healthcare system (Licqurish et al., 2017; Lin et al., 2014). In addition, the ethnic disparity might be related to lower levels of smoking rates among ethinic minority communities (Joshi, Jatrana, & Paradies, 2018) as well in our participants. Tobacco smoking is the major cause of lung cancer (Malhotra, Malvezzi, Negri, La Vecchia, & Boffetta, 2016), but Asian women in particular have higher rates of lung cancer in non-smokers than other populations (J. Emery & Mitchell, 2017). Importantly, there is some evidence that non-smokers took longer to seek medical care after the onset of symptoms (Dias, Linhas, Campainha, Conde, & Barroso, 2017).

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To our knowledge, this is the first study to compare the lung cancer intervals prior to the hospital setting amongst ethnic minority patients to those of Caucasian patients, and we found a trend towards longer intervals amongst ethnic minority patients. This result warrants larger-scale studies with greater statistical power to more precisely examine possible ethnic disparities in lung cancer diagnostic intervals prior to hospital referral.

There are a number of strengths in the design of our study that could be considered in future studies. First, we examined the entire lung cancer diagnostic and pre-treatment pathways. Second, we used internationally accepted frameworks to conceptualise and measure these pathways. These approaches enabled a systematic approach in data collection and a more complete picture of lung cancer pathways. It also allowed for data comparison between studies and across cancer types.

Our main limitation was including only five CALD groups; therefore, caution is needed when generalising these findings to other CALD groups. Furthermore, we had to combine all five groups as a single entity in the analyses even though factors relating to diagnostic intervals could vary between CALD groups. While focusing on only five CALD groups was necessary due to practical considerations with translating study materials, this approach created great challenges in recruiting CALD patients because the composition of CALD communities varied across study sites and the five CALD groups were not the top CALD communities for some sites. Our study was also limited in that we recruited fewer participants than we initially anticipated, leading to some intervals having relatively small sample size and insufficient power for statistical analyses. There were a number of reasons for the lower-than-expected recruitment outcomes. First, as noted above, we focused only five CALD groups which limited the number of CALD patients we could recruit. Second, the original 50% patient survey response rate and 80% GP review response rate were likely over ambitious given the relatively high mortality rate for lung cancer (Ferlay et al., 2019) and the time-poor and increasing part-time nature among GPs (Pit, Vo, & Pyakurel, 2014). Therefore, collected from the patient survey likely reflected that of the relative healthy sub-group of lung cancer patients who were willing to participate in research. Given this, caution is needed when generalising the findings from this study to the general population. On the other

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hand, the 33% survey response rate and the 63% GP response reported in this study were comparable to survey studies set among patients with lung cancer and GPs (Menon et al., 2019). Finally, the selection of covariates included in the multivariable models were based on the results of univariable models. Such selection depends on a specific value of significance level and sample size, and may be unstable. For example, no potential covariates can be significant in a very small size, whereas all potential covariates may be significant in a very large sample.

Despite these limitations, our study represents an important extension of research on ethnic disparity along the diagnostic and treatment pathways for lung cancer. Our study provides further evidence on ethnic disparity in the hospital diagnostic interval, which is likely to have negative consequences on outcomes, such as poorer psychological wellbeing and quality of life, among patients with lung cancer from ethnic minorities and their families. Our study is also the first to examine lung cancer diagnostic intervals prior to the hospital setting in ethnic minority patients and found a trend towards longer intervals among this group. However, caution is needed when generalising this result to the general population given the relatively small sample sizes of pre-hospital intervals and potential selection issues. Taken together, these results highlight the need for further studies on these intervals and the need for interventions aimed to reduce ethnic disparities in these intervals. These might include a campaign to increase awareness of common lung cancer symptoms in the ethnic minority communities and an education program for GPs to increase their understanding on ethnic differences in the lung cancer diagnostic and treatment pathway.

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Table 1 Characteristics of participants in the case-note analysis

	Whole sample (n = 577)	Anglo (n = 407, 71%)	CALD[1] (n = 170, 29%)	*p*
Age (Median, IQR[2])	69 (16)	68 (16)	70 (15)	.008[6]
Gender				
Male	329 (57%)	222 (55%)	107 (63%)	.063[7]
Female	248 (43%)	185 (45%)	63 (37%)	
Marital Status				
Single	79 (14%)	69 (17%)	10 (6%)	<.001[7]
Married	311 (54%)	199 (49%)	112 (66%)	
Widowed	62 (11%)	43 (11%)	19 (11%)	
Divorced or separated	74 (13%)	59 (15%)	15 (9%)	
Not stated	51 (8%)	37 (8%)	14 (8%)	
Socio-economic status				
IRSAD[3]	7 (5)	6 (6)	7 (5)	. 173[8]
Referral source				
GP[4]	264 (46%)	178 (44%)	86 (51%)	.244[7]
Private specialist	58 (10%)	36 (9%)	22 (13%)	
Self-referred to ED[5]	85 (15%)	66 (16%)	19 (11%)	
Internal referral	104 (18%)	77 (19%)	27 (16%)	
External referral	37 (6%)	28 (7%)	9 (5%)	
Other	29 (5%)	22 (5%)	7 (4%)	
Type of lung cancer				
Non-small	473 (82%)	334 (82%)	139 (82%)	. 391[7]
Small	81 (14%)	60 (15%)	21 (12%)	
Other	22 (4%)	13 (3%)	9 (5%)	
Stage of lung cancer				
Stage 1	116 (20%)	76 (19%)	40 (24%)	. 514[7]
Stage 2	75 (13%)	54 (13%)	21 (12%)	
Stage 3	112 (19%)	85 (21%)	27 (16%)	
State 4	171 (30%)	122 (30%)	49 (29%)	
Not recorded	102 (18%)	70 (17%)	32 (19%)	

[1]CALD – Culturally and Linguistically Diverse, [2]IQR- Inter-Quarter Range, [3]Socio-ecnomic status was measured through the IRSD (i.e., Index of Relative Socio-economic Disadvantage) of the postcodes of participants' home address. The IRSAD is calculated by the Australian Bureau of Statistics as an indicator of the socio-economic status of people living in a particular area. The IRSAD ranges from 1 to 10, with higher values indicating higher levels of advantage and lower levels of relative socio-economic disadvantage, [4]GP – General Practitioner, [5]ED – Emergency Department, [6]Mann-Whitney U test, [7]Pearson's Chi-squared test, [8]Gamma test

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Table 2 Characteristics of participants in the patient survey

	Whole sample (n = 156)	Anglo (n = 112, 72%)	CALD[1] (n = 44, 28%)	*p*
Age (Median, IQR[2])	70 (13)	69 (13)	72 (13)	.252[5]
Education level (n=152)				.175[2]
Primary school or lower	16 (10%)	8 (7%)	8 (19%)	
High school	74 (49%)	57 (52%)	17 (41%)	
TAFE[3] or trade training	29 (19%)	20 (18%)	9 (21%)	
University or higher	33 (22%)	25 (23%)	8 (19%)	
Employment (n=153)				.127[6]
Full time	14 (9%)	13 (12%)	1 (2%)	
Part time	11 (7%)	9 (8%)	2 (5%)	
Casual	4 (3%)	3 (3%)	1 (2%)	
Retired	105 (69%)	69 (63%)	36 (84%)	
Not in paid employment	19 (12%)	16 (14)	3 (7%)	
Smoking history (n=152)				<.001[7]
Current smoker	18 (12%)	17 (16%)	1 (2%)	
Former smoker	112 (73%)	85 (77%)	27 (61%)	
Non-smoker	24 (16%)	8 (7%)	16 (36%)	
Having family history of lung cancer (n=152)	37 (24%)	26 (24%)	11 (25%)	.904[7]
HLQ-Understand[4] (n=154) (mean, SD)	3.18 (0.76)	3.23 (0.78)	3.08 (0.79)	.272[8]
HLQ-Engage[4] (n=153)	4.05 (0.73)	4.06 (0.71)	4.03 (0.79)	.848[8]
HLQ-Navigate[4] (n=154)	3.91 (0.74)	3.92 (0.72)	3.87 (0.79)	.701[8]

[1]CALD – Culturally and Linguistically Diverse, [2]IQR- Inter-Quarter Range, [3]TAFE - Technical and Further Education [4]HLQ refers to the Health Literacy Questionnaire (Osborne et al., 2013). HLQ-Understand refers to the HLQ domain of "Feeling understood and supported by healthcare providers" and its scores range from 1 to 4 with higher scores indicating higher ability HLQ-Engage refers to the domain of "Ability to actively engage with healthcare providers" and HLQ-Navigate refers to the domain of "Navigating the healthcare system". Both scores range from 1 to 5, with higher scores indicating higher ability in the target HLQ domain, [5]Mann-Whitney U test, [6]Fisher's exact test, [7]Pearson's Chi-squared test, [8]t-test

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Table 3 Results of Cox regression analyses examining covariates of the hospital diagnostic interval

Variable name	Univariable analysis		Multivariable analysis	
	HR[1] (95% CI[2])	*p*	HR (95% CI)	*p*
Ethnicity				
CALD[3] vs Anglo-Australian	1.32 (1.09-1.60)	.005	1.~~46~~26 (1.~~17~~03-1.~~83~~54)	~~.001~~.022
Age	1.00 (1.00-1.02)	.042	~~1.01~~0.99 (~~1.00~~0.98-1.~~02~~00)	.~~07~~1043
Gender				-[16]
Female vs Male (ref[4])	1.04 (0.87-1.25)	.660		
State		<.001		≤.001
VIC[5] vs QLD[6]	1.53 (1.19-1.96)	.001	1.~~64~~67 (1.~~22~~27-2.~~20~~17)	≤.001
NSW[7] vs QLD	0.91 (0.66-1.25)	.561	~~0.99~~1.09 (0.~~60~~75-1.~~62~~59)	.~~96~~7652
Socio-economic status – IRSAD[8]	1.01 (0.99-1.04)	.340		-
Marital status				-
Married vs Not married	0.94 (0.79-1.12)	.500		
Nature of lung cancer		.316		-
Non-small vs Small	1.21 (0.95-1.56)	0.129		
Other vs Small	1.19 (0.73-1.93)	0.484		
~~**Stage of lung cancer**~~		~~<.001~~		~~<.001~~
~~1 vs 4~~	~~2.02 (1.56-2.60)~~	~~<.001~~	~~1.89 (1.42-2.51)~~	~~<.001~~
~~2 vs 4~~	~~1.81 (1.35-2.43)~~	~~<.001~~	~~1.85 (1.35-2.53)~~	~~<.001~~
~~3 vs 4~~	~~1.30 (1.00-1.68)~~	~~.047~~	~~1.24 (0.94-1.64)~~	~~.128~~
Referral type		.095		-
Private specialist vs GP[9]	0.81 (0.59- 1.12)	.197		
Self-referred to ED[10] vs GP	0.81 (0.63-1.05)	.112		
Internal referral vs GP	1.08 (0.85-1.38)	.521		
External referral vs GP	0.71 (0.49-1.02)	.061		
Other vs GP	1.31 (0.73-2.34)	.363		
Type of specialist seen		.031		.~~10~~9006
General surgeon vs Respiratory physician	0.61 (0.29-1.28)	.191	0.~~42~~45 (0.~~19~~21-0.~~91~~96)	.~~02~~7040
Thoracic surgeon vs Respiratory physician	1.02 (0.76-1.37)	.878	0.~~83~~98 (0.~~59~~72-1.~~18~~33)	.~~30~~9900
Medical oncologist vs Respiratory physician	0.68 (0.51-0.91)	.010		.~~20~~5003
Radiation oncologist vs Respiratory physician	0.62 (0.38-1.00)	.049	0.~~80~~63 (0.~~57~~47-~~1.13~~0.86)	.~~44~~8030
Other vs Respiratory physician	1.04 (0.81-1.34)	.734	0.~~81~~57 (0.~~48~~35-~~1.39~~0.94)	.~~40~~6960

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Variable name		Univariable analysis HR[1] (95% CI[2])	*p*	Multivariable analysis HR (95% CI)	*p*
				1.~~13~~01 (0.~~84~~78-1.~~52~~30)	
Bronchoscopy			.545		-
	No vs Yes	1.06 (0.88-1.27)			
EBUS[11]			.160		-
	No vs Yes	0.87 (0.72-1.06)			
Chest X ray			.186		-
	No vs Yes	0.85 (0.66-1.08)			
CT[12]			.038		.439~~0.222~~
	No vs Yes	0.69 (0.49-0.98)		0.~~71~~86 (0.~~41~~58-1.~~23~~26)	
PET[13]			.101		-
	No vs Yes	0.83 (0.66-1.04)			
FNA[14]			.021	~~0.90~~1.03 (0.~~72~~84-1.~~12~~26)	.763~~0.356~~
	No vs Yes	1.23 (1.03-1.48)			
MDT[15] discussion			.012		.160~~0.004~~
	No vs Yes	0.61 (0.41-0.90)		0.~~44~~72 (0.~~25~~47-~~0.77~~1.14)	
Source of diagnosis			.003		.005~~0.002~~
Radiology report vs Pathology report		0.69 (0.53-0.89)	.005	0.~~54~~65 (0.~~38~~49-0.~~76~~86)	~~<.001~~.003
Medical record vs Pathology report		1.87 (0.93-3.77)	.081	1.~~21~~45 (0.~~58~~71-2.~~51~~94)	~~0.615~~.312

[1]HR – Hazard Ratio, [2]CI – Confidence Interval, [3]CALD – Culturally and Linguistically Diverse, [4]ref – Reference group, [5]VIC – Victoria, [6]QLD – Queensland, [7]NSW – New South Wales, [8]Socio-ecnomic status was measured through the IRSD (i.e., Index of Relative Socio-economic Disadvantage) of the postcodes of participants' home address. The IRSAD is calculated by the Australian Bureau of Statistics as an indicator of the socio-economic status of people living in a particular area. The IRSAD ranges from 1 to 10, with higher values indicating higher levels of advantage and lower levels of relative socio-economic disadvantage, [9]GP – General Practitioner, [10]ED – Emergency Department, [11]EBUS - Endobronchial Ultrasound, [12]CT - Computerised Tomography, [13]PET - Positron Emission Tomography, [14]FNA - Fine Needle Aspiration, [15]MDT – Multidisciplinary Team, [16]variables with this sign indicating that it is not included in the multivariable analysis

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Title

Do ethnic patients report longer lung cancer intervals than Anglo-Australian patients? - Findings from a prospective, observational cohort study

Abstract

Introduction: Lung cancer patients from ethnic minorities have poorer outcomes than their Caucasian counterparts. We compared lung cancer intervals between culturally and linguistically diverse (CALD) and Anglo-Australian patients to identify ethnic disparities.

Material and methods: This was a prospective, observational cohort study comprising a patient survey and reviews of patients' hospital and general practice records. Across three states, 577 (407 Anglo-Australian and 170 CALD) patients were recruited and their hospital records reviewed. The survey was returned by 189 (135 Anglo-Australian and 54 CALD) patients and a review was completed by general practitioners (GPs) of 99 (76 Anglo-Australian and 23 CALD) patients. Survival and Cox regression analyses were conducted.

Results: CALD patients had longer hospital diagnostic interval (median 30 days, 95% CI 26 – 34) than Anglo-Australian patients (median 17, 95% CI 14 – 20), p = .005, hazard ratio (HR) = 1.32 (95% CI 1.09 - 1.60). This difference persisted after relevant factors were taken into consideration, adjusted HR = 1.26 (95% CI 1.03 - 1.54, p =.022). CALD patients also reported longer pre-hospital intervals, however, these differences were not statistically significant.

Discussion: Target interventions need to be developed to address ethnic disparity in hospital diagnostic interval.

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Key words

Lung cancer, ethnicity, diagnostic intervals, cancer pathway, immigrants

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Introduction

Lung cancer is the leading cause of cancer mortality, estimated in 2018 to be responsible for 1.76 million (or 18.4% of the total) cancer deaths worldwide (Ferlay et al., 2019). One reason for this high mortality rate is that lung cancer is often diagnosed at a late stage when curative treatment is an unlikely option (Walters et al., 2013). Therefore, early diagnosis and treatment is a key focus for reducing lung cancer mortality and improving patient outcomes (Walters et al., 2013). It is important to analyse intervals along the lung cancer pathway to identify where delays are ocurring so as to better focus the development of interventions that can address these delays and achieve more timely diagnosis and appropriate treatment (Walter, Webster, Scott, & Emery, 2012; Weller et al., 2012).

Patients from ethnic minority backgrounds are a vulnerable group of patients with lung cancer. Compared to Caucasians, they are often diagnosed at more advanced stages, have poorer survival rates, and are less likely to receive timely and appropriate treatment (Lin et al., 2014; Richards et al., 2017; Varlotto et al., 2018). They also face additional barriers to accessing healthcare, such as holding more fatalistic beliefs towards cancer and its treatment, language barriers, unfamilarity with the healthcare system (Licqurish et al., 2017; Lin et al., 2014).

Relatively few studies have examined intervals along the lung cancer diagnostic and treatment pathways amongst ethnic minority patients. Jacobsen et al's (2017) scoping review on lung cancer diagnostic intervals identified only six studies reporting on ethnic minority patients. All of these studies were conducted in the United States (US) and only examined hospital intervals. Of them, five reported longer intervals among ethnic minority patients than Caucasian patients (Jacobsen et al., 2017). Another study conducted in Australia found that of patients with lung cancer, those born overseas had a 5-day longer interval from referral to diagnosis than Australian-born patients (Evans et al., 2016).

Given the great differences in healthcare systems and the composition and history of the ethnic communities between the US and other multicultural countries such as Australia, there is a need for further studies on ethnic disparity in the lung cancer intervals in countries outside the US. In addition,

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even though the pre-hospital intervals account for a significant proportion of the lung cancer diagnostic pathway (Jacobsen et al., 2017), to our knowledge, no study has examined intervals prior to hospital involvement amongst ethnic minority patients.

The LEAD project (Lung cancer diagnostic and treatment pathways: a comparison between culturally and linguistically diverse [CALD] and Anglo-Australian patients) was designed to address these limitations through comparing intervals along the lung cancer diagnostic and treatment pathways between CALD and Anglo-Australian patients. Australia is one of the most culturally diverse countries in the world (Pison, 2019). More than a quarter (29%) of Australia's population were born overseas and over 200 languages are spoken in Australian homes (Australian Bureau of Statistics, 2017). Based on earlier studies, we hypothesised that CALD patients would report longer intervals along the lung cancer pathway than Anglo-Australian patients. We also hypothesised that the differences in the intervals would persist after the impact of other relevant factors, such as age and stage of lung cancer at the time of diagnosis, was taken into consideration.

Methods

Study design and participants

LEAD was a prospective, observational cohort study using a mixed-method approach *(blinded for reviewers)*. Here we report on the quantitative sub-study, which comprised a case-note analysis of patients' hospital records, a patient survey, and a record review by the patients' general practitioners (GPs). The study was conducted in five study sites across three states in Australia: three Integrated Cancer Services in Melbourne, Victoria; one public hospital in Sydney, New South Wales; and, one public hospital in Brisbane, Queensland. These health services provide coverage for all the metropolitan regions of Melbourne, Sydney and Brisbane, which account for 49% of Australian population (Australian Bureau of Statistics, 2017), and have significant numbers of patients with lung cancer and CALD patients.

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The patient eligibility criteria were: (1) having a new diagnosis of primary lung cancer within the previous month or during the recruitment phase (May 2017 to July 2018), and (2) being either Anglo-Australian or CALD. We used prospective recruitment and also included patients diagnosed within the previous month to minimise the risk of recall bias and participant attrition due to death.

Anglo-Australian patients were defined as those born in Australia and four other major English-speaking countries (Canada, New Zealand, the United Kingdom, and the US). CALD patients were defined as those born overseas and from one of five ethnic groups: Arabic, Chinese, Greek, Italian, and Vietnamese. These are the most common ethnic groups for overseas-born people in Australia (Australian Bureau of Statistics, 2017). Patients who were pregnant or aged under 18 years were excluded because lung cancer is uncommon among these two groups and those patients tend to have a different diagnostic pathway to the general lung cancer population (Mitrou, Petrakis, Fotopoulos, Zarkavelis, & Pavlidis, 2016; Yu et al., 2010).

As outlined in our protocol paper *(blinded for reviewers)*, we aimed to recruit 724 patients (362 per group) (assuming a 50% patient survey completion rate and a 80% GP review completion rate, based on previous studies, e.g., Emery et al., 2013) in order to achieve a final sample of 290 participants (145 per group). This sample size provides 90% power for a log-rank test with a two-sided alpha of 0.05 to detect a difference in median intervals of 60 versus 88 days (assuming an exponential distribution of survival times). A 28 day difference in median intervals was judged clinically important based on previous studies that indicate tumour size increases by about 20% every 28 days (Henschke et al., 2012; Torring, Frydenberg, Hansen, Olesen, & Vedsted, 2013).

We obtained ethics approval for a multiple-site study from Monash Health Human Research Ethics Committee (HREC/16/MonH/311) and research governance approval from all participating sites.

Procedure

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The study coordinators at each site identified eligible patients from the list of new cases presented at their respective lung cancer multidisciplinary team (MDT) meetings. Additional recruitment sources, such as the bronchoscopy lists, were also used in some study sites. The site coordinators went through these lists regularly throughout the recruitment phase. The recruitment target for the Anglo-Australia group was reached at some sites before the recruitment period finished. For these sites, Anglo-Australian participants were recruited at a slower speed (i.e., one of every two or three patients was recruited into the study depending on how fast the site reaching the recruitment target) once the recruitment target was reached.

After an eligible patient was identified, the site coordinators conducted a case-note analysis of the patients' hospital medical records using an audit tool developed based on those previously used by the research team *(blinded for reviewers)*. This tool collected data relevant to the lung cancer diagnostic and pre-treatment treatment pathway (e.g., dates of referral, dates of diagnosis, and the nature and stage of lung cancer at the time of diagnosis) and the patients' demographic background (e.g. age, gender, and country of birth). Waiver of consent was used for this component and identifiable patient information was removed in the case-note analysis.

The site coordinators sent an invitation letter to the patient, together with the patient survey and a reply-paid envelope. Two weeks after the initial invitation, the patients who had not already returned the survey received a reminder phone call, as well as a reminder letter. For CALD patients who did not speak English, we sent the invitation letter and the survey in English and in their preferred languages, and the reminder phone call was made to the contact person listed in their medical records instead of the patients themselves.

The patient survey comprised the Cancer Symptom Interval Measure (C-SIM) instrument (J Emery et al., 2013) plus questions on patients' socio-demographic characteristics (e.g. education level), clinical history (e.g. smoking history), and health literacy. Implied consent was used for this component. In addition, we asked for patients' written consent for the research team to access their hospital and general practice medical records in the patient survey. For those who provided written consent, we then

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contacted their GP and also conducted data linkage between their survey data and their case-note analysis data. This was achieved by site coordinator providing patients' case-note ID upon receipt of written consent forms from the research team.

For those who returned the survey but did not provide written consent, we had their case-note and survey data, but these data were saved separately and were not linked. For those who did not return survey, we only had their case-note data which were de-identified.

We contacted the GPs of the patients who had provided written consent in the patient survey by mail to invite them to complete a review of the patients' general practice medical records. The invitation letter was sent together with a GP review proforma, the patient's written consent, and a reply-paid envelope. A reminder letter was sent two weeks later and a reminder phone call was made to the GP practice. To increase GPs' interest in completing the review, a certificate of participation was offered to GPs who completed the review. This certificate could be used by the GPs to self-report to relevant medical colleges for Continuing Professional Development points.

The GP review proforma was posted with patients' survey IDs only, so there was no identifiable patient information on the review proforma when returned, whereas the survey ID enabled data linkage between the patient survey and the GP review. The review proforma was based on an earlier one used by the research team (J Emery et al., 2013) and captured key data on presentations to general practice and investigations conducted by GPs prior to referrals.

Outcomes

The primary outcomes were nine intervals along the lung cancer diagnostic and pre-treatment pathway (see Figure 1). These intervals were developed based on the Model of Pathways to Treatment (Scott, Walter, Webster, Sutton, & Emery, 2013; Walter et al., 2012) and the Aarhus Statement (Weller et al., 2012), which provide internationally accepted theoretical and methodological guidance in cancer early diagnosis research. In situations where there was uncertainty about specific dates, we used the mid-

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point rule proposed by Allgar and Neal (2005). However, unlike Allgar and Neal (2005) who did not include intervals greater than one year, we included these intervals to maximum the number of participants in analyses, but coded them as 366 days as the intervals were unlikely to be accurate in number of days. Negative intervals sometimes arose because the lung cancer diagnostic and treatment pathways might not always occur in a linear fashion (Walter et al., 2012; Weller et al., 2012). These intervals were converted to 0 before entering the analyses.

Statistical analyses

Data from the patient surveys and the GP reviews were entered centrally into separate databases using SPSS Version 25. Data from the case-note analysis were entered locally by the site coordinators into an online database using Research Electronic Data Capture (REDCap) (Harris et al., 2009) and then downloaded into the SPSS. As noted above, for participants who provided written consent in the patient survey, their case-note analysis, patient survey and GP review data were linked. For participants who did not provide this consent, their case-note analysis data were de-identified and were not linked to their survey data (for those who returned the survey without written consent).

Differences between CALD and Anglo-Australian groups in socio-demographic variables were compared using Pearson's chi-squared tests for categorical variables (e.g. smoking status), t-tests for continuous variables that are normally distributed (e.g. health literacy measures), and Mann-Whitney U test for continuous variables that are not normally distributed (e.g., age). The distribution of intervals was characterised using the Kaplan–Meier method, and the log-rank test was used to compare the intervals between CALD and Anglo-Australian groups. Each interval reflects the time elapsed from a starting point (e.g. noticing symptoms) until an event occurs (e.g. presenting symptoms to GPs). Proportional Hazards (PH) regression was used estimate the ratio of the hazards in the two participant groups. A hazard ratio (HR) > 1 indicates a longer interval in the CALD group, and a HR < 1 a shorter interval in the CALD group.

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PH regression was also used to examine the sensitivity of results to adjustment for selected covariates. The covariates investigated included: (1) patient demographic factors (e.g., age and gender), (2) disease and symptom factors (e.g., nature of lung cancer, and whether or not the patient reported particular lung cancer symptoms), (3) investigation related factors (e.g., referral source, and whether or not the patient was discussed at a lung MDT meeting). The relevance of these covariates for each interval was established by evaluating each covariate individually in a series of univariable PH models (see Supplemental Table 1 for covariates examined for each time interval). Covariates from these PH models that were significant at < 0.05 were selected for inclusion in the multivariable models and the assumptions for PH regression were checked and confirmed.

Role of the funding source

The funder of this study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

A total of 577 patients were recruited into the study, of whom 189 (33%) returned the survey, 156/189 (83%) patients provided written consent, and the GPs of 99 (63%) patients returned the review (see Figure 2). There was no difference between CALD and Anglo-Australian patients in the survey response rate ($p = .74$), the consent rate ($p = .81$), and the GP review return rate ($p = .07$), respectively. There was also no difference between the two groups in the availability of key data in the case-note analysis, the patient survey and the GP review (see Supplemental Table 2).

As can be seen in Tables 1 and 2, compared to Anglo-Australian patients, CALD patients were older, less likely to be single or divorced, and less likely to be a current or former smoker. There was, however,

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no difference in other variables, such as socio-economic status and health literacy, or the types and stages lung cancer at the time of diagnosis.

In the comparisons of the intervals between ethnic groups, a difference was found in the hospital diagnostic interval with the estimate HR of 1.32 (95% CI: 1.09-1.60, p = .005), reflecting a longer interval for the CALD group (median of 30 days; 95% CI: 26 to 44 days) compared to the Anglo-Australian group (median 17 days; 95% CI 14 to 20, log-rank p =. 003) (see Figure 3). This effect remained statistically significant even after taking into account the nine comparisons of intervals performed (using the Bonferroni method where the p-value for an individual test amongst the set of nine performed must fall below the critical value of 0.05/9 = 0.0056 to be declared statistically significant). Among the remaining intervals, there was a statistically insignificant trend towards longer intervals amongst CALD patients for: 1) total diagnostic and treatment interval; 2) total diagnostic interval; 3) help-seeking interval; 4) GP diagnostic interval, and 5) hospital care interval (see Figure 3).

The univariable PH regression analyses for the hospital diagnostic interval identified the following covariates for inclusion in the multivariable PH model: age, state of residence, the type of specialists seen at the first appointment, whether the patient had computed tomography (CT) scan or fine needle aspiration (FNA) biopsy completed, whether the patients were discussed at the MDT, and the source of diagnosis (see Table 3). After adjustment of covariates of interest, the HR for CALD patients was 1.26 (95% CI: 1.03 to 1.54, p=.022).

Discussion

Guided by the Model of Pathways to Treatment (Scott et al., 2013; Walter et al., 2012) and the Aarhus Statement (Weller et al., 2012), we measured and compared the lung cancer diagnostic and pre-treatment pathways between CALD and Anglo-Australian patients through nine intervals. We found that CALD patients experienced a longer hosptial diagnostic interval than Anglo-Australian patients (HR = 1.32, p = .005).

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The difference in medians between groups was 30 days (95% CI 26 – 34) vs 17 days (95% CI 14 – 20). The effect persisted after adjustment for other relevant factors, such as the age and the source of diagnosis, adjusted HR = 1.26, p =.022. These results are consistent with those from earlier studies (Evans et al., 2016; Jacobsen et al., 2017) and provide further evidence of a longer hospital diagnostic interval among patients with lung cancer from ethnic minorities.

The size of the difference between groups in median hospital diagnostic interval is unlikely to lead to significant differences in clinical outcomes, because tumour size is only thought to increase by 20% every 28 days (Henschke et al., 2012; Torring et al., 2013). This suggestion is supported by our finding that there was no difference in the stages of lung cancer at the time of diagnosis between CALD and Anglo-Australian patients.

In spite of this, the 13-day difference may still have negative consequences on outcomes, such as poorer psychological wellbeing and quality of life, among patients with lung cancer from ethnic minorities and their families. There is clear evidence that waiting for a cancer diagnosis is a distressing time for patients and families and that they have high levels of anxiety and depression and low levels of health-related quality of life during this time (Brocken, Prins, Dekhuijzen, & van der Heijden, 2012; Moseholm et al., 2016; Wiljer et al., 2012). In addition, studies have found that ethnic minority cancer patients have worse psychological outcomes and quality of life than locally-born patients (Sze et al., 2015).

There are a number of factors that might explain the ethnic disparity that we observed in the study, including different beliefs towards cancer and its treatment, language barriers and unfamilarity with the healthcare system (Licqurish et al., 2017; Lin et al., 2014). In addition, the ethnic disparity might be related to lower levels of smoking rates among ethinic minority communities (Joshi, Jatrana, & Paradies, 2018) as well in our participants. Tobacco smoking is the major cause of lung cancer (Malhotra, Malvezzi, Negri, La Vecchia, & Boffetta, 2016), but Asian women in particular have higher rates of lung cancer in non-smokers than other populations (J. Emery & Mitchell, 2017). Importantly, there is some evidence that non-smokers took longer to seek medical care after the onset of symptoms (Dias, Linhas, Campainha, Conde, & Barroso, 2017).

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To our knowledge, this is the first study to compare the lung cancer intervals prior to the hospital setting amongst ethnic minority patients to those of Caucasian patients, and we found a trend towards longer intervals amongst ethnic minority patients. This result warrants larger-scale studies with greater statistical power to more precisely examine possible ethnic disparities in lung cancer diagnostic intervals prior to hospital referral.

There are a number of strengths in the design of our study that could be considered in future studies. First, we examined the entire lung cancer diagnostic and pre-treatment pathways. Second, we used internationally accepted frameworks to conceptualise and measure these pathways. These approaches enabled a systematic approach in data collection and a more complete picture of lung cancer pathways. It also allowed for data comparison between studies and across cancer types.

Our main limitation was including only five CALD groups; therefore, caution is needed when generalising these findings to other CALD groups. Furthermore, we had to combine all five groups as a single entity in the analyses even though factors relating to diagnostic intervals could vary between CALD groups. While focusing on only five CALD groups was necessary due to practical considerations with translating study materials, this approach created great challenges in recruiting CALD patients because the composition of CALD communities varied across study sites and the five CALD groups were not the top CALD communities for some sites. Our study was also limited in that we recruited fewer participants than we initially anticipated, leading to some intervals having relatively small sample size and insufficient power for statistical analyses. There were a number of reasons for the lower-than-expected recruitment outcomes. First, as noted above, we focused only five CALD groups which limited the number of CALD patients we could recruit. Second, the original 50% patient survey response rate and 80% GP review response rate were likely over ambitious given the relatively high mortality rate for lung cancer (Ferlay et al., 2019) and the time-poor and increasing part-time nature among GPs (Pit, Vo, & Pyakurel, 2014). Therefore, collected from the patient survey likely reflected that of the relative healthy sub-group of lung cancer patients who were willing to participate in research. Given this, caution is needed when generalising the findings from this study to the general population. On the other

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hand, the 33% survey response rate and the 63% GP response reported in this study were comparable to survey studies set among patients with lung cancer and GPs (Menon et al., 2019). Finally, the selection of covariates included in the multivariable models were based on the results of univariable models. Such selection depends on a specific value of significance level and sample size, and may be unstable. For example, no potential covariates can be significant in a very small size, whereas all potential covariates may be significant in a very large sample.

Despite these limitations, our study represents an important extension of research on ethnic disparity along the diagnostic and treatment pathways for lung cancer. Our study provides further evidence on ethnic disparity in the hospital diagnostic interval, which is likely to have negative consequences on outcomes, such as poorer psychological wellbeing and quality of life, among patients with lung cancer from ethnic minorities and their families. Our study is also the first to examine lung cancer diagnostic intervals prior to the hospital setting in ethnic minority patients and found a trend towards longer intervals among this group. However, caution is needed when generalising this result to the general population given the relatively small sample sizes of pre-hospital intervals and potential selection issues. Taken together, these results highlight the need for further studies on these intervals and the need for interventions aimed to reduce ethnic disparities in these intervals. These might include a campaign to increase awareness of common lung cancer symptoms in the ethnic minority communities and an education program for GPs to increase their understanding on ethnic differences in the lung cancer diagnostic and treatment pathway.

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Table 1 Characteristics of participants in the case-note analysis

	Whole sample (n = 577)	Anglo (n = 407, 71%)	CALD[1] (n = 170, 29%)	*p*
Age (Median, IQR[2])	69 (16)	68 (16)	70 (15)	.008[6]
Gender				
Male	329 (57%)	222 (55%)	107 (63%)	.063[7]
Female	248 (43%)	185 (45%)	63 (37%)	
Marital Status				
Single	79 (14%)	69 (17%)	10 (6%)	<.001[7]
Married	311 (54%)	199 (49%)	112 (66%)	
Widowed	62 (11%)	43 (11%)	19 (11%)	
Divorced or separated	74 (13%)	59 (15%)	15 (9%)	
Not stated	51 (8%)	37 (8%)	14 (8%)	
Socio-economic status				
IRSAD[3]	7 (5)	6 (6)	7 (5)	. 173[8]
Referral source				
GP[4]	264 (46%)	178 (44%)	86 (51%)	.244[7]
Private specialist	58 (10%)	36 (9%)	22 (13%)	
Self-referred to ED[5]	85 (15%)	66 (16%)	19 (11%)	
Internal referral	104 (18%)	77 (19%)	27 (16%)	
External referral	37 (6%)	28 (7%)	9 (5%)	
Other	29 (5%)	22 (5%)	7 (4%)	
Type of lung cancer				
Non-small	473 (82%)	334 (82%)	139 (82%)	. 391[7]
Small	81 (14%)	60 (15%)	21 (12%)	
Other	22 (4%)	13 (3%)	9 (5%)	
Stage of lung cancer				
Stage 1	116 (20%)	76 (19%)	40 (24%)	. 514[7]
Stage 2	75 (13%)	54 (13%)	21 (12%)	
Stage 3	112 (19%)	85 (21%)	27 (16%)	
State 4	171 (30%)	122 (30%)	49 (29%)	
Not recorded	102 (18%)	70 (17%)	32 (19%)	

[1]CALD – Culturally and Linguistically Diverse, [2]IQR- Inter-Quarter Range, [3]Socio-ecnomic status was measured through the IRSD (i.e., Index of Relative Socio-economic Disadvantage) of the postcodes of participants' home address. The IRSAD is calculated by the Australian Bureau of Statistics as an indicator of the socio-economic status of people living in a particular area. The IRSAD ranges from 1 to 10, with higher values indicating higher levels of advantage and lower levels of relative socio-economic disadvantage, [4]GP – General Practitioner, [5]ED – Emergency Department, [6]Mann-Whitney U test, [7]Pearson's Chi-squared test, [8]Gamma test

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Table 2 Characteristics of participants in the patient survey

	Whole sample (n = 156)	Anglo (n = 112, 72%)	CALD[1] (n = 44, 28%)	*p*
Age (Median, IQR[2])	70 (13)	69 (13)	72 (13)	.252[5]
Education level (n=152)				.175[2]
Primary school or lower	16 (10%)	8 (7%)	8 (19%)	
High school	74 (49%)	57 (52%)	17 (41%)	
TAFE[3] or trade training	29 (19%)	20 (18%)	9 (21%)	
University or higher	33 (22%)	25 (23%)	8 (19%)	
Employment (n=153)				.127[6]
Full time	14 (9%)	13 (12%)	1 (2%)	
Part time	11 (7%)	9 (8%)	2 (5%)	
Casual	4 (3%)	3 (3%)	1 (2%)	
Retired	105 (69%)	69 (63%)	36 (84%)	
Not in paid employment	19 (12%)	16 (14)	3 (7%)	
Smoking history (n=152)				<.001[7]
Current smoker	18 (12%)	17 (16%)	1 (2%)	
Former smoker	112 (73%)	85 (77%)	27 (61%)	
Non-smoker	24 (16%)	8 (7%)	16 (36%)	
Having family history of lung cancer (n=152)	37 (24%)	26 (24%)	11 (25%)	.904[7]
HLQ-Understand[4] (n=154) (mean, SD)	3.18 (0.76)	3.23 (0.78)	3.08 (0.79)	.272[8]
HLQ-Engage[4] (n=153)	4.05 (0.73)	4.06 (0.71)	4.03 (0.79)	.848[8]
HLQ-Navigate[4] (n=154)	3.91 (0.74)	3.92 (0.72)	3.87 (0.79)	.701[8]

[1]CALD – Culturally and Linguistically Diverse, [2]IQR- Inter-Quarter Range, [3]TAFE - Technical and Further Education [4]HLQ refers to the Health Literacy Questionnaire (Osborne et al., 2013). HLQ-Understand refers to the HLQ domain of "Feeling understood and supported by healthcare providers" and its scores range from 1 to 4 with higher scores indicating higher ability HLQ-Engage refers to the domain of "Ability to actively engage with healthcare providers" and HLQ-Navigate refers to the domain of "Navigating the healthcare system". Both scores range from 1 to 5, with higher scores indicating higher ability in the target HLQ domain, [5]Mann-Whitney U test, [6]Fisher's exact test, [7]Pearson's Chi-squared test, [8]t-test

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Table 3 Results of Cox regression analyses examining covariates of the hospital diagnostic interval

Variable name	Univariable analysis		Multivariable analysis	
	HR[1] (95% CI[2])	*p*	HR (95% CI)	*p*
Ethnicity				
CALD[3] vs Anglo-Australian	1.32 (1.09-1.60)	.005	1.26 (1.03-1.54)	.022
Age	1.00 (1.00-1.02)	.042	0.99 (0.98-1.00)	.043
Gender				-[16]
Female vs Male (ref[4])	1.04 (0.87-1.25)	.660		
State		<.001		< .001
VIC[5] vs QLD[6]	1.53 (1.19-1.96)	.001	1.67 (1.27-2.17)	<.001
NSW[7] vs QLD	0.91 (0.66-1.25)	.561	1.09 (0.75-1.59)	.652
Socio-economic status – IRSAD[8]	1.01 (0.99-1.04)	.340		-
Marital status				-
Married vs Not married	0.94 (0.79-1.12)	.500		
Nature of lung cancer		.316		-
Non-small vs Small	1.21 (0.95-1.56)	0.129		
Other vs Small	1.19 (0.73-1.93)	0.484		
Referral type		.095		-
Private specialist vs GP[9]	0.81 (0.59- 1.12)	.197		
Self-referred to ED[10] vs GP	0.81 (0.63-1.05)	.112		
Internal referral vs GP	1.08 (0.85-1.38)	.521		
External referral vs GP	0.71 (0.49-1.02)	.061		
Other vs GP	1.31 (0.73-2.34)	.363		
Type of specialist seen		.031		.006
General surgeon vs Respiratory physician	0.61 (0.29-1.28)	.191	0.45 (0.21-0.96)	.040
Thoracic surgeon vs Respiratory physician	1.02 (0.76-1.37)	.878	0.98 (0.72-1.33)	.900
Medical oncologist vs Respiratory physician	0.68 (0.51-0.91)	.010	0.63 (0.47-0.86)	.003
Radiation oncologist vs Respiratory physician	0.62 (0.38-1.00)	.049	0.57 (0.35-0.94)	.030
Other vs Respiratory physician	1.04 (0.81-1.34)	.734	1.01 (0.78-1.30)	.960
Bronchoscopy		.545		-
No vs Yes	1.06 (0.88-1.27)			
EBUS[11]		.160		-
No vs Yes	0.87 (0.72-1.06)			
Chest X ray		.186		-
No vs Yes	0.85 (0.66-1.08)			
CT[12]		.038		.439
No vs Yes	0.69 (0.49-0.98)		0.86 (0.58-1.26)	
PET[13]		.101		-
No vs Yes	0.83 (0.66-1.04)			

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Variable name	Univariable analysis		Multivariable analysis	
	HR[1] (95% CI[2])	*p*	HR (95% CI)	*p*
FNA[14]		.021		.763
No vs Yes	1.23 (1.03-1.48)		1.03 (0.84-1.26)	
MDT[15] **discussion**		.012		.160
No vs Yes	0.61 (0.41-0.90)		0.72 (0.47-1.14)	
Source of diagnosis		.003		.005
Radiology report vs Pathology report	0.69 (0.53-0.89)	.005	0.65 (0.49-0.86)	.003
Medical record vs Pathology report	1.87 (0.93-3.77)	.081	1.45 (0.71-2.94)	.312

[1]HR – Hazard Ratio, [2]CI – Confidence Interval, [3]CALD – Culturally and Linguistically Diverse, [4]ref – Reference group, [5]VIC – Victoria, [6]QLD – Queensland, [7]NSW – New South Wales, [8]Socio-ecnomic status was measured through the IRSD (i.e., Index of Relative Socio-economic Disadvantage) of the postcodes of participants' home address. The IRSAD is calculated by the Australian Bureau of Statistics as an indicator of the socio-economic status of people living in a particular area. The IRSAD ranges from 1 to 10, with higher values indicating higher levels of advantage and lower levels of relative socio-economic disadvantage, [9]GP – General Practitioner, [10]ED – Emergency Department, [11]EBUS - Endobronchial Ultrasound, [12]CT - Computerised Tomography, [13]PET - Positron Emission Tomography, [14]FNA - Fine Needle Aspiration, [15]MDT – Multidisciplinary Team, [16]variables with this sign indicating that it is not included in the multivariable analysis

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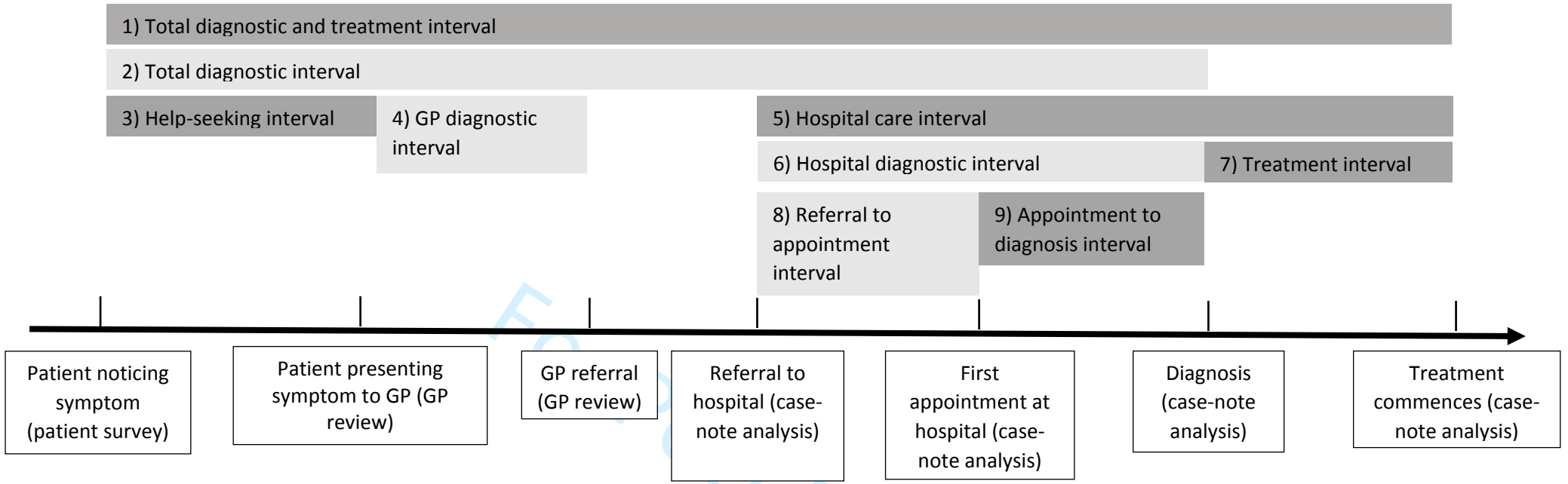

Figure 1 Time intervals examined in LEAD and their data sources

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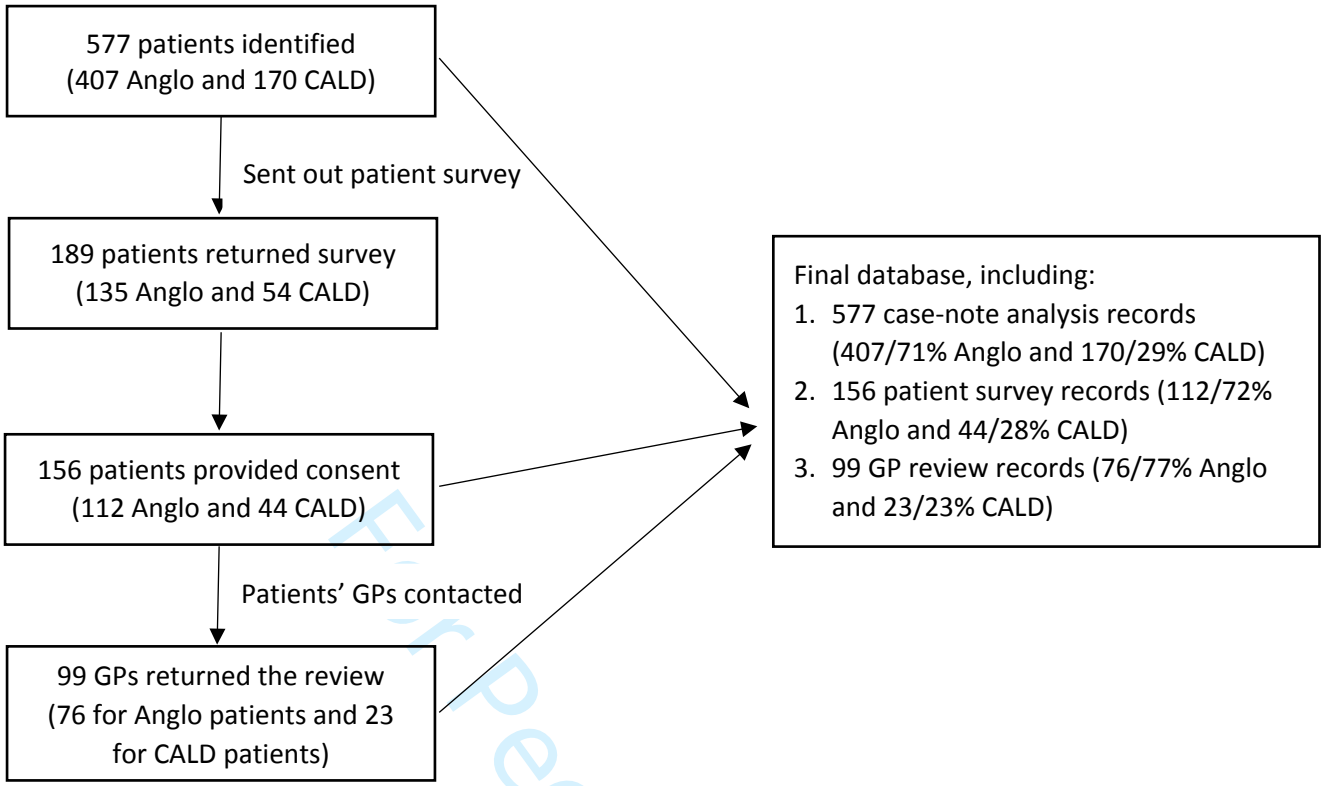

Figure 2 Data flow in the LEAD project

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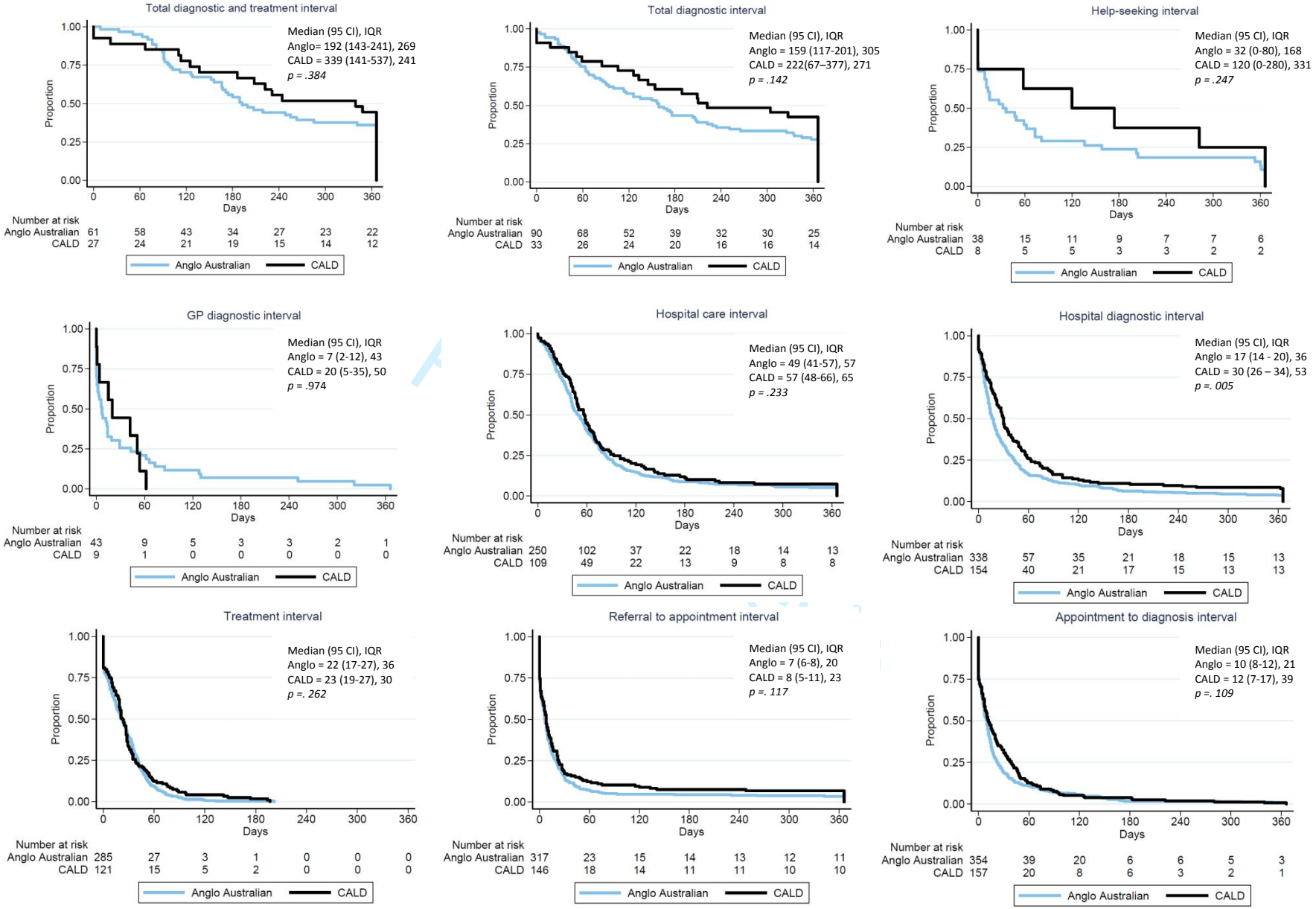

Figure 3 Kaplan-Meier survival graphs of the nine time intervals