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Title: Factors influencing treatment selection and thirty-day mortality following chemotherapy for people with small cell lung cancer: an analysis of national audit data

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Abstract

Background

Thirty-day mortality after treatment for lung cancer is a measure of unsuccessful outcome and where treatment should have been avoided. Guidelines recommend offering chemotherapy to individuals with small cell lung cancer (SCLC) who have poorer performance status (PS) because of its high initial response rate. However, this comes with an increased risk of toxicity and early death. We quantified real-world 30-day mortality in SCLC following chemotherapy, established the factors associated with this and compared these to the factors that influence receipt of chemotherapy.

Methods

We used linked national English datasets to define the factors associated with both receiving chemotherapy and 30-day mortality following chemotherapy.

Results

We identified 3,715 people diagnosed with SCLC, of which 2,235 (60.2%) received chemotherapy. There were 174 (7.8%) deaths within 30 days of chemotherapy. The adjusted odds of receiving chemotherapy decreased with older age, worsening PS and increasing comorbidities. Thirty-day mortality was independently associated with poor PS (PS 2 vs PS 0 adjusted OR 3.75 95% CI 1.71-8.25) and stage (extensive vs limited adjusted OR 1.68 95% CI 1.03-2.74) but in contrast was not associated with increasing age. Both chemotherapy administration and 30-day mortality varied by hospital network.

Conclusions

To reduce variation in chemotherapy administration predictors of 30-day mortality could be used as an adjunct to improve sub-optimal patient selection. We have quantified 30-day mortality risk by the two independently associated factors, PS and stage, so that patients and clinicians can make better informed decisions about the potential risk of early death following chemotherapy.

Keywords

Small cell lung cancer

Chemotherapy

Epidemiology

30-day mortality

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This research was funded by the Roy Castle lung cancer foundation (2015 14 Hubbard) and the University of Nottingham John Turland charitable fund. Neither were involved in the design, analysis or interpretation of results.

Abbreviations

CAV- Cyclophosphamide, doxorubicin and vincristine

CbE- Carboplatin + etoposide SCLC- Small cell lung cancer

CI – Confidence interval

ED-SCLC- Extensive stage small cell lung cancer

EP- Cisplatin + etoposide

LD-SCLC- Limited stage small cell lung cancer

NLCA- National lung cancer audit

OR- Odds ratio

PS- Performance status

SACT- Systemic anti-cancer therapies

TNM- Tumour, Node Metastasis

WHO- World health organisation

VALSG- Veterans Administration Lung Study Group

Introduction

The median survival for people with small cell lung cancer (SCLC) who do not receive chemotherapy is short, and this, coupled with the fact that this aggressive tumour is responsive to chemotherapy reflects treatment guidelines which recommend chemotherapy for extensive stage (ED-SCLC) even in elderly people with poor performance status (PS) and significant comorbidities.[1-4] Administration of chemotherapy in this frail population means some individuals die shortly after treatment. It is recognised that deaths within 30 days of anti-cancer treatment are an indicator of avoidable harm and sub-optimal patient selection as they reflect that treatment was either; directly toxic or, in the case of non-treatment related early death e.g. disease progression, was futile and unnecessary.[5] To minimise 30-day mortality and improve patient selection for chemotherapy we have determined what factors influence receipt of chemotherapy and investigated how these are associated with 30-day mortality from the first chemotherapy dose.

Materials and Methods

Study population

Ethical approval for this study was obtained from the NHS Health Research Authority (16/LO/0503). Our primary dataset, the National Lung Cancer Audit (NLCA), consisted of people diagnosed with lung cancer in English hospitals between 1st January 2015 and 31st December 2015. These data were linked with Systemic Anticancer Therapies (SACT) and Hospital Episode Statistics data. All data were prospectively collected via clinical coding or electronic prescription. People with SCLC were identified from their systematized nomenclature of medicine histological code.

Chemotherapy

If an individual had a date for administration of chemotherapy recorded within 6 months from the date of diagnosis, they were defined as having received chemotherapy. Those who did not have a date for chemotherapy administration or received chemotherapy after 6 months from diagnosis were assumed not to have received chemotherapy. We defined the location where chemotherapy was received by lung cancer network. In England, there are 13 cancer networks based on geographical location and each is composed of several hospitals. The chemotherapy received was grouped according to the combination administered. The remaining groups were: Single platinum (cisplatin or carboplatin), other (single agent etoposide, topotecan and clinical trials) and missing (date of administration present but no drug details given).

Death date

We used a death date derived from the Office of National Statistics records. For this study, the date of death had last been updated on the 19th October 2016. We used these dates along with the SACT record for date of first chemotherapy dose received to calculate 30-day mortality.

Covariates

Our variables were primarily derived from NLCA data. Socioeconomic status was calculated from postcode of residence and formatted into Townsend index of deprivation (1- least to 5 –most). PS is a marker of a person's well-being and fitness. It is based upon WHO criteria (0- asymptomatic to 4- bedbound, unable to carry out self-care) and taken at the time of diagnosis.

Stage was obtained from pre-treatment tumour node metastases (TNM) records. We divided stage into limited (LD-SCLC) and extensive (ED-SCLC), based on similar

criteria to the Veterans Administration Lung Study Group (VALSG).[6] ED-SCLC consisted of any tumour with M1a/b or any T and M0 with N3 nodal involvement. If TNM was not recorded stage was classed as missing.

We used a previously derived method to calculate a Charlson comorbidity index using a list of diagnoses (excluding lung cancer) from previous hospital admissions up to the date of chemotherapy.[7,8] People with no hospital admissions or comorbidities were assigned a score of 0. The Charlson index was grouped into 4 categories (0, 1, 2-3 and ≥4).

Statistical analysis

All analyses were completed using Stata V15 (Stata Corp, TX, USA). We performed a descriptive analysis of the whole cohort and those who received chemotherapy. We then did multiple logistic regression to estimate odds ratios for receiving chemotherapy and adjusted for the aforementioned factors along with cancer network where chemotherapy was given or where the patient was first seen (if chemotherapy was not given).

We calculated the proportion of deaths within 30 days for those who received chemotherapy. We used multiple logistic regression to estimate odds ratios (OR) for 30-day mortality by patient, tumour, chemotherapy and network factors in those who received chemotherapy. Our final logistic regression model contained factors that were a-priori (age, sex, social deprivation) or showed significant association with early death on univariate analysis ($p<0.05$). We assessed the significance of each variable by using the likelihood ratio test or Wald's p value.

We compared lung cancer network performance with receipt of chemotherapy and 30-day mortality by generating a pooled mean national proportion for both outcome

measures. Then, in a separate multiple logistic regression model, adjusting for our measured factors, we clustered patients by network and generated odds ratios of receiving chemotherapy and early death for each network by comparing with the mean national proportion.

Results

We identified 3,715 individuals with SCLC. The cohort demographics are shown in *Table 1*. The median age was 70 years (IQR 63-76). Most people had ED-SCLC (n=2,818 (75.8%)) whilst 785 (21.1%) had LD-SCLC. Stage and PS were not recorded in 112 (3.0%) and 1,031 (27.8%) people respectively.

A total of 2,235 people (60.2%) received chemotherapy, 1,133 (50.7%) were male. The median age of those who received chemotherapy was 69 years (IQR 62-74) and 1,130 (50.5%) had a PS of 0-1, 421 people (18.8%) had a PS of 2 and 160 (7.2%) had a PS of 3-4. PS was not recorded for 524 (23.5%) people. The chemotherapy administered by lung cancer stage is shown in *Table 2*.

Receiving chemotherapy

There was a reduction in the odds of receiving chemotherapy with increasing age (*Table 1*). The adjusted OR for those aged 50-59 years vs. those aged 70-79 years was 1.61 (95% CI 1.25-2.06). Worsening PS was associated with less chance of receiving chemotherapy (PS 3 vs PS 0, adjusted OR 0.28 95% CI 0.21-0.38). People with a Charlson comorbidity index of ≥4, were less likely to receive chemotherapy compared to those with no comorbidity (adjusted OR 0.52 95% CI 0.42-0.64). Sex, social deprivation and stage did not affect receipt of chemotherapy. When compared to the national proportion of people treated there was significant variation in the odds of receiving chemotherapy by cancer network, this is demonstrated in *Figure 1*. Three

networks were less likely to administer chemotherapy and 3 were more likely. The odds ranged from 0.70 (95% CI 0.56-0.88) to 1.95 (95% CI 1.36-2.80).

30-day mortality

The median survival from diagnosis to death for individuals who received chemotherapy was 406 days (95% CI 386-420) and 244 days (95% CI 233-253) for LD-SCLC and ED-SCLC respectively. This was markedly different for people who did not receive chemotherapy (LD-SCLC 300 days (95%CI 262-308 days) and ED-SCLC 36 days (95% CI 32-39 days)).

The overall 30-day mortality after chemotherapy was 7.8% (n=174). This was associated with patient, tumour and geographical factors (*Table 3*). Worsening PS, was overwhelmingly associated with 30-day mortality. The adjusted odds ratio for people with PS 2 vs PS 0 was 3.75 (95% CI 1.71-8.25). People ≥80 years were less likely to die within 30 days compared to people aged 70-79 years (adjusted OR 0.42 95% CI 0.20-0.91) however, there was no trend across all ages (p trend= 0.8). ED-SCLC was associated with greater odds of early death (adjusted OR 1.68 95% CI 1.03-2.74). Early mortality was not independently associated with the chemotherapy received, however, there was a signal that a single platinum agent increased 30-day mortality risk compared to carboplatin + etoposide (CbE) (adjusted OR 1.71 95% CI 0.99-2.95). There was significant variability in 30-day mortality by cancer network (p <0.001). *Figure 2* shows the case-mix adjusted proportion of patients who died within 30 days of chemotherapy by different network and demonstrates that one network had an increased proportion of deaths while another had significantly fewer. There was no correlation between the proportion of individuals treated and the proportion of early deaths by network (p=0.487).

Discussion

Main findings

From these observational data we have found that the administration of chemotherapy for SCLC was associated with PS, age, comorbidity and cancer network. The preferred choice of chemotherapy in LD-SCLC was CbE followed by cisplatin + etoposide (EP). In ED-SCLC CbE was preferred followed by single platinum.

We have quantified the up to date median survival for people who do not receive chemotherapy in SCLC and have shown that the difference between ED-SCLC and LD-SCLC is much greater than previously thought.[1] Thirty-day mortality was associated with stage and PS and varied by network. Although increasing age did not show a trend, people aged ≥80 years were less likely to die within 30 days, yet, were also less likely to receive chemotherapy.

Strengths

This is the first time that factors associated with 30-day mortality have been explored in detail for SCLC using real-world data. Clinical trials provide limited data on 30-day mortality and compared to these, our study population is unselected and therefore more relevant to clinical practice. We have demonstrated variation in SCLC treatment and outcomes in England but this finding will be relevant to other countries. The untreated median survival in SCLC is often cited from VALSG research conducted in the 1970s but we have described the current median survival, this is important as healthcare has changed with time.[1]

Limitations

Our dataset consisted of histologically confirmed SCLC but there is a small proportion of patients who were diagnosed with lung cancer that were too frail to obtain a

histological diagnosis. This number is too small to affect our findings as histological confirmation for lung cancers diagnosed in 2015 was reported as 74% in the NLCA.[9] Radiotherapy data was limited. Radiotherapy may add further toxicity to chemotherapy, however, it is not usually given in the first 30 days. We cannot describe the causes of early death, though, the information that matters to the patient is the risk of death from any cause. We have reported stage based on VALSG criteria. TNM staging offers a more precise method of grouping patients, however, using this would result in subgroups being too small for our statistical analysis. Similarly, guidelines use VALSG criteria to recommend treatment, hence, our findings can be easily related to these.

Comparisons with other research

Receipt of chemotherapy

The findings of increasing age, poorer PS, greater comorbidity and network have all been associated with a negative effect on the likelihood of receiving chemotherapy.[10-12] PS is a subjective measure by the clinician and therefore one expects this to correlate with receiving chemotherapy as the clinician also controls the prescription.

Rich et al identified that patients were more likely to receive chemotherapy if they were diagnosed in a hospital recruiting for clinical trials.[10] This may explain the differences between networks in our study as some contain more clinical trial units than others. However, ambiguous selection criteria and expertise may also contribute to variation.

Chemotherapy

Some of the chemotherapy given, such as CAV, is not recommended in current guidelines. Previously CAV was favoured in poor prognosis SCLC, unlike EP, which was not used for this group.[13] A survey conducted 20 years ago found CbE was favoured over EP because of patient convenience, toxicity and quality of life.[13] This may explain why CbE was favoured for LD-SCLC in our study.

30-day mortality

Our finding that 30-day mortality was 4.0% and 9.1% for people with LD-SCLC and ED-SCLC respectively, is similar to *Wallington et al's* study (4.0% for curative intent chemotherapy and 12.0% for palliative intent).[14] Likewise, a systematic review of phase III clinical trials in SCLC found that 2.95% of people died within 4 weeks of completing chemotherapy.[15] In this study the population mostly consisted of individuals with PS 0-1 and deaths that were a result of disease progression were excluded. With these caveats considered our findings are similar when 30-day mortality risk is stratified by PS and stage, as shown in Table 4.

We found the oldest age group had a lower risk of death with no significant trend across all ages. Despite this, the oldest group were less likely to receive chemotherapy. This contrasts with previous research which assessed overall survival in patients entered into clinical trials for chemotherapy in SCLC.[16] They found that increasing age was a risk factor for death. The most likely explanation is that the oldest patients in our study who received chemotherapy were in fact fitter than their younger counterparts. This originates from them either being less likely to be offered or accept chemotherapy when fitness levels are equivalent to younger patients.

Comorbidity was not independently associated with early mortality. In previous work, we found that an increase in Charlson index was associated with reduced overall survival.[10] Our discrepancies are explained by the different length survival was measured. Thirty days is a short time-frame and if survival is measured over longer periods it permits an increased exposure time to the slower rate of death from comorbidities to occur.[8] Similarly, chemotherapy given to people with more comorbidities might be under-dosed.

Using more than 2 chemotherapy drugs in combination is linked with increased early treatment-related deaths in SCLC.[17,18] Contrary to this we found a signal that a single platinum agent increased 30-day mortality risk when compared to CbE. Selection bias may explain this i.e. frailer individuals were given a single chemotherapy drug to limit toxicity. If this is the case then it implies that an "all or nothing" approach should be taken for combination chemotherapy.

Median survival

In our study, the median survival for untreated LD-SCLC was considerably longer than *Zelen et al's* estimate of 11.7 weeks.[1] This difference is explained by the broad range of TNM stages captured under the limited stage umbrella, differing cohort sizes (*Zelen et al* n=38) and the advances of routine healthcare since the 1970s.

Relevance

Our research demonstrates geographical variation in the administration of chemotherapy for SCLC with no apparent correlation to the risk of 30-day mortality, indicating uncertainty in patient selection. In surgery for lung cancer global risk scores have been proposed as an aid to inform shared decision making, but none are yet considered accurate enough for this purpose.[19-21] Instead, tables have been produced showing recent mortality figures stratified by the most important associated factors.[19]

We propose that a similar method should be considered when assessing eligibility for chemotherapy and have therefore stratified 30-day mortality risk by the two independently associated factors PS and stage (*Table 4*). However, further work is needed to develop a robust risk prediction model for 30-day mortality following chemotherapy which could incorporate other biological markers.[22-24]

Conclusion

The degree of physical impairment, as reflected in PS, is the overwhelming factor determining receipt of chemotherapy and 30-day mortality. However, it is evident that age and comorbidity are given too much weight in the decision to administer chemotherapy which may result in suboptimal decision making and variation between networks. We propose that 30-day mortality risk can be used in conjunction with our median survival estimates to assist the patient selection process. Table 4 provides a practical solution to this, conveying 30-day mortality risk by the independently associated factors, PS and stage allowing better informed treatment decisions going forward.

Conflict of interest statement:

David Baldwin received payment from Astra Zeneca for a biopsy masterclass. The other authors have no conflict of interest.

Table 1: Features of patients who had chemotherapy and the odds ratios for receiving chemotherapy									
	Total population		Had chemotherapy						
Factor	N= 3,715	%	N=2,235 (60.2%)	%	OR	95% CI	Adjusted OR*	95% CI	P value (LR test)
Sex									
Female	1,797	48.4	1,102	61.3	1		1		
Male	1,918	51.6	1,133	59.1	0.91	0.80-1.04	0.97	0.84-1.12	0.666*
Age group									
<50	104	2.8	69	66.3	1.27	0.83-1.93	1.20	0.77-1.89	
50-59	477	12.8	342	71.7	1.63	1.30-2.05	1.61	1.25-2.06	
60-69	1,211	32.6	789	65.2	1.20	1.03-1.41	1.16	0.97-1.38	
70-79	1,401	37.7	852	60.8	1		1		
≥80	522	14.1	183	35.1	0.35	0.28-0.43	0.37	0.29-0.46	<0.001¥
Townsend Quintile									
Least deprived-1	466	12.5	278	59.7	1		1		
2	659	17.8	400	60.7	1.04	0.82-1.33	1.01	0.77-1.32	
3	698	18.8	424	60.7	1.05	0.82-1.33	1.11	0.85-1.45	
4	841	22.6	509	60.5	1.04	0.82-1.31	1.02	0.79-1.32	
Most deprived- 5	1,051	28.3	624	59.4	0.99	0.79-1.23	0.92	0.71-1.18	0.568
Performance status									
0	450	12.1	334	74.2	1		1		
1	1,031	27.8	796	77.2	1.18	0.91-1.52	1.44	1.11-1.97	
2	663	17.9	421	63.5	0.60	0.46-0.79	0.85	0.64-1.13	
3	423	11.4	148	35.0	0.19	0.14-0.25	0.28	0.21-0.38	
4	117	3.2	12	10.3	0.04	0.02-0.07	0.05	0.03-0.10	
Missing	1,031	27.8	524	50.8	0.36	0.28-0.46	0.44	0.34-0.58	<0.001
Charlson comorbidity index									
0	625	16.8	445	71.2	1		1		
1	575	15.5	426	74.1	1.16	0.90-1.549	1.19	0.91-1.57	
2-3	514	13.8	330	64.2	0.73	0.56-0.93	0.86	0.65-1.14	
≥4	2,001	53.9	1,034	51.7	0.43	0.36-0.53	0.52	0.42-0.64	<0.001
Stage									
Limited	785	21.1	547	69.7	1		1		
Extensive	2,818	75.9	1,633	57.9	0.60	0.51-0.71	0.88	0.73-1.08	
Missing	112	3.0	55	49.1	0.42	0.28-0.63	0.68	0.44-1.06	0.191
Network (separate logistic regression model to other factors)									
National pooled	3,715		2,235	60.2	1		1		
N1	214	5.8	108	50.5	0.67	0.52-0.87	0.88	0.66-1.18	
N2	207	5.6	120	58.0	0.91	0.70-1.19	0.75	0.57-1.00	
N3	441	11.9	276	62.6	1.11	0.92-1.33	1.0	0.82-1.22	
N4	341	9.2	178	52.2	0.72	0.59-0.89	0.70	0.56-0.88	
N5	490	13.2	318	64.9	1.22	1.03-1.46	1.31	1.08-1.58	
N6	382	10.3	237	62.0	1.08	0.89-1.32	0.93	0.75-1.15	
N7	287	7.7	182	63.4	1.15	0.91-1.43	1.24	0.97-1.59	
N8	358	9.7	196	54.7	0.80	0.66-0.98	0.71	0.57-0.89	
N9	294	7.9	191	65.0	1.23	0.98-1.55	1.30	1.00-1.69	
N10	273	7.4	137	50.2	0.67	0.53-0.84	0.70	0.54-0.90	
N11	103	2.8	67	65.0	1.23	0.83-1.84	1.33	0.87-2.03	
N12	162	4.4	119	73.5	1.83	1.30-2.58	1.95	1.36-2.80	
N13	163	4.4	106	65.0	1.23	0.90-1.69	1.45	1.03-2.04	<0.001‡

LR= likelihood ratio test, Adjusted for all other variables ¥: LR test trend *: Wald's P value. ‡:LR test in multivariate logistic model without clustering

Table 2: Chemotherapy regimens received by lung cancer stage		
Chemotherapy regimen	**Number of people**	**% of those who received chemotherapy**
Limited stage		
Carboplatin + etoposide	368	67.3
Cisplatin + etoposide	104	19.0
CAV	2	0.4
Single platinum	32	5.9
Other chemotherapy	10	1.8
Missing	31	5.7
Extensive stage		
Carboplatin + etoposide	1 257	77.0
Cisplatin + etoposide	105	6.4
CAV	17	1.0
Single platinum	118	7.2
Other chemotherapy	44	2.7
Missing	92	5.6

Table 3: Features of patients who died within 30 days of receiving chemotherapy and odds ratios for death within 30 days							
Factor	**Total 30 day deaths N=174**	**% who died from those who received chemotherapy**	**OR**	**95% CI**	**Adjusted OR**	**95% CI**	**P value (LR test)**
Sex							
Female	80	7.3	1		1		
Male	94	8.3	1.16	0.85-1.58	1.12	0.81-1.55	0.491*
Age group							
<50	5	7.3	0.83	0.33-2.14	0.87	0.33-2.32	
50-59	19	5.6	0.63	0.37-1.06	0.71	0.41-1.22	
60-69	69	8.8	1.02	0.72-1.44	1.13	0.79-1.63	
70-79	73	8.6	1		1		
≥80	8	4.4	0.49	0.23-1.03	0.42	0.20-0.91	0.773¥
Townsend quintile							
Least deprived- 1	14	5.0	1		1		
2	32	8.0	1.64	0.86-3.13	1.44	0.74-2.80	
3	38	9.0	1.86	0.99-3.49	1.55	0.81-2.98	
4	41	8.1	1.65	0.88-3.09	1.53	0.80-2.91	
Most deprived- 5	49	7.9	1.61	0.87-2.96	1.57	0.83-2.98	0.667
Performance status							
0	8	2.4	1		1		
1	42	5.3	2.27	1.05-4.89	2.15	0.99-4.69	
2	43	10.2	4.64	2.15-10.00	3.75	1.71-8.25	
3-4	30	18.8	9.40	4.20-21.05	6.92	3.02-15.86	
Missing	51	9.7	4.39	2.06-9.38	4.17	1.93-9.04	<0.001
Charlson comorbidity index							
0	25	5.6	1		1		
1	19	4.5	0.78	0.43-1.45	0.72	0.38-1.36	
2-3	20	6.1	1.08	0.59-1.99	0.94	0.50-1.76	
≥4	110	10.6	2.00	1.28-3.13	1.28	0.80-2.06	0.130
Stage							
Limited	22	4.0	1		1		
Extensive	149	9.1	2.40	1.51-3.79	1.68	1.03-2.74	
Missing	3	5.5	1.38	0.40-4.75	1.12	0.31-4.04	0.057
Chemotherapy							
Carboplatin+ etoposide	130	7.8	1		1		
Cisplatin + etoposide	7	3.2	0.39	0.18-0.85	0.48	0.21-1.07	
CAV	2	10.5	1.39	0.32-6.08	1.59	0.34-7.47	
Other	5	9.1	1.18	0.46-3.01	0.93	0.35-2.49	
Single platinum	22	14.6	2.01	1.24-3.27	1.71	0.99-2.95	
Missing	8	6.3	0.79	0.38-1.66	0.84	0.38-1.82	0.141
Network (separate logistic regression model to other factors)							
Pooled networks	174	7.8	1		1		
N1	10	9.3	1.21	0.64-2.28	1.10	0.58-2.10	
N2	6	5.0	0.62	0.28-1.40	0.66	0.29-1.51	
N3	23	8.3	1.08	0.72-1.60	1.10	0.73-1.67	
N4	6	3.4	0.41	0.19-0.92	0.40	0.18-0.88	
N5	32	10.1	1.33	0.95-1.85	1.17	0.84-1.64	
N6	20	8.4	1.09	0.71-1.68	1.26	0.81-1.96	
N7	23	12.6	1.71	1.14-2.58	1.79	1.14-2.80	
N8	10	5.1	0.64	0.34-1.18	0.66	0.36-1.23	
N9	23	12.0	1.62	1.08-2.44	1.50	0.97-2.31	
N10	7	5.1	0.64	0.30-1.34	0.65	0.31-1.35	
N11	2	3.0	0.36	0.09-1.48	0.39	0.09-1.67	
N12	4	3.4	0.41	0.15-1.10	0.43	0.16-1.15	
N13	8	7.6	0.97	0.48-1.96	1.03	0.49-2.14	0.015‡
*: Wald's P value test ¥: LR test for trend ‡: LR test in multivariate logistic model without clustering. Adjusted OR for all other factors							

Table 4: Proportion of individuals who died within 30 days of receiving chemotherapy stratified by stage and performance status.

		Table 4: Proportion of individuals who died within 30 days of receiving chemotherapy stratified by stage and performance status.			
		Performance Status			
		PS 0	PS 1	PS 2	PS 3-4
Stage	Limited	2.0% (0.0%-7.9%) (n=99)	3.0% (1.4%-6.1%) (n=235)	7.6% (3.3%-16.1%) (n=79)	16.0% (5.7%-37.5%) (n=25)
	Extensive	2.6% (1.1%-5.7%) (n=230)	6.3% (4.6%-8.7%) (n=553)	10.9% (7.8%-14.7%) (n=340)	19.4% (13.5%-27.1%) (n=134)
Parenthesis contains 95% confidence interval, n represents the total number of individuals who received chemotherapy in that group.					

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