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Lung cancer survival and stage at diagnosis in Australia, Canada, Denmark, Norway, Sweden and the United Kingdom: a population-based study, 2004-2007

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What is the key question?
Do differences in stage at diagnosis explain wide international differences in lung cancer survival?

What is the bottom line?
Differences in stage at diagnosis explain some of the international variation in lung cancer survival, but wide disparities in stage-specific survival suggest that other factors such as treatment are also important.

Why read on?
This is the first international population-based study of lung cancer survival by stage at diagnosis and includes nearly 60,000 patients. We describe how far stage explains international inequalities in lung cancer survival.

Abstract

Background

We consider whether differences in stage at diagnosis could explain the variation in lung cancer survival between six developed countries in 2004-7.

Methods

Routinely collected, population-based data were obtained on all adults (15-99 years) diagnosed with lung cancer in 2004-7 and registered in regional and national cancer registries in Australia, Canada, Denmark, Norway, Sweden and the UK. Stage data for 57,352 patients were consolidated from various classification systems . Flexible parametric hazard models on the log cumulative scale were used to estimate net survival at one year and the excess hazard up to 18 months after diagnosis.

Results

Age-standardised one-year net survival from non-small cell lung cancer ranged from 30% (UK) to 46% (Sweden). Patients in the UK and Denmark had lower survival than elsewhere, partly because of a more adverse stage distribution. However, there were also wide international differences in stage-specific survival. Net survival from TNM stage I NSCLC was 10% lower in the UK than in Sweden, and for TNM stage IV disease survival was 16% lower. Similar patterns were found for small-cell lung cancer.

Conclusion

There are comparability issues when using population-based data but even given these constraints, this study shows that while differences in stage at diagnosis explain some of the international variation in overall lung cancer survival, wide disparities in stage-specific survival exist, suggesting that other factors are also important such as differences in treatment. Stage should be included in

international cancer survival studies, and the comparability of population-based data should be improved.

INTRODUCTION

Lung cancer remains the leading cause of cancer death worldwide.[1] Survival has not improved greatly over the past three decades, and remains low for patients with all but the least invasive tumours.[2] Wide international inequalities in lung cancer survival remain apparent,[3;4] even between European countries.[5]

Governments monitor the implementation and efficacy of their cancer plans by comparing survival outcomes to those achieved in other countries with similar levels of economic development.[6] The highest survival among such countries is a benchmark against which progress can be monitored, representing what could be attained with optimal treatment and public awareness.[7] The International Cancer Benchmarking Partnership (ICBP), a consortium of clinicians, epidemiologists and policy-makers, has described lung cancer survival differences between six developed countries in 1995-2007.[8]

Understanding why these survival differences occur will facilitate policy designed to bring survival up to the highest international standard. Stage at diagnosis is an important prognostic factor, and international population-based studies suggest that differences in stage explain some of the survival variation for several cancers, including the ICBP for ovarian cancer.[9-12] Few such studies exist for lung cancer, although stage explains some of the survival differences between Nordic countries[13] and within countries over time.[2] Here, using population-based data, we investigate whether lung cancer survival differences may be attributable to differences in stage at diagnosis, reflecting delays in diagnosis or differences in staging procedures, or to differences in stage-specific survival, which could indicate differences in treatment, staging or co-morbidity.

Clinical trials are the gold standard for testing the efficacy of new therapies, but they usually exclude elderly, frail and socially-marginalised patients. Trials cannot be used for international comparisons of the effectiveness of entire health systems to underpin public health policy: population-based data on the survival of all patients are required.

DATA

Data were originally collected for patients diagnosed during 1995-2007 and followed up to the end of 2007 in six countries: Norway; Denmark; the UK (Northern Ireland, Wales and England); Australia (New South Wales and Victoria); Canada (Alberta, British Columbia, Manitoba and Ontario) and Sweden (clinical database of the Uppsala-Örebro and Stockholm-Gotland health regions;). Adults (15-99 years) diagnosed with an invasive, primary, malignant tumour of the lung or bronchus (ICD-10 C34.0-C34.9) were included. Patients whose tumour registration was made from a death certificate only (DCO) were excluded. Details of inclusion criteria and quality control have been published.[8]

Analyses were restricted to the period 2004-7 (232,278 patients), when stage data were more complete, and further to registries where at least 50% of patients were staged, thereby excluding Ontario, Victoria, Wales and six of the eight regional registries in England. A total of 57,352 patients were finally included in the analyses.

We requested stage data in three separate fields, on the extent of the tumour (T), the degree of nodal involvement (N) and the presence of metastases (M), coded to the TNM classification.[14] We prioritised pathological T and N and clinical M where both clinical and pathological data were available. Norway and New South Wales provided a locally-defined stage, classified as 'local, regional, distant'.

In order to include Norway and New South Wales in the comparisons, we mapped the TNM system used in the four other countries to the US Surveillance, Epidemiology and End Results Summary Stage 2000 classification (SEER),[15] which is similar to both the Norwegian and the New South Wales 'localised, regional, distant' classifications, but better documented and more widely known.[16] This mapping was straightforward where we had information on each of T, N and M, but it was not possible for England, which only provided a grouped TNM stage (I-IV). We therefore present two sets of analyses: one in which stage is categorised to the TNM classification system, which may be more relevant for clinicians but excludes Australia and Norway, and another in which stage is classified as 'localised, regional, distant' (SEER), which excludes England.

We examined non-small cell (NSCLC) and small-cell lung cancer (SCLC) separately, because of their different aetiology and clinical behaviour. NSCLC represents over 80% of lung cancers, and we included non-microscopically verified tumours in this group. NSCLCs grow more slowly and are generally more amenable to treatment, whereas SCLC is more aggressive, although short-term survival can be extended with chemotherapy.

STATISTICAL ANALYSES

We estimated net survival and its mortality equivalent the excess hazard, using a flexible parametric model implemented in the Stata command stpm2[17] (StataCorp LP, College Station, Texas, webappendix para 1). Net survival (or excess hazard) is the survival (or the mortality) of cancer patients after background mortality in the general population has been taken into account. Background mortality was taken from life tables specific to sex, single year of age, region of residence and year of death.[8]

Analysis was first stratified by stage at diagnosis with age at diagnosis and country of residence included as covariates and their effects allowed to vary with time since diagnosis. Non-linear effects of continuous covariates and time-dependent effects were modelled with cubic splines. Interactions between age and country were assessed with likelihood ratio test. Final models were selected based on the Akaike Information Criterion and examination of Martingale residuals (webappendix para 2). Patients were censored three years after diagnosis, but we provide estimates up to 18 months after diagnosis, because model stability requires follow-up beyond the last survival estimate.[18]

We first treated patients with missing stage as a separate category. Multiple imputation by chained equations was then conducted to include patients with missing stage in the analyses using the Stata command ice[19] (webappendix para 3). We ran the imputation model 15 times and combined the results under Rubin's rules.[19] We then re-estimated stage-specific survival using the 15 imputed datasets, by repeating the survival analysis modelling strategy described above, and compared the range of survival estimates to the estimates for patients with known stage.

We present survival estimates by age, stage and country. All-ages estimates were standardised using stage-specific weights based on the age distribution observed across all countries (web appendix, tables 1 and 2).

RESULTS

Descriptive statistics

Men represented between 52.3% (Sweden) and 62.2% (Australia) of all patients (Table 1). In the UK, 26.0% of tumours were not microscopically verified, compared with 5.2% in Sweden (Table 1). Among microscopically confirmed tumours, the percentage of SCLC varied from 12.9% in Australia to 18.0% in Norway. The proportion of adenocarcinomas ranged from 25.2% (UK) to 44.8% (Sweden). The age distribution at diagnosis was similar in all countries, with mean age about 70 years (Table 2). Patients for whom information on stage at diagnosis was missing tended to be older (mean age about 73 years). Patients diagnosed at a more advanced stage tended to be younger than those diagnosed at an earlier stage, and older patients were more likely to be missing data on stage (web appendix figure 1).

Table 1. Sex of patients, proportion not microscopically verified and histological subtypes

	Australia[1]	Canada[2]	Denmark	Norway	Sweden[3]	UK[4]
Number of patients[5]	12,233	9,805	16,058	9,445	5,246	26,243
% men	62.2	52.9	53.6	59.1	52.3	60.1
% without microscopic verification[6]	14.4	18.2	13.5	10.1	5.2	26.0
Histological subtype as % of microscopically verified tumours (ICD-O-3 code)						
Adenocarcinoma (8140-8576)	35.6	41.0	35.4	36.5	44.8	25.2
Squamous cell (8050-8084)	20.0	20.9	22.1	22.6	21.8	27.6
Large cell (8012-8035, 8046)	26.7	20.0	14.8	17.2	15.6	23.3
Small cell (8040-8045)	12.9	14.4	17.1	18.0	13.6	16.7
Other[7]	4.9	3.7	10.7	5.8	4.2	7.1

[1] Australia: New South Wales

[2] Canada: Alberta and Manitoba

[3] Sweden: Uppsala-Örebro and Stockholm-Gotland health regions

[4] United Kingdom (TNM analysis): West Midlands Cancer Intelligence Unit (WMCIU) and the Eastern Cancer Registry and Information Centre (ECRIC) in England and Northern Ireland; United Kingdom (SEER analysis): Northern Ireland

[5] This table refers to patients included in the TNM analyses for Canada, Denmark, Sweden and the UK, and to the patients included in the SEER analyses for Australia and Norway

[6] Includes patients with morphological verification but missing morphology (ICD-O-3 code 9990 and above)

[7] Carcinomas (8010-8011), basal cell (8090-8110), transitional cell (812-813), sarcomas (8800-8921), other, Not Otherwise Specified (8000-8005, 8580-8790, 8930-9989)

Table 2. Number of non-small cell and small-cell lung cancer patients diagnosed during 2004-2007: country and stage at diagnosis (TNM and SEER Summary Stage 2000), before and after imputation

		TNM stage								SEER Summary Stage 2000								
		Non-small cell				Small-cell					Non-small cell				Small-cell			
				%				%					%				%	
	Stage	Number[5]	Mean age at diagnosis	Observed	After imputation	Number[5]	Mean age at diagnosis	Observed	After imputation	Stage	Number[5]	Mean age at diagnosis	Observed	After imputation	Number[5]	Mean age at diagnosis	Observed	After imputation
Australia[1]										All patients	10,878	70.5			1,355	69.1		
										Missing stage	2,541	73.4	23.4		252	69.2	18.6	
										Localised	2,500	70.8	30.0	30.8	249	68.2	22.6	23.8
										Regional	1,878	69.0	22.5	22.8	178	69.3	16.1	16.6
										Distant	3,959	69.3	47.5	46.4	676	69.5	61.3	59.6
Canada[2]	All patients	8,648	70.2			1,157	67.7			All patients	8,648	70.2			1,157	67.7		
	Missing stage	485	72.9	5.6		24	72.8	2.1		Missing stage	568	73.2	6.6		46	70.6	4.0	
	I	1,635	70.6	20.0	20.1	37	70.3	3.3	3.3	Localised	1,635	70.6	20.2	20.3	37	70.3	3.3	3.3
	II	409	69.3	5.0	5.0	19	66.1	1.7	1.7	Regional	2,141	70.9	26.5	26.5	292	67.9	26.3	26.2
	III	2,155	71.0	26.4	26.4	360	67.7	31.8	31.8	Distant	4,304	69.3	53.3	53.1	782	67.3	70.4	70.5
	IV	3,964	69.3	48.6	48.4	717	67.4	63.3	63.3									
Denmark	All patients	13,681	69.0			2,377	67.7			All patients	13,681	69.0			2,377	67.7		
	Missing stage	1,535	74.8	11.2		194	70.6	8.2		Missing stage	1,535	74.8	11.2		194	70.6	8.2	
	I	1,749	69.0	14.4	14.0	63	69.6	2.9	3.7	Localised	1,749	69.0	14.4	14.0	63	69.6	2.9	2.9
	II	701	68.4	5.8	5.7	36	67.5	1.6	2.2	Regional	2,959	68.5	24.4	24.1	333	67.7	15.3	15.1
	III	3,019	68.2	24.9	24.6	511	67.2	23.4	23.1	Distant	7,438	68.0	61.2	61.9	1,787	67.4	81.9	82.0
	IV	6,677	68.1	55.0	55.7	1,573	67.5	72.1	71.0									
Norway	All patients									All patients	7,921	70.0			1,524	67.8		
	Missing stage									Missing stage	787	73.4	9.9		111	68.1	7.3	
	I									Localised	1,256	70.2	17.6	17.7	72	69.4	5.1	5.3
	II									Regional	2,382	69.8	33.4	33.6	372	66.7	26.3	26.6
	III									Distant	3,496	69.3	49.0	48.6	969	68.1	68.6	68.2
	IV																	

Sweden[3]

All patients	4,570	69.3			676	68.8		
Missing stage	266	74.8	5.8		31	70.7	4.6	
I	850	69.0	19.7	19.6	23	69.8	3.6	3.6
II	152	70.4	3.5	3.5	8	70.1	1.2	1.3
III	1,286	69.6	29.9	29.9	203	68.4	31.5	31.4
IV	2,016	68.4	46.8	47.0	411	68.7	63.7	63.7

All patients	4,570	69.3			676	68.8		
Missing stage	266	74.8	5.8		31	70.7	4.6	
Localised	850	69.0	19.7	19.6	23	69.8	3.6	3.5
Regional	1,090	70.1	25.3	25.2	116	68.7	18.0	17.9
Distant	2,364	68.4	54.9	55.2	506	68.6	78.4	78.6

UK[4]

All patients	22,993	71.8			3,250	68.2		
Missing stage	6,975	73.9	30.3		1,249	69.2	38.4	
I	2,376	71.8	14.8	13.5	96	69.1	4.8	4.9
II	1,165	70.9	7.3	6.8	67	68.4	3.3	3.3
III	4,718	71.6	29.5	28.6	529	67.9	26.4	26.0
IV	7,759	70.2	48.4	51.0	1,309	67.4	65.4	65.7

All patients	3,311	70.6			451	66.4		
Missing stage	1,299	73.1	39.2		192	68.5	42.6	
Localised	346	71.3	17.2	15.9	18	66.1	6.9	8.4
Regional	588	69.4	29.2	28.1	28	66.7	10.8	11.0
Distant	1,078	68.2	53.6	56.0	213	64.5	82.2	80.7

[1] Australia: New South Wales

[2] Canada: Alberta and Manitoba

[3] Sweden: Uppsala-Örebro and Stockholm-Gotland health regions

[4] United Kingdom (TNM analysis): Northern and Yorkshire Cancer Registry and Information Service (NYCRIS), Eastern Cancer Registration and Information Centre (ECRIC) in England and Northern Ireland; United Kingdom (SEER analysis): Northern Ireland

[5] Number of patients before imputation

Stage at diagnosis

The UK had the highest proportion of patients for whom data on stage (TNM) at diagnosis were missing, both for NSCLC (30.3% *vs.* 5.6-11.2% elsewhere) and for SCLC (38.4% *vs.* 2.1-8.2%). The proportion was also relatively high in Australia (SEER), both for NSCLC (23.4%) and SCLC (18.6%) (Table 2).

Lung cancer is generally diagnosed at an advanced stage. For NSCLC, the proportion with metastatic disease (TNM stage IV) ranged from 46.8% in Sweden to 55% in Denmark, or (SEER 'distant') from 47.5% (Australia) to 61.2% (Denmark). The proportion of early stage NSCLC was lowest in Denmark and the UK.

For SCLC, 72.1% of patients in Denmark had metastatic disease (TNM stage IV), compared to less than 66% elsewhere. For SEER ('distant'), the proportion ranged from 61.3% in Australia to around 82% in Denmark and the UK (Table 2).

Imputing TNM or SEER stage where it was missing did not consistently shift stage distribution towards more or less advanced stage. The increase in the proportion of TNM stage IV was 0.2-2.6% for NSCLC patients (Table 2), and -1.1% to +0.3% for SCLC.

Survival from non-small cell lung cancer

Overall, age-standardised one-year net survival from NSCLC ranged from 30% in the UK to 46% in Sweden (Table 3). Survival was also high (42%) in Australia and Canada, and intermediate (34-39%) in Denmark and Norway. Overall estimates differ slightly between the TNM and SEER analyses because patients in England were only included in the TNM analyses (40% of all TNM-staged patients), and Australian and Norwegian patients were only included in the SEER analyses (38% of all SEER patients). These exclusions affect the model results for the other countries.

One-year survival for patients with TNM stage I and II disease was significantly lower in the UK (I 72.5%; II 59.8%) and Denmark (I 73.3%; II 59.1%) than in Canada (I 86.3%; II 78.5%) and Sweden (I 88.4%; II 70.7%) (Table 3). Survival was also lower in the UK for stage III (35.3% *vs.* 42.8-46.4% elsewhere) and IV (15.9% *vs.* 20.8-25.6% in Denmark and Sweden). The apparent survival advantage

in Canada for early-stage NSCLC was not evident at more advanced stage, and survival for stage IV disease was 16.8%, similar to that for UK patients.

For TNM stage I-II, the excess hazard in the UK and Denmark was higher than in Canada and Sweden at all time points up to 18 months, but the differences were widest soon after diagnosis, narrowing over the first year (Figure 1). The excess hazard for stage III-IV NSCLC was consistently high in the UK.

Patients with 'localised' NSCLC in Australia had low survival, but survival for more advanced disease was average (Table 3, Figure 2). The excess hazard for Australian patients with 'regional' NSCLC declined more steeply with time than in other countries (Figure 1). Norwegian patients had average stage-specific survival (Table 3).

The inclusion of patients with imputed stage made no material difference to the survival patterns (Figure 2)

Table 3. One-year net survival (%) overall, age-standardised and age-specific, by stage at diagnosis and country for non-small cell lung cancer patients diagnosed during 2004-2007

	Australia[1]			Canada[2]			Denmark			Norway			Sweden[3]			UK[4]		
	NS (%)	95% CI		NS (%)	95% CI		NS (%)	95% CI		NS (%)	95% CI		NS (%)	95% CI		NS (%)	95% CI	
TNM stage																		
All patients																		
All ages				41.8	40.7	42.8	35.4	34.6	36.2				46.1	44.7	47.5	28.8	28.3	29.4
Age-standardised				41.7	40.9	42.5	34.1	33.5	34.7				45.5	44.5	46.6	29.6	29.1	30.0
15-54				50.4	47.9	53.0	45.4	43.3	47.4				54.2	50.6	57.7	41.5	39.6	43.5
55-74				44.2	42.9	45.5	39.3	38.4	40.3				48.0	46.4	49.7	32.5	31.7	33.2
75-99				36.0	34.5	37.5	24.9	23.8	26.0				40.7	38.5	42.9	22.6	21.8	23.3
Stage I																		
All ages				86.2	84.6	87.8	75.0	73.1	76.9				88.8	86.7	90.9	71.1	69.4	72.9
Age-standardised				86.3	85.3	87.3	73.3	71.9	74.6				88.4	87.0	89.8	72.5	71.4	73.6
15-54				95.5	94.1	96.9	92.4	90.6	94.2				94.5	92.1	96.8	90.0	88.0	92.0
55-74				89.5	88.0	91.0	79.7	77.8	81.6				89.9	87.9	91.8	77.5	75.6	79.3
75-99				79.5	76.6	82.3	59.8	56.2	63.5				85.2	81.6	88.8	60.9	58.2	63.6
Stage II																		
All ages				79.0	75.2	82.7	60.8	57.1	64.5				70.3	63.1	77.6	58.6	55.7	61.5
Age-standardised				78.5	76.3	80.7	59.1	56.8	61.5				70.7	66.8	74.7	59.8	57.9	61.7
15-54				89.7	86.6	92.8	79.0	73.6	84.4				88.7	83.2	94.1	79.9	74.5	85.2
55-74				82.4	79.0	85.9	64.9	61.1	68.8				75.5	69.0	82.1	65.3	62.1	68.5
75-99				69.0	63.6	74.5	46.0	40.8	51.2				58.2	48.6	67.8	45.5	41.6	49.4
Stage III																		
All ages				43.2	41.3	45.2	45.0	43.3	46.8				47.1	44.5	49.8	34.4	33.1	35.8
Age-standardised				44.0	42.5	45.4	42.8	41.5	44.1				46.4	44.5	48.4	35.3	34.3	36.3
15-54				53.5	48.1	58.9	57.8	53.6	61.9				55.4	48.3	62.4	44.4	40.2	48.6
55-74				49.3	46.7	51.8	49.4	47.4	51.5				52.5	49.4	55.7	39.6	37.9	41.4
75-99				33.2	30.4	35.9	30.8	28.0	33.5				35.7	31.8	39.6	26.3	24.6	28.1
Stage IV																		
All ages				16.8	15.7	17.8	21.4	20.5	22.3				25.9	24.1	27.7	15.5	14.7	16.2
Age-standardised				16.8	16.0	17.6	20.8	20.1	21.5				25.6	24.3	27.0	15.9	15.3	16.4
15-54				24.0	21.0	27.1	27.4	24.9	29.8				31.1	26.3	35.9	24.5	22.0	27.1
55-74				17.5	16.1	18.8	23.5	22.4	24.6				27.1	24.9	29.2	17.1	16.1	18.0
75-99				13.2	11.7	14.6	14.4	13.2	15.7				21.7	19.0	24.5	10.9	9.9	11.8
Missing stage																		
All ages				42.2	38.4	46.0	19.2	17.3	21.0				34.4	29.0	39.9	20.6	19.7	21.5
Age-standardised				38.7	35.4	42.0	19.6	18.1	21.1				34.7	30.4	39.1	20.6	19.9	21.2
15-54				88.4	82.4	94.4	40.5	31.7	49.3				49.7	31.0	68.5	42.1	38.0	46.1
55-74				40.8	34.4	47.2	21.3	18.4	24.1				40.2	31.5	48.9	23.7	22.4	25.0
75-99				33.2	28.0	38.5	15.8	13.6	18.1				29.7	23.1	36.3	16.0	14.9	17.0

SEER Summary Stage 2000

All patients	All ages	41.8	40.9	42.7	41.8	40.8	42.8	35.4	34.6	36.2	38.4	37.4	39.5	46.0	44.6	47.5	30.4	28.8	31.9
	Age-standardised	42.4	41.7	43.1	42.0	41.3	42.8	34.6	34.0	35.2	38.5	37.7	39.3	45.8	44.7	46.8	30.9	29.7	32.0
	15-54	53.5	51.1	56.0	50.1	47.5	52.7	45.0	43.0	47.1	49.8	46.9	52.7	53.8	50.3	57.4	46.1	41.3	50.9
	55-74	46.4	45.3	47.6	44.2	42.9	45.4	39.2	38.3	40.2	42.9	41.6	44.2	47.9	46.3	49.6	32.5	30.6	34.4
	75-99	32.8	31.5	34.0	36.2	34.7	37.6	25.1	24.0	26.2	29.0	27.6	30.5	40.8	38.6	42.9	24.3	22.2	26.4
Localised	All ages	63.2	61.5	64.9	85.8	84.2	87.5	73.9	71.9	75.8	74.9	72.6	77.1	88.3	86.2	90.5	67.5	62.9	72.1
	Age-standardised	64.4	63.3	65.5	86.1	85.1	87.0	72.5	71.3	73.7	74.9	73.6	76.2	87.8	86.5	89.0	68.1	65.7	70.6
	15-54	83.8	81.3	86.2	94.1	93.1	95.2	87.4	85.5	89.3	89.1	87.2	91.0	95.4	94.2	96.6	85.9	82.7	89.0
	55-74	71.4	69.6	73.2	89.7	88.3	91.0	78.3	76.5	80.1	80.3	78.3	82.3	90.8	89.1	92.6	74.1	70.0	78.2
	75-99	48.5	46.1	50.9	78.5	76.0	80.9	60.5	57.5	63.4	63.4	60.1	66.6	81.7	78.5	85.0	55.8	50.0	61.6
Regional	All ages	52.8	50.7	54.9	53.6	51.5	55.7	51.2	49.4	53.0	47.4	45.4	49.4	54.2	51.3	57.1	46.5	42.4	50.7
	Age-standardised	52.3	51.1	53.6	55.2	54.1	56.4	50.0	48.9	51.1	47.6	46.4	48.7	54.7	53.2	56.3	46.3	44.1	48.5
	15-54	67.1	64.1	70.2	69.7	67.1	72.4	64.9	62.1	67.6	63.1	60.2	66.1	68.9	65.6	72.3	61.6	57.0	66.1
	55-74	58.4	56.2	60.6	61.2	59.0	63.3	56.1	54.2	58.0	54.1	52.1	56.2	60.9	58.1	63.7	52.2	48.0	56.3
	75-99	37.8	35.2	40.4	39.9	37.4	42.4	36.3	34.0	38.6	32.9	30.6	35.3	40.3	36.9	43.7	32.6	28.1	37.1
Distant	All ages	17.6	16.5	18.6	18.5	17.4	19.6	22.9	22.0	23.8	18.3	17.1	19.5	27.3	25.6	28.9	18.6	16.4	20.8
	Age-standardised	17.9	17.1	18.7	18.7	17.9	19.5	22.4	21.8	23.1	18.5	17.7	19.4	27.1	25.9	28.4	18.3	16.7	20.0
	15-54	30.1	26.8	33.4	25.0	22.1	28.0	29.3	27.0	31.7	26.3	22.8	29.8	31.9	27.4	36.4	25.1	18.9	31.4
	55-74	19.6	18.2	21.0	19.4	18.0	20.7	25.1	24.0	26.2	20.6	19.1	22.2	29.0	26.9	31.0	19.3	16.8	21.9
	75-99	10.1	8.9	11.4	15.0	13.5	16.5	15.6	14.3	16.8	12.1	10.6	13.5	22.3	19.8	24.8	14.3	11.2	17.5
Missing stage	All ages	45.8	44.0	47.7	42.3	38.6	45.9	19.3	17.4	21.2	42.2	38.9	45.4	35.0	29.5	40.5	23.2	21.0	25.4
	Age-standardised	45.6	44.2	47.0	40.2	37.1	43.2	19.9	18.4	21.5	41.8	39.3	44.4	35.5	31.2	39.9	23.1	21.4	24.8
	15-54	61.0	55.2	66.8	88.5	83.0	94.0	40.5	31.6	49.4	72.1	62.3	82.0	50.0	31.2	68.7	55.5	47.1	63.8
	55-74	50.4	47.9	52.9	42.9	37.1	48.7	21.8	18.9	24.7	49.7	45.1	54.3	41.0	32.3	49.8	24.3	21.3	27.3
	75-99	39.9	37.5	42.4	33.3	28.3	38.2	15.7	13.4	17.9	32.2	28.0	36.4	30.1	23.4	36.8	18.6	15.9	21.3

[1] Australia: New South Wales

[2] Canada: Alberta and Manitoba

[3] Sweden: Uppsala-Örebro and Stockholm-Gotland health regions

[4] United Kingdom (TNM analysis): Northern and Yorkshire Cancer Registry and Information Service (NYCRIS), Eastern Cancer Registration and Information Centre (ECRIC) in England and Northern Ireland; United Kingdom (SEER analysis): Northern Ireland

(Insert Figure 1 and Figure 2)

Survival from small-cell lung cancer

One-year, age-standardised net survival from SCLC ranged from 24.9% in the UK to 36.6% in Sweden (TNM analyses), and from 23.1% (UK) to 38.7% (Sweden) in the SEER analysis (Table 4). The estimates differ because patients in England (38% of all patients) were only included in analyses by TNM stage, while Australian and Norwegian patients (38% of all patients) were only included in analyses by SEER stage.

Among early-stage SCLC patients (TNM I and II), survival was lower in the UK (55.9%) and Denmark (64.5%) than in Canada (71.1%) and Sweden (71.7%) (Table 4). The UK had lower survival among stage III (37.3% *vs*. 47.9-52.2%) and IV (14.4% *vs*. 17.9-27.6%) patients. The excess hazard of death for UK patients with stage III SCLC was very high immediately after diagnosis, but became average by 18 months (Figure 3). Among patients with stage IV disease, the excess hazard in the UK and in Canada was high throughout the first 18 months.

Norway had average survival for patients diagnosed at each SEER stage, and the excess hazard was generally average through follow-up (Figure 3). Australian patients had quite low stage-specific survival from SCLC (Table 4). The range in the excess hazard between SEER stages was narrower in Australia than in other countries throughout follow-up (Figure 3).

Survival estimates including patients with imputed stage were generally close to those for patients with known stage. The main exception was for the UK (Northern Ireland only) in the SEER analyses, where the number of patients was small (Figure 4).

Table 4. One-year net survival (%) overall, age-standardised and age-specific, by stage at diagnosis and country for small-cell lung cancer patients diagnosed during 2004-2007

		Australia[1]			Canada[2]			Denmark			Norway			Sweden[3]			UK[4]		
		NS (%)	95% CI		NS (%)	95% CI		NS (%)	95% CI		NS (%)	95% CI		NS (%)	95% CI		NS (%)	95% CI	
TNM stage																			
All patients	All ages				30.7	28.3	33.0	30.8	29.1	32.5				36.1	32.9	39.3	24.7	23.3	26.1
	Age-standardised				30.0	28.0	32.1	30.6	29.1	32.0				36.6	33.8	39.4	24.9	23.7	26.1
	15-54				44.6	38.1	51.0	41.2	36.2	46.1				48.9	38.6	59.3	33.2	29.1	37.3
	55-74				32.9	30.1	35.8	33.9	31.9	36.0				39.2	35.4	43.0	27.9	26.2	29.6
	75-99				17.5	14.0	20.9	18.1	15.7	20.5				26.0	21.1	30.8	14.4	12.5	16.2
Stage I & II	All ages				71.7	60.4	83.1	65.2	56.5	73.9				70.3	56.7	83.9	56.0	48.7	63.4
	Age-standardised				71.1	61.5	80.7	64.5	57.1	71.9				71.7	59.8	83.7	55.9	49.6	62.2
	15-54				94.9	88.6	100.0	82.6	66.9	98.4				99.9	99.6	100.0	82.2	70.5	93.8
	55-74				77.2	65.0	89.4	71.7	61.8	81.5				72.5	55.4	89.6	57.3	48.7	65.9
	75-99				48.6	25.7	71.6	44.6	29.3	59.9				60.0	38.6	81.4	44.9	32.4	57.5
Stage III	All ages				48.5	43.8	53.1	51.0	46.8	55.3				51.6	45.0	58.1	36.9	32.8	41.0
	Age-standardised				47.9	43.9	52.0	50.6	47.1	54.2				52.2	46.6	57.8	37.3	33.9	40.7
	15-54				71.0	59.6	82.3	74.3	66.3	82.3				63.0	45.4	80.5	50.8	40.5	61.0
	55-74				51.1	45.6	56.7	52.7	47.8	57.7				54.7	47.0	62.4	42.2	37.3	47.1
	75-99				29.4	21.9	36.9	35.3	28.4	42.1				41.6	31.4	51.8	18.8	13.1	24.5
Stage IV	All ages				18.3	15.8	20.8	23.0	21.1	24.9				26.8	23.0	30.6	14.4	12.7	16.2
	Age-standardised				17.9	16.1	19.8	23.0	21.5	24.4				27.6	24.6	30.6	14.4	13.1	15.8
	15-54				31.5	25.6	37.4	35.5	31.0	39.9				39.4	30.1	48.7	19.9	15.8	24.0
	55-74				18.7	16.1	21.3	23.8	21.8	25.7				28.6	24.5	32.8	14.7	12.9	16.5
	75-99				10.0	7.1	13.0	15.0	12.3	17.7				19.5	13.9	25.2	11.1	8.7	13.6
Missing stage	All ages				20.5	6.1	35.0	23.2	17.9	28.6				16.9	5.4	28.4	24.4	22.3	26.6
	Age-standardised				23.0	13.6	32.4	24.3	20.7	27.9				16.8	9.5	24.2	24.2	22.4	26.1
	15-54				not possible to estimate			38.2	29.2	47.2				29.3	14.0	44.5	38.2	30.8	45.6
	55-74				25.7	9.7	41.7	27.3	21.3	33.3				21.1	7.8	34.4	28.0	25.3	30.8
	75-99				13.3	0.9	25.7	14.3	9.4	19.2				7.9	0.0	16.1	13.7	11.0	16.4
SEER Summary Stage 2000																			
All patients	All ages	37.5	35.0	39.9	32.9	30.4	35.5	33.4	31.6	35.2	33.4	31.2	35.5	38.2	34.8	41.5	23.9	20.1	27.6
	Age-standardised	38.6	36.5	40.6	32.3	30.2	34.4	33.1	31.5	34.6	33.3	31.4	35.1	38.7	35.8	41.5	23.1	19.9	26.4
	15-54	54.5	48.3	60.6	46.7	40.2	53.2	43.8	38.8	48.9	54.2	48.1	60.2	51.2	40.9	61.4	34.5	25.5	43.6
	55-74	41.6	38.6	44.5	35.2	32.2	38.2	36.4	34.3	38.6	37.2	34.4	39.9	41.3	37.3	45.2	24.3	19.8	28.8
	75-99	24.8	21.3	28.2	19.8	16.1	23.5	20.7	18.1	23.2	16.7	14.0	19.5	28.0	22.9	33.0	15.3	9.4	21.2

Localised	All ages	53.7	48.2	59.1	74.4	61.9	86.9	60.8	49.8	71.7	65.9	55.5	76.2	72.4	56.5	88.4	43.6	23.7	63.5
	Age-standardised	53.0	49.0	57.0	75.8	67.8	83.7	61.7	54.6	68.7	65.9	59.1	72.6	74.0	64.1	83.9	41.2	27.9	54.5
	15-54	77.2	70.1	84.3	90.4	84.1	96.6	80.9	72.8	89.0	83.8	76.7	90.9	90.0	82.6	97.4	74.0	58.7	89.4
	55-74	57.9	52.1	63.8	78.6	67.3	89.8	65.5	55.0	75.9	68.8	58.9	78.8	77.1	63.1	91.2	44.1	22.7	65.5
	75-99	35.1	27.3	42.8	62.2	44.5	79.9	46.5	32.5	60.4	52.8	39.1	66.5	62.3	41.3	83.2	24.3	2.9	45.8
Regional	All ages	35.4	29.2	41.5	50.6	44.9	56.2	54.0	48.6	59.5	50.7	45.8	55.5	56.6	47.8	65.3	51.0	34.0	67.9
	Age-standardised	37.2	31.8	42.6	50.1	45.4	54.8	54.1	49.6	58.6	49.3	45.1	53.4	57.4	50.1	64.8	51.9	37.0	66.7
	15-54	52.1	36.1	68.2	74.7	63.2	86.2	70.2	59.3	81.1	75.2	66.0	84.4	71.7	51.1	92.2	76.5	41.1	100.0
	55-74	41.1	33.3	48.9	53.9	47.3	60.4	56.3	50.2	62.4	55.1	49.1	61.0	60.2	50.0	70.4	59.1	36.4	81.8
	75-99	19.7	11.1	28.2	30.1	21.5	38.7	41.6	32.2	50.9	25.4	17.5	33.2	44.8	31.2	58.5	22.0	0.7	43.3
Distant	All ages	19.8	17.1	22.4	23.4	20.7	26.1	28.8	26.8	30.7	22.9	20.5	25.3	32.1	28.5	35.8	14.1	9.6	18.6
	Age-standardised	20.9	18.5	23.3	22.8	20.5	25.0	28.4	26.7	30.0	23.3	21.2	25.4	32.6	29.5	35.8	14.0	9.9	18.1
	15-54	31.3	22.2	40.4	37.5	30.2	44.7	40.3	34.7	45.9	40.1	32.0	48.3	38.7	27.4	50.0	11.7	4.6	18.8
	55-74	23.0	19.6	26.4	24.4	21.2	27.6	31.1	28.8	33.5	25.8	22.7	28.8	35.5	31.2	39.8	14.9	9.8	20.0
	75-99	10.9	7.6	14.2	12.6	8.9	16.3	16.2	13.4	18.9	11.1	8.4	13.7	22.3	16.7	27.9	13.4	2.9	24.0
Missing stage	All ages	57.8	52.3	63.3	26.0	14.4	37.7	25.5	19.8	31.1	39.0	31.0	46.9	17.1	6.1	28.2	26.3	20.5	32.1
	Age-standardised	57.8	53.9	61.7	26.8	19.3	34.3	26.7	22.7	30.7	37.5	32.1	42.9	16.9	9.6	24.1	25.6	21.4	29.7
	15-54	75.7	67.9	83.5	not possible to estimate			47.5	35.6	59.3	59.3	47.5	71.2	32.9	16.7	49.1	45.7	34.7	56.7
	55-74	62.4	56.7	68.1	31.7	18.9	44.5	30.2	23.6	36.8	43.6	35.0	52.3	22.0	8.5	35.5	29.8	22.9	36.7
	75-99	44.8	37.6	52.0	15.4	5.1	25.7	14.4	9.1	19.6	21.3	13.0	29.6	6.3	0.0	13.1	12.9	7.7	18.1

[1] Australia: New South Wales

[2] Canada: Alberta and Manitoba

[3] Sweden: Uppsala-Örebro and Stockholm-Gotland health regions

[4] United Kingdom (TNM analysis): Northern and Yorkshire Cancer Registry and Information Service (NYCRIS), Eastern Cancer Registration and Information Centre (ECRIC) in England and Northern Ireland; United Kingdom (SEER analysis): Northern Ireland

(Insert Figure 3 and Figure 4)

DISCUSSION

Lung cancer survival varied widely between these six wealthy countries in 2004-7. Age-standardised one-year net survival for non-small cell lung cancer ranged from 30% in the UK to 46% in Sweden. Survival was relatively low in Denmark, intermediate in Norway, and high in Australia and Canada. For small-cell lung cancer, one-year survival was 12-16% lower in the UK than in Sweden and Australia, and intermediate elsewhere.

These survival differences are partly explained by differences in stage at diagnosis. Denmark in particular had a more adverse stage distribution. However, international differences in survival were also evident within each stage of disease, for both types of lung cancer: generally low in the UK and high in Sweden. Denmark had low survival for patients with early-stage disease, but average survival for those with more advanced disease, while in Canada, the comparatively high survival for early disease was not apparent for patients with more advanced disease. International differences in stage at diagnosis may arise because of differences in disease aetiology (which may affect the aggressiveness of disease), or delays in diagnosis, or in the staging procedures themselves. Stage-specific survival may also vary because of differences in the quality of and access to stage-specific treatment.

Population-based survival estimates are invaluable for public health surveillance because they include all patients - young and old, rich and poor, with early or late disease and with or without co-morbidity - not just the small percentage of younger, fitter patients typically recruited to clinical trials. This study was based on 57,352 unselected lung cancer patients from population-based registries.

However, using such data requires extensive quality control[16] to ensure comparability of stage data. We consider our consolidation of raw data from different staging classifications to have been largely successful; the stage distributions by age, survival and morphology are clinically coherent, as well as internally consistent and comparable with previous estimates,[20-22] but some potential for misclassification remains. For example, small differences between the New South Wales coding scheme and SEER could explain why New South Wales has an apparently higher proportion of

localised disease than elsewhere (e.g. the distance of main-stem bronchial tumours from the carina is not considered in the New South Wales system, whereas it is in SEER). This down-staging in New South Wales produces lower stage-specific survival because their localised disease category includes some patients who would be classified as having more advanced stage within SEER. We detailed the potential misclassification when mapping T, N and M data to SEER.[16] We make recommendations on the coding of stage at diagnosis for international surveillance of cancer control.

Differences in the thoroughness of staging may also contribute to international variation in stage distributions and stage-specific survival. The proportion of histologically-verified tumours varied widely, from 74.0% in the UK to 94.8% in Sweden. The high proportion in Sweden was consistent with published estimates,[23] and lower levels of histological verification in the UK are also well known, with mounting evidence that elderly patients are much less likely to undergo these invasive procedures in the UK due to concerns about their frailty.[24]

Low stage-specific survival in the UK could conceivably arise in part because of sub-optimal staging and this misclassification of stage in a proportion of patients could lead to inappropriate treatment and therefore overall lower survival. In order to understand the impact of different staging procedures on international differences in survival, cancer registries will need to capture information on the staging procedures used for each patient, e.g. whether sensitive investigations such as PET-CT were used, enabling patients with very low-volume metastatic NSCLC to be correctly identified as having advanced disease, or whether liver function tests were used to identify advanced-stage SCLC. At the very least, registries should record whether the recorded stage was defined clinically (based on physical examination, imaging or endoscopy) or following histological examination.

Stage data were missing for 2-43% of patients, despite restriction to those registries where at least 50% of patients were staged. Patients with missing data on stage tended to be older and to have poorer survival than staged patients. To reduce bias, we imputed stage where it was missing using the available covariables.[19]

We used standard approaches to deal with other potential biases that face all international comparisons of cancer survival using population-based data, such as age-standardisation to control for differences in the age-distribution.[25] Nonetheless, some compositional differences remained: men made up over 59% of the patients in Australia, Norway and the UK compared to less than 54% elsewhere, and men generally have lower lung cancer survival than women.[26] The histological sub-types of lung cancer also varied. Non-microscopically verified cancers were grouped with NSCLC but those could have included some patients with SCLC or misdiagnosed cancer. Any effect would have been small, but probably more important in the UK, which had the lowest proportion of patients with histological confirmation (74.0%). The UK also had the lowest proportion of adenocarcinomas, which have a better prognosis, and this was true even after imputing morphology where it was missing (results not shown).

In general, the completeness of all these registries is high, but small differences in information capture could also contribute to differences in survival. In Sweden, cancer registrations are not initiated from death certificates as they are elsewhere, which may mean some patients with very poor survival are missed. The effect on overall survival will be minimal given the very high completeness of the Swedish data.[27]

Despite these issues of data quality and comparability, there remains evidence of large international differences in lung cancer survival. For NSCLC, the low survival in Denmark is driven partly by more advanced stage at diagnosis. In the UK, the proportion of patients diagnosed at an early stage is also lower than elsewhere. A more advanced stage distribution may arise because of faster disease progression (possibly related to higher incidence of smoking[28]), or because of delays in diagnosis. Research has pointed to diagnostic delay in Denmark,[13;29] and policies are now in place in Denmark and the UK to shorten the time to diagnosis.[29;30]

However, survival from NSCLC in the UK was also comparatively low for each stage of disease. Compared to Sweden, one-year survival in the UK was statistically significantly 10-16% lower within

each TNM stage I-IV, and 9-19% lower than in Canada for stages I-III (survival for stage IV was low in Canada). Danish patients had low stage-specific survival for TNM stages I-II.

Patients in the UK also had lower overall survival from SCLC despite the relatively favourable stage distribution, because stage-specific survival at each stage was generally lower than elsewhere.

Low stage-specific survival may indicate poorer levels of stage-specific treatment. Previous studies have shown that surgery for lung cancer is less frequently performed in the UK[31;32] than elsewhere in Europe[33;34] or Canada.[20;35] Similarly, lower provision of chemotherapy and radiotherapy has been reported in the UK[32] than in Australia,[36] Canada[20] and Sweden.[34] These studies are not directly comparable, because they use different methods, data and calendar periods. The overall pattern is nevertheless suggestive of the need for wider access to optimal treatment.

We are currently examining how far differences in treatment between the six ICBP countries may explain the variation in survival. Other explanations that may be considered include factors such as obesity, smoking, performance status and co-morbidity. It would be desirable to have data on these factors, which may be more common in the countries with lower overall survival,[33] but such factors would have to be both highly prevalent and powerfully prognostic to explain the survival differences between countries reported here. Clinical choices may also be more conservative in some countries than others in the face of co-morbidities, older age and lower performance status.

This study demonstrates wide differences between six wealthy countries in short-term survival from lung cancer, the most common cause of cancer death world-wide. These differences seem unlikely to be explained by artefacts of method or unrecorded confounders, and differences in stage at diagnosis and stage-specific treatment are likely to be important explanations.

The study also shows the importance of including stage at diagnosis in international survival comparisons. It is essential that the quality, completeness and comparability of stage data are improved, both in clinical settings and in population-based cancer registries, in order to facilitate surveillance of international trends in survival. Such comparisons incentivise policy development and they act as benchmarks for setting national cancer plans.

Acknowledgements

Conflicts of interest

Michael A Richards is the National Cancer Director (England, funded by the Department of Health). Other authors declare that they have no conflicts of interest.

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Tables and Figures

Table 1 Sex of patients, proportion not microscopically verified and histological subtypes

Table 2 Number of non-small cell and small-cell lung cancer patients diagnosed during 2004-2007: country and stage at diagnosis (TNM and SEER Summary Stage 2000), before and after imputation

Table 3 One-year net survival (%) overall, age-standardised and age-specific, by stage at diagnosis and country for non-small cell lung cancer patients diagnosed during 2004-2007

Figure 1 Age-standardised excess hazard (per 1,000 person-years, log scale) from non-small cell lung cancer by stage, country and time since diagnosis: TNM stage (upper figure) and SEER Summary Stage 2000 (lower figure)
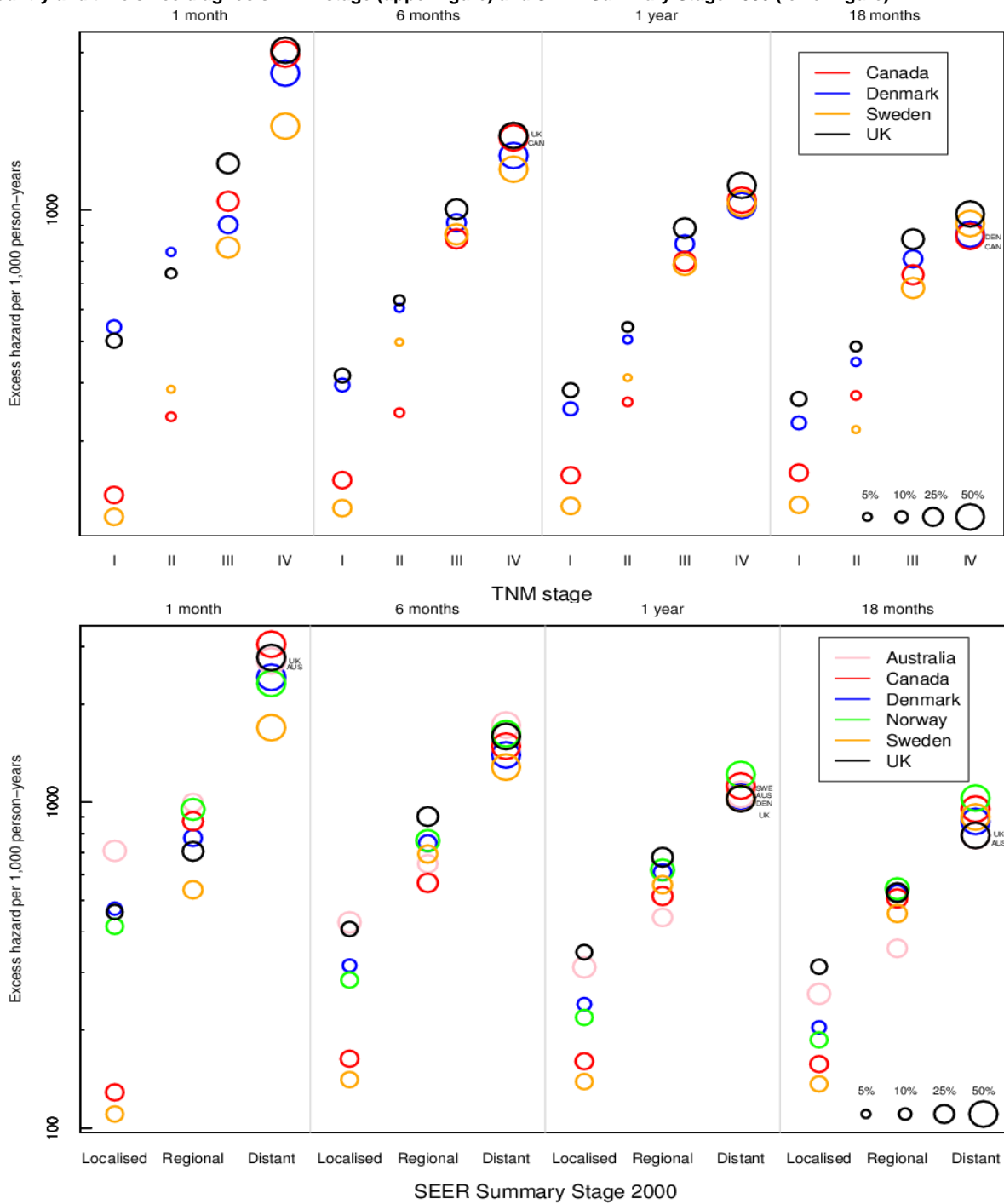
Notes
1. National data are used for Denmark and Norway. Other countries are represented by regional registries: Australia: New South Wales; Canada: Alberta and Manitoba; Sweden: Uppsala-Örebro and Stockholm-Gotland health regions; the United Kingdom (TNM analysis): West Midlands Cancer Intelligence Unit (WMCIU), the Eastern Cancer Registration and Information Centre (ECRIC) in England and Northern Ireland; the United Kingdom (SEER analysis): Northern Ireland
2. Bubbles are scaled to represent stage distribution at diagnosis

Figure 2 Age-standardised one-year net survival from non-small cell lung cancer by stage at diagnosis and country using known stage and imputed stage, TNM (upper figure) and SEER Summary Stage 2000 (lower figure)

Notes:
Australia: New South Wales; Canada: Alberta and Manitoba; Sweden: Uppsala-Örebro and Stockholm-Gotland health regions; the United Kingdom (TNM analysis): West Midlands Cancer Intelligence Unit (WMCIU), the Eastern Cancer Registration and Information Centre (ECRIC) in England and Northern Ireland; the United Kingdom (SEER analysis): Northern Ireland

Table 4 One-year net survival (%) overall, age-standardised and age-specific, by stage at diagnosis and country for small-cell lung cancer patients diagnosed during 2004-2007

Figure 3 Age-standardised excess hazard (per 1,000 person-years, log scale) from small-cell lung cancer by stage, country and time since diagnosis: TNM stage (upper figure) and SEER Summary Stage 2000 (lower figure)
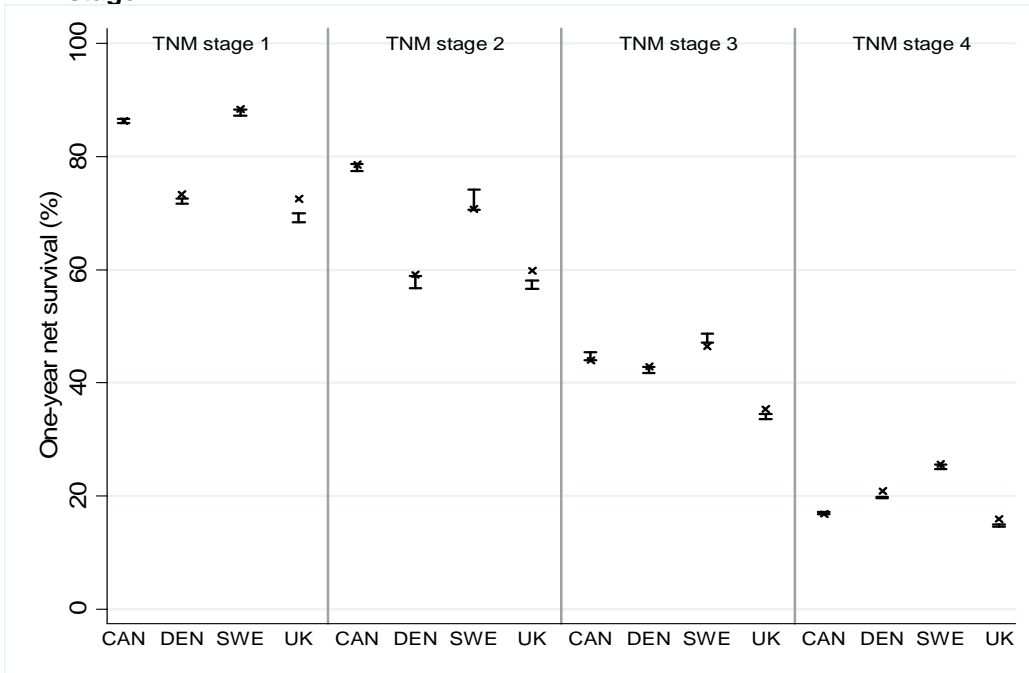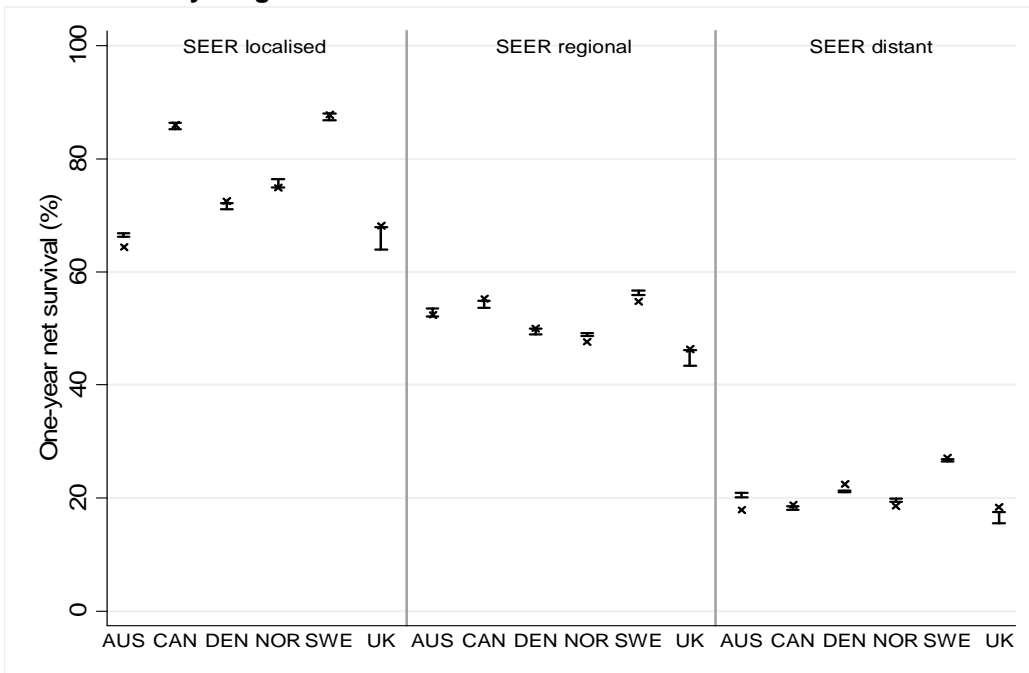
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Figure 1. Age-standardised excess hazard (per 1,000 person-years, log scale) from non-small cell lung cancer by stage, country and time since diagnosis: TNM stage (upper figure) and SEER Summary Stage 2000 (lower figure)

Notes
1. National data are used for Denmark and Norway. Other countries are represented by regional registries: Australia: New South Wales; Canada: Alberta and Manitoba; Sweden: Uppsala-Örebro and Stockholm-Gotland health regions; the United Kingdom (TNM analysis): West Midlands Cancer Intelligence Unit (WMCIU), the Eastern Cancer Registration and Information Centre (ECRIC) in England and Northern Ireland; the United Kingdom (SEER SS2000 analysis): Northern Ireland
2. Bubbles are scaled to represent stage distribution at diagnosis

Figure 2. Age-standardised one-year net survival from non-small cell lung cancer by stage at diagnosis and country using known stage and imputed stage, TNM (upper figure) and SEER Summary Stage 2000 (lower figure)

TNM stage

SEER Summary Stage 2000

X survival estimate derived from women with known stage

⊥ range of survival estimates derived for all women after imputation of stage where it was missing (see text)

Notes:
Australia: New South Wales; Canada: Alberta and Manitoba; Sweden: Uppsala-Örebro and Stockholm-Gotland health regions; the United Kingdom (TNM analysis): West Midlands Cancer Intelligence Unit (WMCIU), the Eastern Cancer Registration and Information Centre (ECRIC) in England and Northern Ireland; the United Kingdom (SEER SS2000 analysis): Northern Ireland

Figure 3. Age-standardised excess hazard (per 1,000 person-years, log scale) from small-cell lung cancer by stage, country and time since diagnosis: TNM stage (upper figure) and SEER Summary Stage 2000 (lower figure)
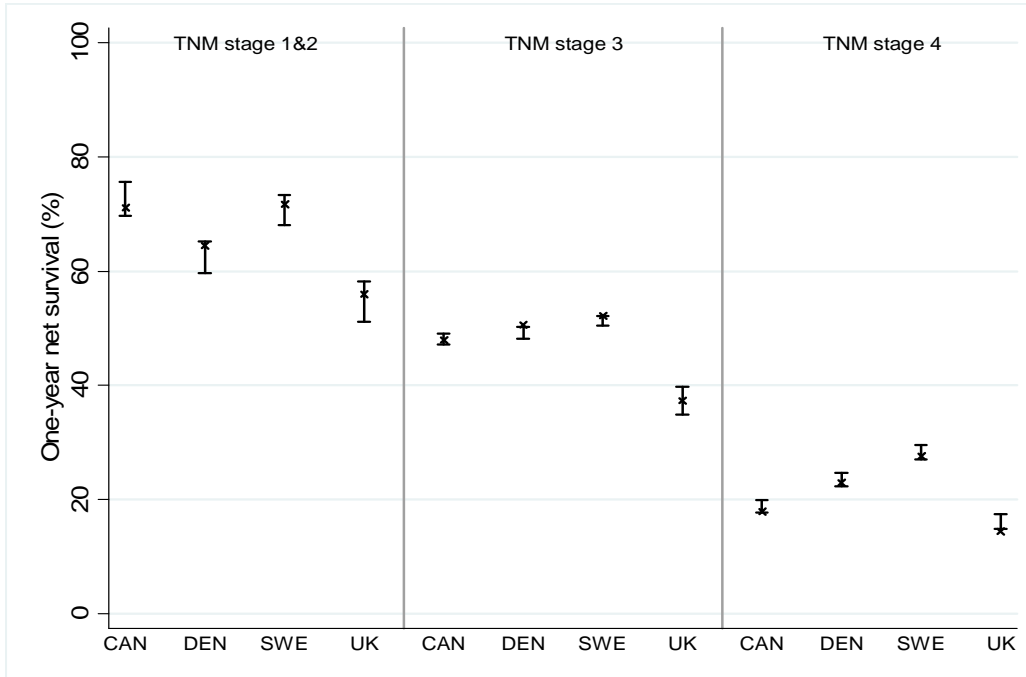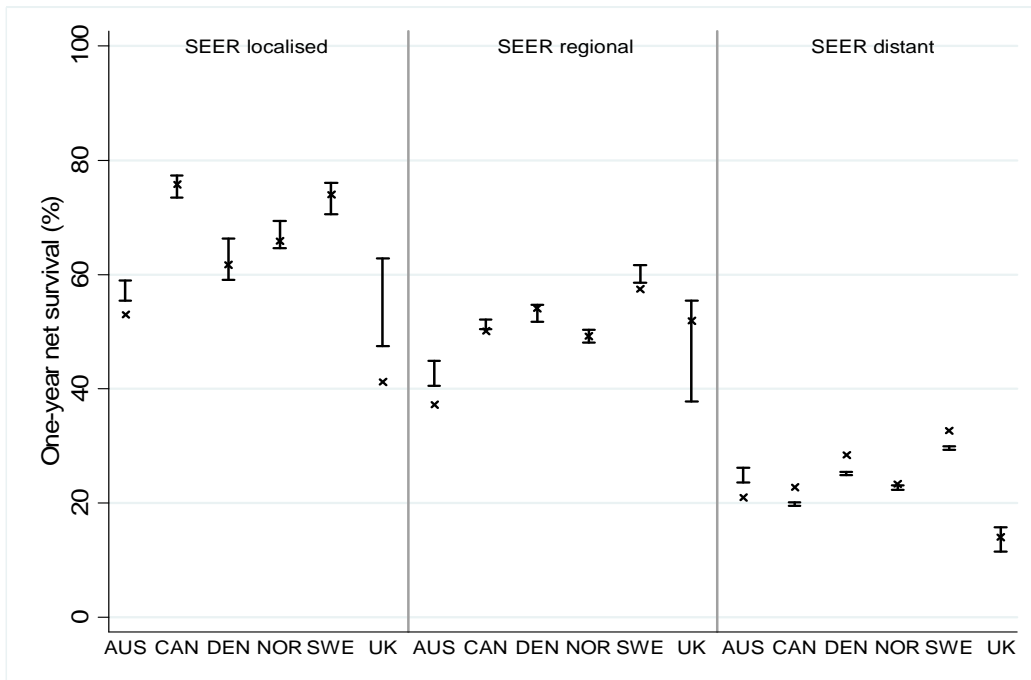
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WEB APPENDIX

Web appendix table 1 Stage-specific sets of weights used for age standardisation of non-small cell lung cancer estimates

Web appendix table 2 Stage-specific sets of weights used for age standardisation of small-cell lung cancer estimates

Web appendix figure 1 Proportions of non-small cell (top panel) and small-cell (bottom panel) lung cancer patients with missing data on stage and observed cumulative stage distribution by age at diagnosis and country, TNM and SEER Summary Stage 2000

Web appendix table 1. Stage-specific sets of weights used for age standardisation of non-small cell lung cancer estimates
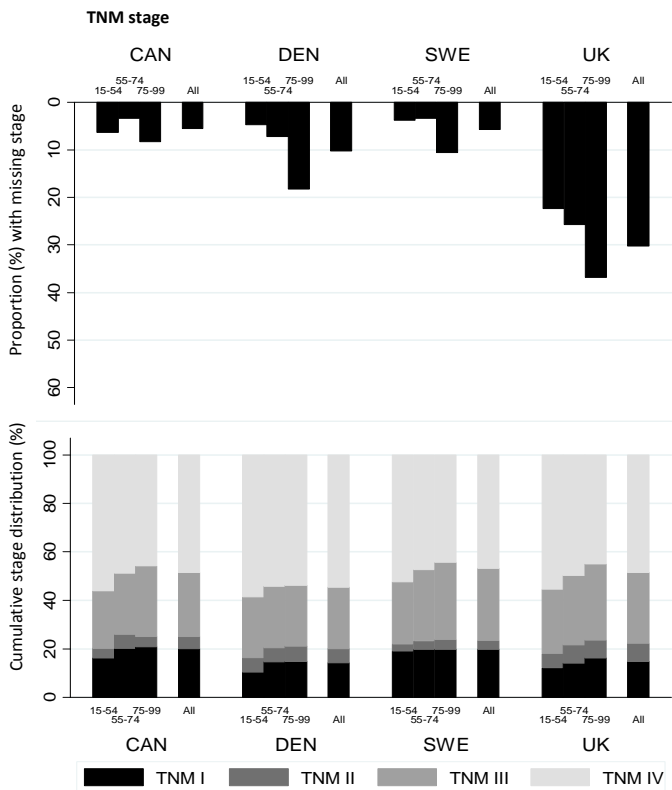
TNM stage	Age	Weights	SEER Summary Stage 2000	Age	Weights
All patients	15-44	0.01	All patients	15-44	0.02
	45-54	0.07		45-54	0.08
	55-64	0.22		55-64	0.23
	65-74	0.32		65-74	0.32
	75-84	0.31		75-84	0.29
	85-99	0.07		85-99	0.07
TNM stage I	15-44	0.02	Localised	15-44	0.02
	45-54	0.06		45-54	0.06
	55-64	0.22		55-64	0.22
	65-74	0.34		65-74	0.34
	75-84	0.30		75-84	0.30
	85-99	0.06		85-99	0.06
TNM stage II	15-44	0.01	Regional	15-44	0.02
	45-54	0.07		45-54	0.07
	55-64	0.23		55-64	0.24
	65-74	0.34		65-74	0.34
	75-84	0.29		75-84	0.28
	85-99	0.05		85-99	0.06
TNM stage III	15-44	0.01	Distant	15-44	0.02
	45-54	0.07		45-54	0.10
	55-64	0.22		55-64	0.25
	65-74	0.33		65-74	0.32
	75-84	0.30		75-84	0.26
	85-99	0.07		85-99	0.05
TNM stage IV	15-44	0.02	Missing stage	15-44	0.01
	45-54	0.09		45-54	0.05
	55-64	0.24		55-64	0.15
	65-74	0.33		65-74	0.27
	75-84	0.27		75-84	0.38
	85-99	0.05		85-99	0.14
Missing stage	15-44	0.01			
	45-54	0.04			
	55-64	0.15			
	65-74	0.27			
	75-84	0.39			
	85-99	0.14			

Web appendix table 2. Stage-specific sets of weights used for age standardisation of small-cell lung cancer estimates

TNM stage	Age	Weights	SEER Summary Stage 2000	Age	Weights
All patients	15-59	0.21	All patients	15-59	0.21
	60-74	0.53		60-74	0.53
	75-99	0.26		75-99	0.26
TNM stage I & II	15-59	0.18	Localised	15-59	0.19
	60-74	0.53		60-74	0.52
	75-99	0.29		75-99	0.29
TNM stage III	15-59	0.21	Regional	15-59	0.21
	60-74	0.55		60-74	0.54
	75-99	0.24		75-99	0.25
TNM stage IV	15-59	0.22	Distant	15-59	0.22
	60-74	0.55		60-74	0.53
	75-99	0.24		75-99	0.25
Missing stage	15-59	0.18	Missing stage	15-59	0.18
	60-74	0.49		60-74	0.48
	75-99	0.32		75-99	0.33

Web appendix figure 1. Proportions of non-small cell (top panel) and small-cell (bottom panel) lung cancer patients with missing data on stage and observed cumulative stage distribution by age at diagnosis and country, TNM and SEER Summary Stage 2000

NON-SMALL CELL LUNG CANCER

SMALL-CELL LUNG CANCER