Lung Cancer Incidence, Mortality, Treatment and Survival in the Republic of Ireland: 1994-2008

National Cancer Registry Ireland

ABBREVIATIONS

Acronyms	
95% CI	95% confidence interval
APC	Annual percentage change
CSO	Central Statistics Office
DCO	Death certificate only (cases)
DNML	Dublin Mid Leinster
DNNE	Dublin North East
EASIR	European age standardised incidence rate
EASMR	European age standardised mortality rate
ENCR	European network of cancer registries
GH	General hospital
HSE	Health service executive
ICD	International statistical classification of diseases and related health problems
NCR	National Cancer Registry
NOS	Not otherwise specified
NSCLC	Non small cell lung cancer
RH	Regional hospital
RoI	Republic of Ireland
SCLC	Small cell lung cancer
SMR	Standardised mortality ratio
SRR	Standardised rate ratio
UH	University hospital
WASIR	World age standardised incidence rate
XNOS	Unknown or not otherwise specified

Published by National Cancer Registry, 2011

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This report should be cited as:

Lung cancer incidence, mortality, treatment and survival in the Republic of Ireland: 1994-2008. National Cancer Registry, Cork, Ireland (2011).

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EXECUTIVE SUMMARY

This report examines patterns and trends of lung cancer incidence, mortality, treatment and survival in Ireland during the period 1994-2008.

The burden of lung cancer is higher in males. 1,059 men and 652 women were diagnosed with lung cancer each year on average between the years 1994 and 2008.

In 2008 the age standardised incidence rate of lung cancer in males was 57/100,000 compared to 36/100,000 in females. From 1994-2008 there was a downward trend in the incidence rate of lung cancer in males (1% per annum) along with a falling trend in mortality (2% per annum). However, in females the picture was quite different. The incidence rate in women increased at 2.3% per annum throughout the period and the mortality rate increased at 0.5% per annum.

International comparisons show that incidence and mortality rates for Irish men compared quite favourably with our European neighbours. However, for women the incidence and mortality rates were among the highest in Europe.

There was a trend towards improved survival across the three diagnostic periods examined in this report: 1994-1999, 2000-2003, and 2004-2007. There was also evidence of greater uptake of the various treatment options available. The percentage of cases who received chemotherapy increased significantly from 15% in the period 1996-1999 to 32% in the period 2004-2008. Similarly, the percentage undergoing radiotherapy increased significantly from 37% in the period 1996-1999 to 40% in the period 2004-08. The number of cases who received no tumour directed treatment decreased from 49% in the period 1996-1999 to 40% in the period 2004-2008.

It is estimated that 90% of lung cancer cases can be directly attributed to tobacco smoking, which is a modifiable risk factor. Therefore, if progress is to be made in reducing the incidence of lung cancer in Ireland in the future, renewed efforts must be made to reduce tobacco use, especially in women.

SUMMARY

Lung cancer is the third most common cancer in Ireland in men and in women, accounting for 13.9% of cancers in men and 9.4% in women during 1994-2008 (excluding non melanoma skin cancer).

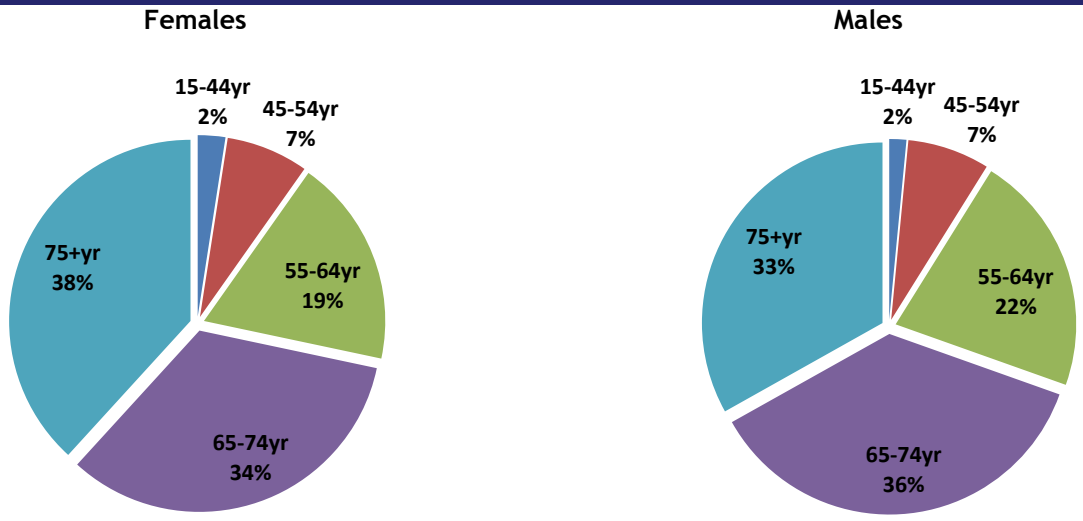
1,059 men and 652 women were diagnosed with lung cancer each year on average between the years 1994 and 2008. In women the age standardised incidence rate rose significantly between 1994 and 2008, by 2.3% per annum, while in men it fell by 1% per annum (Table 1).

The majority of those diagnosed with lung cancer were aged 65 years and over (Figure 1). Approximately 2% of cases presented in those aged less than 45 years. Male lung cancer patients were younger on average than females; 31% of males and 28% of females were aged less than 65 years.

Table 1
Summary data for lung cancer in Ireland, 1994-2008

	Females	Males
% of all new cancer cases	5.4%	9.3%
% of all new cancer cases excluding non melanoma skin cancer	9.4%	13.9%
Average number of new cases per year	652	1,059
Average number of deaths per year	571	966
European age standardised incidence rate per 100,000 in 2008	36.0	57.4
Annual percentage change in incidence rate, 1994-2008	2.3%	-1.0%
European age standardised mortality rate per 100,000 in 2007	27.7	52.6
Annual percentage change in mortality rate, 1994-2007	0.5%	-2.0%
15 year prevalence, 1994-2008[a]	1,393	1,563
10 year prevalence, 1999-2008	1,265	1,378
5 year prevalence, 2004-2008	1,000	1,101

Figure 1
Age distribution of incident lung cancer cases, 1994-2008



[a] The number of cases still alive who were diagnosed during the period 1994-2008

1. RISK FACTORS FOR LUNG CANCER

Table 2
Risk factors for lung cancer, by strength of evidence

Strength of evidence	Increases risk	Decreases risk
Convincing or probable	Tobacco[1]	Fruit[4]
	Passive smoking[1]	Food containing carotenoids[4]
	Asbestos exposure[2]	
	Radon exposure[2, 22]	
	Ionizing radiation (X-rays & gamma radiation)[2]	
	Family history of lung cancer[3]	
	Arsenic in drinking water[4]	
	Beta-carotene supplements (in current smokers)[4]	
	Low socio-economic status[5]	
Possible	Alcohol[6]	Physical activity[4,7]
	Low body fatness[4]	Non starchy vegetables[8]
		Aspirin and other non steroidal anti-inflammatory drugs[9]

Smoking is the major cause of lung cancer (Table 2). 90% of lung cancer cases are directly attributable to cigarette smoking.[1] Duration of smoking is the strongest determinant of risk among smokers; the earlier the starting age, or the longer the period of smoking, the higher the risk. Stopping smoking, at any age but particularly before middle age, avoids most of the subsequent risk. Passive smoking is a cause of lung cancer in those who have never smoked.[1]

A pooled analysis of data from 13 case-control studies of residential radon exposure in nine European countries showed that the underlying lung cancer risk increased by 16% for every 100 Bq/m^3 of radon exposure in the home. The risk to active smokers from radon was observed to be approximately 25 times greater than the risk to lifelong non-smokers.[22]

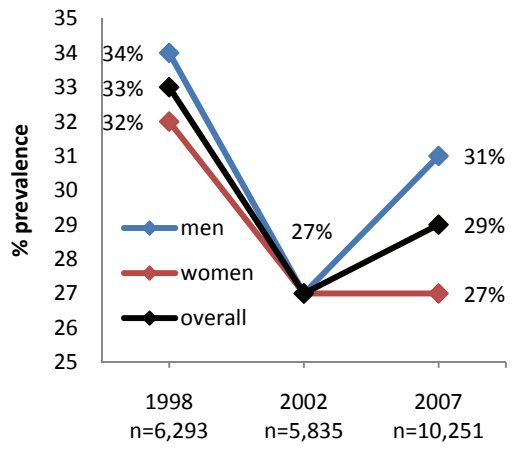
A meta-analysis completed in 2005 suggests that individuals with a family history of lung cancer have an increased risk of developing the disease. This is particularly true for families with a number of affected individuals and where cases have been diagnosed at a young age.[3] Lung cancer risk has consistently been found to be higher in those of low socio-economic status, probably reflecting social class variations in tobacco exposure.[5]

Recent systematic reviews suggest that increased consumption of fruit and vegetables, particularly foods containing carotenoids (generally those which have red or orange pigments) is associated with decreased lung cancer risk, after adjusting for smoking status.[8] In contrast; randomised controlled trials suggest that smokers taking beta-carotene supplements have an increased disease risk.[4]

The chances of developing lung cancer are increased in those exposed to asbestos, ionizing radiation and arsenic in drinking water.[2,4] Various other lifestyle factors such as alcohol intake and physical activity may be related to lung cancer, but the evidence is inconsistent and it is not always possible to rule out the possibility that the findings are due to some residual effect of smoking.[4,6,7]

2. SMOKING PREVALENCE

Figure 2
Prevalence of smoking in RoI by gender: 1998, 2002 and 2007

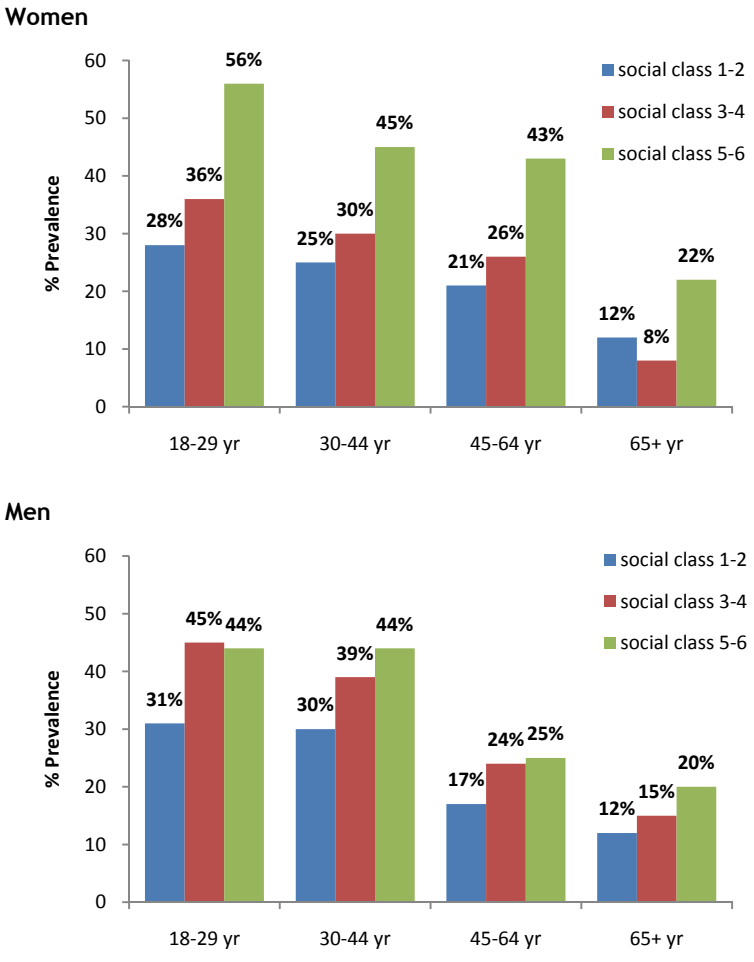


Brugha R, et al (2009) [27]

A recent survey of smoking prevalence was conducted through face-to-face interviews in the homes of 10,251 randomly selected Irish adults (RoI) in 2007.[27] A 'current smoker' was defined as 'smoking every day', or 'some days', and having 'smoked at least 100 cigarettes' during their lifetime.

In 2007, 29% of respondents in the survey reported that they were current smokers. This was lower than in 1998 (33%) and a non-significant increase from 2002 (27%). The downward trend between 1998 and 2002 was seen in both men and women, and across all age groups and social classes (Figure 2). Progress then stalled in all these categories, with no significant change in smoking prevalence between 2002 and 2007.

Figure 3
Prevalence of smoking by gender, age and social class in 2007



Brugha R, et al (2009) [27]

The prevalence of smoking in RoI in 2007 by gender and social class is presented in Figure 3. [27]

Fewer women than men aged 18-29 reported that they were current smokers (32% of women compared to 38% of men).[27] However, the biggest differences in smoking rates were seen between women in the various social classes (SC).

More than half of all women aged 18-29 from SC 5-6 (56%) were smokers, which was twice the rate among women in SC 1-2 (28%) and significantly more than women in SC 3-4 (36%). Differences in smoking prevalence based on social class groups were also seen among young men, but not to the same extent: 44% of young men in SC 5-6 compared to 31% in SC 1-2.

The authors of the report placed much emphasis on the high rate of smoking among young women, especially those in lower social classes.[27] More than half of women aged 18-29 in social classes SC 5-6 were smokers. Such subgroups were singled out for particular policy attention.

3. INCIDENCE OF LUNG CANCER

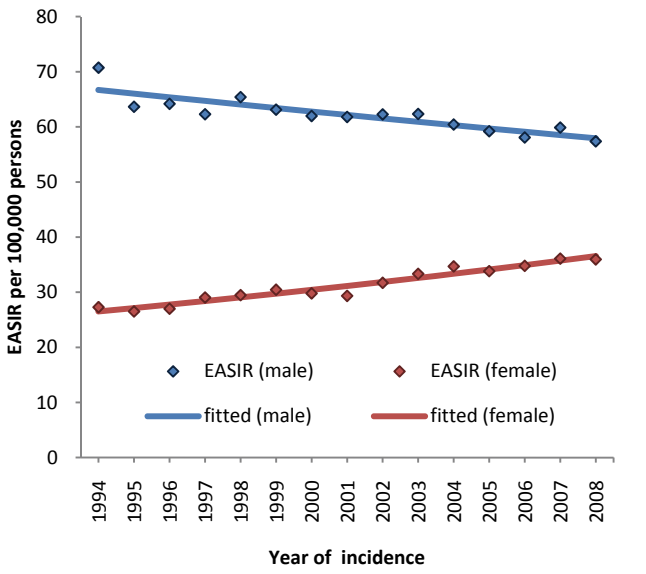
3.1 Lung cancer incidence in the Republic of Ireland

Table 3
Incidence of lung cancer by gender: 1994-2008

	Males		Females	
YEAR	Cases	EASIR	Cases	EASIR
1994	1,064	70.8	510	27.3
1995	976	63.6	510	26.5
1996	1,000	64.2	522	27.0
1997	970	62.3	570	29.1
1998	1,050	65.4	570	29.5
1999	1,020	63.1	609	30.5
2000	1,023	62.0	603	29.8
2001	1,031	61.8	611	29.4
2002	1,063	62.3	659	31.7
2003	1,097	62.3	706	33.3
2004	1,083	60.4	744	34.7
2005	1,100	59.2	749	33.8
2006	1,102	58.1	780	34.8
2007	1,157	59.9	803	36.1
2008	1,147	57.4	839	36.0
Total	**15,883**		**9,785**	
APC*	**1.0%**	**-1.0%**	**3.8%**	**2.3%**
95%CI(APC)	(0.6,1.4%)	(-1.3,-0.7%)	(3.5,4.1%)	(2.0,2.7%)

*APC: Annual percentage change

Figure 4
European age standardised incidence rate (EASIR) and fitted EASIR by gender: 1994-2008



From 1994 until the end of 2008 the total number of cases recorded was 15,883 for men and 9,785 for women (Table 3). 1,059 men and 652 women were diagnosed with lung cancer each year on average between 1994 and 2008. The numbers of lung cancer cases increased for both sexes, by 3.8% annually for women and by 1.0% for men. However, the European age-standardised incidence rate (EASIR) for men fell by 1.0% annually since 1994, while that for women increased by 2.3% annually since 1994 (Figure 4).

From 1994 to 2008 there was a shift in the ratio of male to female lung cancer from 2:1 in 1994 to approximately 4:3 in 2008. The male: female proportion appears to be moving towards parity.

3.2 Summary of patient and tumour characteristics

A summary of patient and tumour characteristics is presented below for patients diagnosed within the periods 1996-1999, 2000-2003 and 2004-2008 (Table 4). The variables and categories considered are explored in more detail in sections 4, 5 and 6. Changes observed over time were:

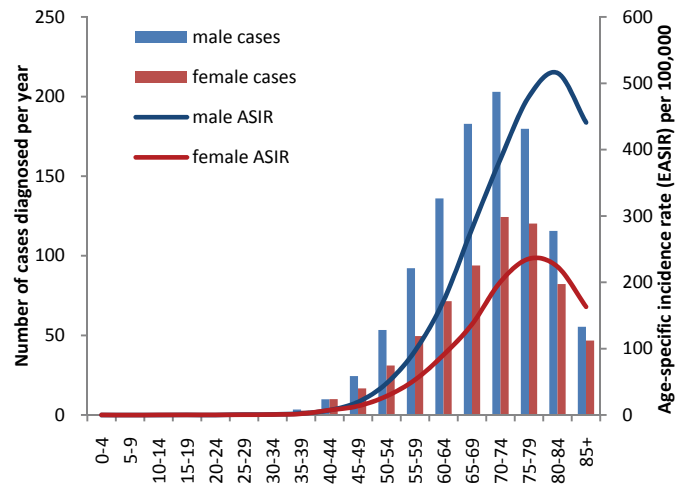
- Increase in the proportion of cases presenting in the 55-64 year age group, with a decrease in the proportion presenting in the 65-74 year age group.
- Increase in the proportion of female cases.
- Increase in the proportion of non small cell lung cancer (NSCLC), with a decrease in the proportion of 'other' and 'unspecified' morphologies.
- Increase in the proportion of cases which were microscopically verified at diagnosis.
- Increase in the proportion of adenocarcinoma tumours, with a decrease in the proportion of squamous cell tumours.
- Increase in the proportion of cases diagnosed at stage III-IV, with a decrease in the proportion diagnosed at stage I-II.
- Increase in the proportion of cases presenting incidentally and a decrease in cases presenting symptomatically.

Table 4
Summary of patient and tumour characteristics for incident lung cancer cases: Diagnostic periods 1996-1999, 2000-2003, 2004-2008

Variable	Category	1996-1999		2000-2003		2004-2008	
		cases	% of cases	cases	% of cases	cases	% of cases
	Total	6,309	100%	6,790	100%	9,500	100%
Age	15-44 yrs	113	2%	127	2%	180	2%
	45-54 yrs	499	8%	484	7%	693	7%
	55-64 yrs	1,165	18%	1,382	20%	2,095	22%
	65-74 yrs	2,375	38%	2,356	35%	3,078	32%
	75+ yrs	2,157	34%	2,441	36%	3,454	36%
Gender	Male	4,040	64%	4,214	62%	5,587	59%
	Female	2,269	36%	2,576	38%	3,913	41%
HSE area of residence	Dublin mid Leinster	1,898	30%	1,992	29%	2,832	30%
	Dublin north east	1,488	24%	1,604	24%	2,149	23%
	South	1,489	24%	1,670	25%	2,338	25%
	West	1,434	23%	1,524	22%	2,181	23%
Marital status	Ever married	4,801	76%	5,267	78%	7,431	78%
	Never married	994	16%	1,095	16%	1,481	16%
	Unknown	514	8%	428	6%	588	6%
Smoking status	Never smoker	519	8%	691	10%	831	9%
	Ex smoker	1,400	22%	1,670	25%	2,504	26%
	Smoker	3,301	52%	3,289	48%	4,543	48%
	Unknown	1,089	17%	1,140	17%	1,622	17%
Socio economic status	1 (Least deprived)	1,002	16%	1,167	17%	1,597	17%
	2	708	11%	784	12%	1,039	11%
	3	706	11%	814	12%	1,016	11%
	4	1,044	17%	1,115	16%	1,474	16%
	5 (Most deprived)	2,406	38%	2,497	37%	3,383	36%
	Unknown	443	7%	413	6%	991	10%
Mode of presentation	Symptomatic	5,554	88%	5,579	82%	7,646	80%
	Incidental	270	4%	460	7%	732	8%
	Screen detected	5	<1%	58	1%	99	1%
	Unknown	480	8%	693	10%	1,023	11%
Method of verification	Microscopic verification (a)	4,523	72%	4,951	73%	7,528	79%
	Clinical diagnosis	1,417	22%	1,546	23%	1,616	17%
	Unknown	369	6%	293	4%	356	4%
Site of tumour	Main bronchus	802	13%	943	14%	1,249	13%
	Upper lobe	2,762	44%	2,887	43%	3,972	42%
	Middle lobe	371	6%	344	5%	394	4%
	Lower lobe	1,273	20%	1,391	20%	2,029	21%
	Overlapping	184	3%	172	3%	188	2%
	Lung, NOS (b)	914	14%	1,050	15%	1,641	17%
	Unknown primary	3	<1%	3	<1%	27	1%
Stage	Stage I	928	15%	917	14%	1,249	13%
	Stage II	510	8%	453	7%	556	6%
	Stage III	1,302	21%	1,596	24%	2,429	26%
	Stage IV	1,602	25%	2,266	33%	3,567	38%
	Stage unknown	1,967	31%	1,558	23%	1,699	23%
Tumour cell type	NSCLC	3,602	57%	3,991	59%	6,143	65%
	SCLC	837	13%	880	13%	1,311	14%
	Other cell type	1,870	30%	1,919	28%	2,046	22%
Morphology	Squamous cell	1,765	28%	1,686	25%	2,370	25%
	Adenocarcinoma	940	15%	1,193	18%	2,043	22%
	Small cell carcinoma	837	13%	880	13%	1,311	14%
	Large/undifferentiated cell carcinoma	179	3%	163	2%	209	2%
	Other morphology	2,588	41%	2,868	42%	3,567	37%
Tumour grade	Grade 1	140	2%	146	2%	202	2%
	Grade 2	712	11%	682	10%	1,123	12%
	Grade 3+	1,533	24%	1,551	23%	2,428	26%
	Grade unknown	3,924	62%	4,411	65%	5,747	60%

(a) microscopic verification includes cytological methods
(b) less specific terms seen in pathology reports, such as: 'bronchus', 'bronchiole', 'bronchogenic' or 'pulmonary not otherwise specified' (NOS)

Figure 5
Number of cases of lung cancer diagnosed per year by gender and age with age-specific incidence rate (ASIR) per 100,000 persons: Diagnostic period: 1994-2008



3.3 Incidence by age

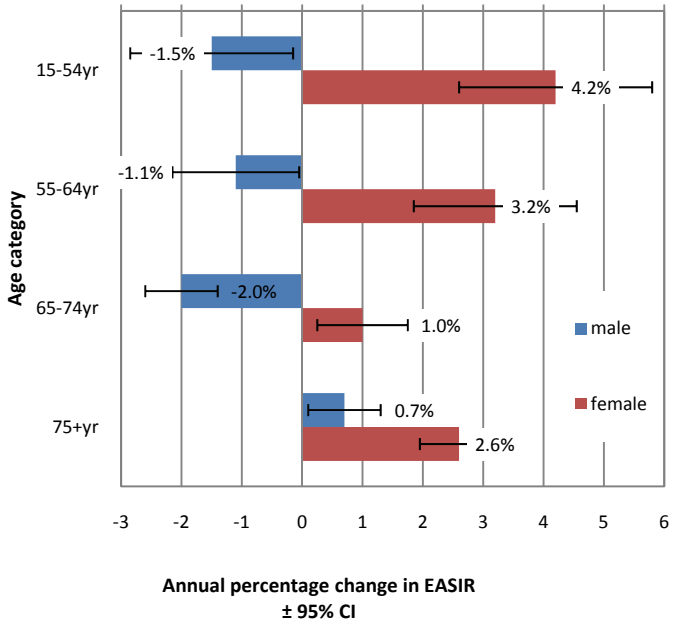
The numbers of cases presenting, and age-specific incidence rates, in each 5-year age group are presented in Figure 5.

The median age for diagnosis of lung cancer in males during the three periods 1996-1999, 2003-2003 and 2004-2008 was 70 years.

The median age for diagnosis in females was 71 years during 2004-2008, and 72 years during 1996-1999 and 2000-2003.

Cases peaked in the age 70-74 year age category for both males and females, which included 19% of all cases for both sexes. The age specific incidence rate (ASIR) was highest in the 80-84 age category for males (516 cases/100,000) and in the 75-79 age category for females (235 cases/100,000).

Figure 6
Annual percentage change (APC) ± 95% CI in European age-standardised incidence rate (EASIR) for lung cancer by gender and age: Diagnostic period: 1994-2008



Changes in incidence (annual percentage change, APC) over the years 1994-2008 in the age categories 15-54 years, 55-64 years, 65-74 years and 75+ years are presented in Figure 6.

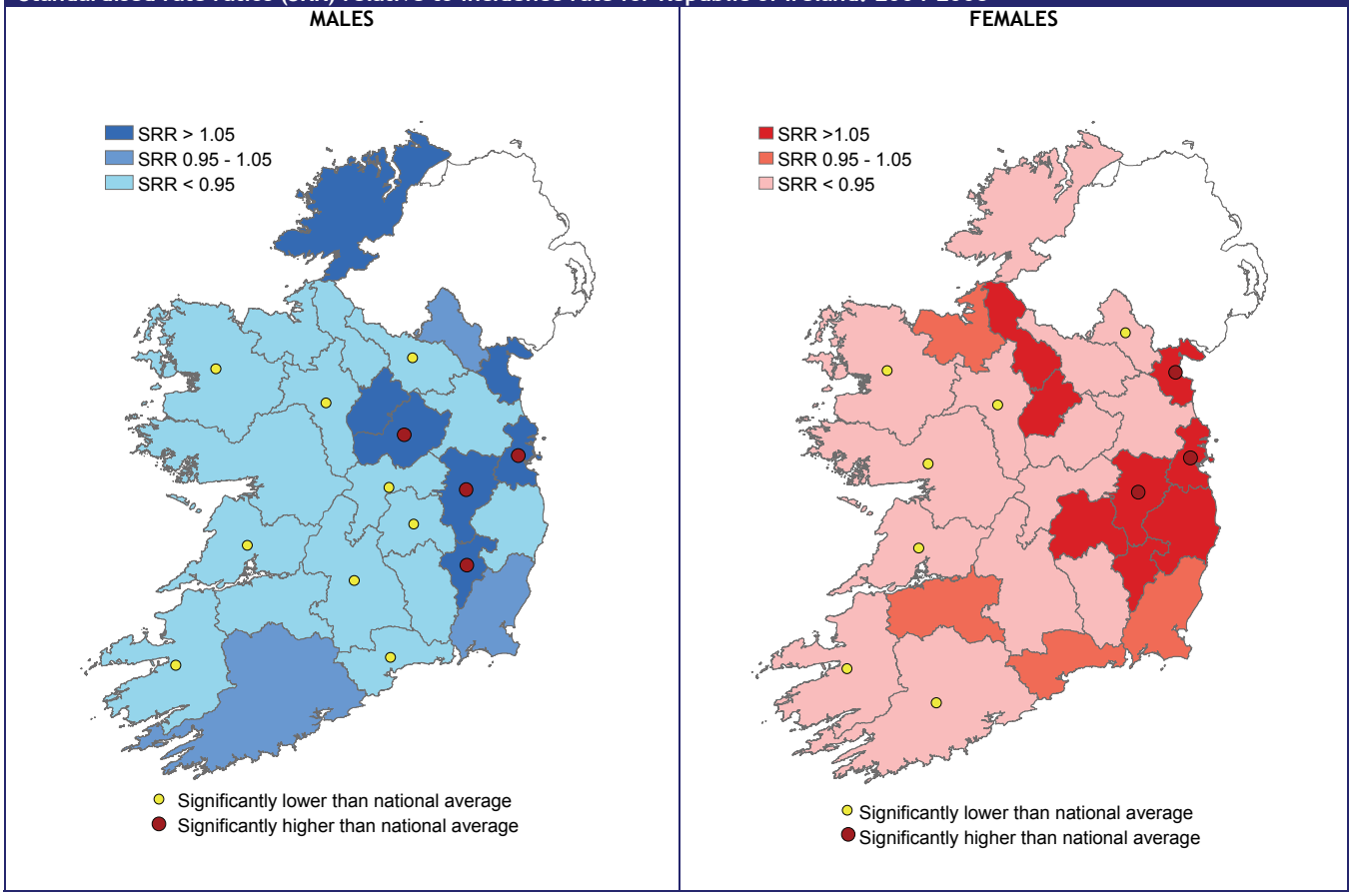
For females, there were significant annual percentage increases in all age categories. Most notably, there was an annual 4.2% increase in the incidence rate in the youngest age group (15-54 years), although this age category included only 9% of all cases.

There were also significant annual increases for females in the 55-64 years category (3.2%), the 65-74 year category (1.0%) and in the 75+ year category (2.6%), which included 38% of cases.

For males, there were significant annual percentage decreases for age categories 15-54 years (-1.5%), 55-64 years (-1.1%), 65-74 (-2.0%) and a significant increase in the oldest age category 75+ years (0.7%), which included 33% of cases.

3.4 Geographic variation in incidence (2004-2008)

Figure 7
County-level variation in lung cancer incidence by gender:
Standardised rate ratios (SRR) relative to incidence rate for Republic of Ireland: 2004-2008



The variation in lung cancer incidence by gender at county level is presented in Figure 7.

European age standardised incidence rates (EASIR) were calculated for the period 2004-2008 for each county. The incidence rate for males in Ireland was 59.0 (95%CI: 57.4, 60.5) per 100,000 persons.[b] The rates in Dublin (77.7), Kildare (72.2), Carlow (71.6) and Westmeath (71.0) stand out as being significantly higher than the average incidence rate for the country as a whole. Conversely, the rates for males in Tipperary (51.2), Mayo (49.7), Cavan (47.1), Waterford (46.8), Offaly (45.4), Laois (43.9), Clare (43.6), Kerry (43.1) and Roscommon (40.4) were significantly lower than the national average rate.

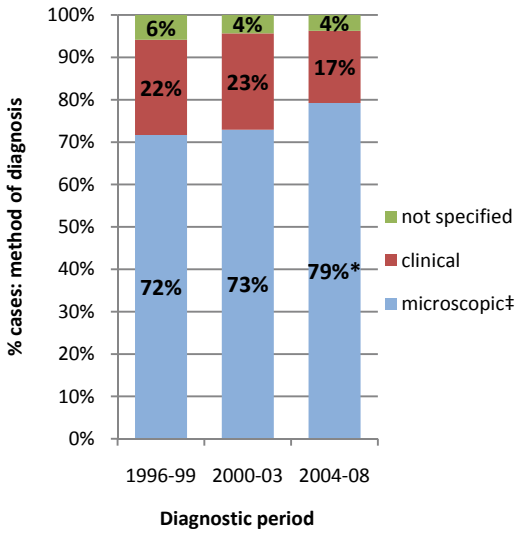
For females, the incidence rate for the country as a whole over the period 2004-2008 was 35.1 (95%CI: 34.0, 36.2) per 100,000 persons. The incidence rates were significantly higher than the national average rate for Louth (59.1), Dublin (44.0), and Kildare (42.5). The rates were significantly lower than the national rate for Cork (28.1), Galway (27.4), Monaghan (26.1), Clare (26.0), Kerry (24.6), Mayo (23.2) and Roscommon (18.5).

Counties are demarcated by largely arbitrary boundaries with great variation in population densities. Geographic variation in incidence rates may be better visualised by consulting the NCR cancer atlas which describes incidence ratios at the level of approximately 3,400 electoral divisions in the Republic of Ireland during 1994-2003 and the forthcoming all-Ireland cancer atlas.[11, 26]

[b] Appendix II statistical methods

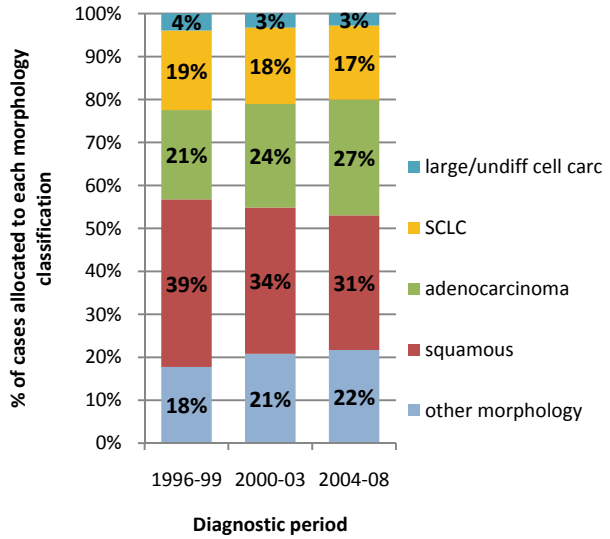
3.5 Incidence by morphology

Figure 8
Percentage of cases by method of diagnosis: Diagnostic periods: 1996-1999, 2000-2003 and 2004-2008



‡ Includes cytological methods,
* p<0.0001, test for linear trend from 1996 to 2008

Figure 9
Percentage of cases allocated to each morphological classification: Diagnostic periods: 1996-1999, 2000-2003 and 2004-2008



Morphology classifications according to Devesa et al, 2005[10]
Data is based on the subset diagnosed microscopically

The proportions of cases diagnosed by microscopic or clinical methods are presented in Figure 8.

There was a significant trend towards diagnosis by microscopic methods relative to clinical methods over the three diagnostic periods. The proportion of cases diagnosed microscopically increased significantly from 72% for 1996-1999 to 79% for 2004-2008

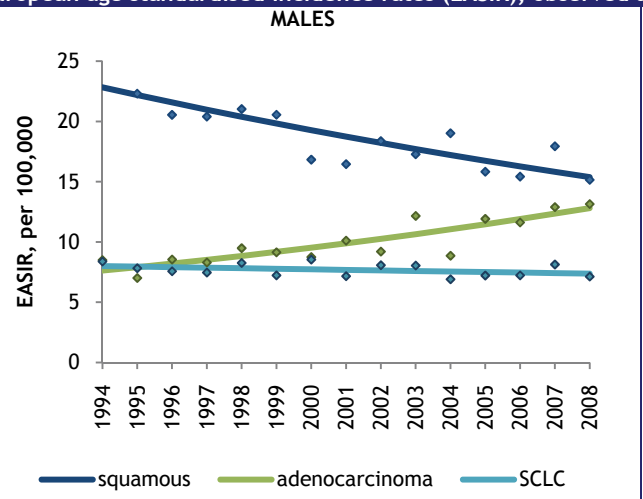
The proportions of cases assigned to each histological classification[c] are presented in Figure 9. Changes in proportions observed across three diagnostic periods were as follows:

- Modest decrease in the proportion of small cell lung cancer (19% to 17%, for 1996-1999 and 2004-2008 respectively)
- Increase in the proportion of adenocarcinoma (21% to 27%, for 1996-1999 and 2004-2008 respectively)
- Decrease in the proportion of squamous cell tumours (39% to 31%, for 1996-1999 and 2004-2008 respectively)
- Increase in the proportion of cases allocated to 'other morphologies' (18% to 22%, for 1996-1999 and 2004-2008 respectively)

[c] Appendix II: Tumour characteristics: morphology

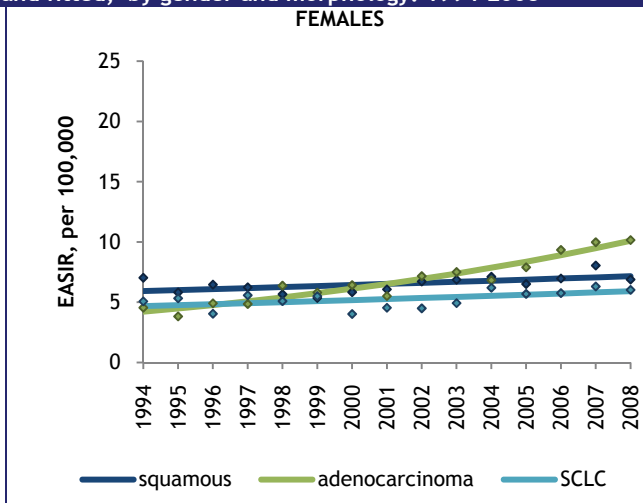
3.6 Trends in morphology (1994-2008)

Figure 10
European age standardised incidence rates (EASIR), observed and fitted, by gender and morphology: 1994-2008



Annual Percent Change (APC) *p<0.0001

Morphology	APC (95%CI)
squamous cell	-2.8*(-3.8,-1.8)
adenocarcinoma	3.8*(2.5, 5.1)
small cell	-0.6 (-1.4, 0.3)



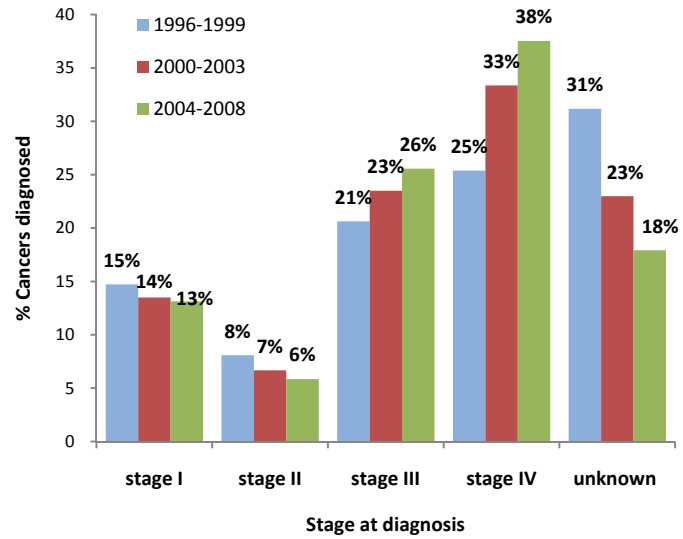
Annual Percent Change (APC) *p<0.0001

Morphology	APC (95%CI)
squamous cell	1.4* (0.2, 2.5)
adenocarcinoma	6.4* (5.2, 7.7)
small cell	1.7* (0.2, 3.2)

Annual percentage changes in the main histological tumour types were calculated using Joinpoint regression[15] for the subset of cases diagnosed microscopically (Figure 10). All three tumour types increased in women. For males, only adenocarcinoma increased, albeit at a much lower rate (3.8%) than that seen in females (6.4%). In males, squamous cell tumours decreased by 2.8% annually. In females, squamous cell tumours increased by 1.4% and small cell (SCLC) tumours by 1.7%.

3.7 Stage at diagnosis (1996-2008)

Figure 11
Stage at diagnosis for lung cancer patients: Diagnostic periods 1996-1999, 2000-2003, 2004-2008



Percentages of cases presenting at various stages of disease over the three diagnostic periods are presented in Figure 11.

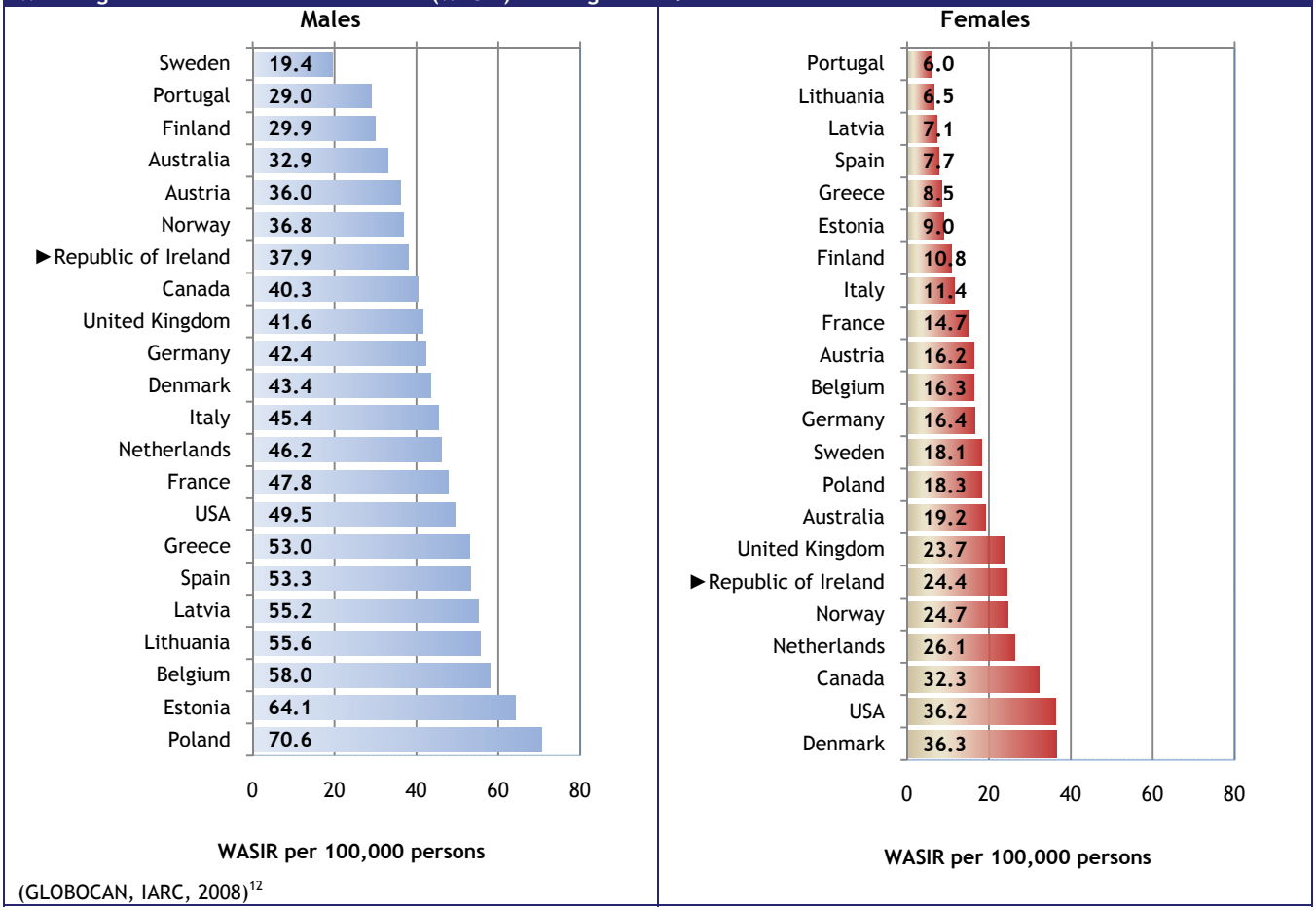
The proportions presenting at stage I and stage II decreased (stage I: 15%, 14%, and 13%, stage II: 8%, 7%, and 6%) for the periods 1996-1999, 2000-2003 and 2004-2008 respectively.

Conversely, the proportions presenting at stage III and stage IV increased (stage III: 21%, 23%, and 26%, stage IV: 25%, 33%, and 38%) for the periods 1996-1999, 2000-2003 and 2004-2008 respectively.

These changes may be accounted for by the increased allocation of unclassified cases to stage III/IV over the three diagnostic periods, and to a lesser extent by stage I/II cases allocated to higher stage, which is probably a reflection of more thorough staging methods.

3.8 International comparisons of incidence

Figure 12
World age standardised incidence rates (WASIR) for lung cancer: 2008



(GLOBOCAN, IARC, 2008)[12]

Estimated world age standardised incidence rates (WASIR) are presented in Figure 12.[12]

In the international data presented, Irish females had a relatively higher incidence rate compared to most other developed countries. In comparison, Irish males showed lower incidence relative to other countries in the survey.

In 2008 the WASIR for males in Ireland (37.9/100,000 persons) was lower than that of Canada (40.3), the United Kingdom (41.6), Germany (42.4), Italy (45.4), France (47.8), Spain (53.3) and the USA (SEER areas, 49.5). The Scandinavian countries (except for Denmark (43.4)) had lower rates than Ireland.

In 2008 the WASIR for females in Ireland (24.4/100,000 persons) was lower than that of Canada (32.2), USA (36.2) and Denmark (36.2). However, females in Ireland had a higher rate of incidence than those of our nearest neighbours in western Europe: Spain (7.7), Italy (11.4), France (14.7), Germany (16.4) and the United Kingdom (23.7).

4. TREATMENT

4.1 Treatment received

Table 5
Treatment received by lung cancer cases†
Annual average number and percentage of cases in receipt of treatment: 1996-1999, 2000-2003, 2004-2008

	1996-99		2000-03		2004-08	
	cases/yr	%	cases/yr	%	cases/yr	%
surgery	212	13%	195	11%	245	13%
chemotherapy*	245	15%	366	21%	635	32%
radiotherapy‡	584	37%	656	38%	770	40%
no treatment*	767	49%	787	46%	752	40%

*p<0.001, ‡p<0.02 for linear trend from 1996 to 2008
†Treatments listed were not mutually exclusive

The annual average number of cases who received various treatment modalities[d] during three diagnostic periods is presented in Table 5.

Approximately 13% of lung cancer cases had tumour directed resective surgery, and the majority of those (96%) underwent only one such procedure during the course of their treatment.

Chemotherapy became an important treatment modality in recent years. The percentage of cases who received chemotherapy increased significantly from 15% in 1996-1999 to 32% in 2004-2008. Similarly, the percentage undergoing radiotherapy increased from 37% in 1996-1999 to 40% in 2004-2008. The number of cases who received no tumour directed treatment decreased from 49% in 1996-1999 to 40% in 2004-2008.

Table 6
Treatment received by non-small cell lung cancer (NSCLC) cases
Annual average number and percentage of cases in receipt of treatment: 1996-1999, 2000-2003, 2004-2008

	1996-99		2000-03		2004-08	
	cases/yr	%	cases/yr	%	cases/yr	%
surgery only	133	15%	119	12%	144	12%
radiotherapy only	290	32%	298	30%	285	23%
chemotherapy only	34	4%	77	8%	131	11%
surgery and chemotherapy	3	<1%	8	1%	43	4%
surgery and radiotherapy	59	7%	47	5%	22	2%
chemotherapy and radiotherapy	61	7%	122	12%	227	19%
surgery, chemotherapy and radio	8	1%	15	2%	29	2%
no treatment	314	35%	311	31%	348	28%
Total	**901**	**100%**	**998**	**100%**	**1,229**	**100%**

The annual average number of cases with NSCLC who received various treatment modalities during three diagnostic periods is presented in Table 6.

The most common treatment combination was chemotherapy & radiotherapy, which increased from 7% in 1996-1999 to 19% in 2004-2008.

Surgery as a single modality decreased from 15% in 1996-1999 to 12% in 2004-2008. Radiotherapy as a single modality decreased from 32% in 1996-1999 to 23% in 2004-2008. Chemotherapy as a single modality increased from 4% in 1996-1999 to 11% in 2004-2008. Surgery & chemotherapy in combination also showed an increase from a low base of <1% in 1996-1999 to 4% in 2004-2008. The proportion of NSCLC cases receiving no treatment decreased from 35% in 1996-1999 to 28% in 2004-2008.

Table 7
Treatment received by small cell lung cancer (SCLC) cases
Annual average number and percentage of cases in receipt of treatment: 1996-1999, 2000-2003, 2004-2008

	1996-99		2000-03		2004-08	
	cases/yr	%	cases/yr	%	cases/yr	%
surgery only	3	1%	1	<1%	1	<1%
radiotherapy only	20	9%	26	12%	27	10%
chemotherapy only	54	26%	50	23%	59	23%
surgery and chemotherapy	1	<1%	1	<1%	-	-
surgery and radiotherapy	1	<1%	-	-	-	-
chemotherapy and radiotherapy	62	30%	66	30%	103	39%
surgery, chemotherapy and radio	2	1%	1	<1%	2	1%
no treatment	68	32%	77	35%	69	26%
Total	**209**	**100%**	**220**	**100%**	**262**	**100%**

The annual average number of cases with SCLC who received various treatment modalities during three diagnostic periods is presented in Table 7.

Surgery was rarely undertaken in SCLC. Less than 1% of cases received surgery in 2004-2008.

The most common treatment was the combination of chemotherapy & radiotherapy, which increased from 30% of cases in 1996-1999 to 39% of cases in 2004-2008. Chemotherapy as the only treatment decreased from 26% of cases in 1996-

[d] Appendix II: Treatment definitions

1999 to 23% in 2004-2008. The proportion of cases with SCLC who received no treatment decreased from 32% in 1996-1999 to 26% in 2004-2008.

4.2 Surgical caseload: Hospitals

Table 8
Lung cancer surgical caseload by hospital:
Diagnostic periods:1996-1999, 2000-2003, 2004-2008

Diagnostic period	1996-99		2000-03		2004-08	
	cases/yr	%	cases/yr	%	cases/yr	%
Totals	**212**	**100%**	**195**	**100%**	**245**	**100%**
St James's Hospital, DN	66	31%	56	28%	98	40%
Mater MUH, DN[e]	20	10%	32	17%	30	12%
St Vincent's University Hospital (UH), DN	26	12%	19	10%	30	12%
Cork University Hospital (UH), CK	30	14%	30	15%	28	11%
Beaumont Hospital, DN	30	14%	23	12%	20	8%
St Vincent's Private Hospital, DN	13	6%	10	5%	14	6%
Mater Private Hospital, DN	13	6%	14	7%	9	4%
University College Hospital (UCH), GY	9	4%	4	2%	7	3%
Hospitals: other or unknown	6	3%	8	4%	10	4%

The annual average number of lung tumour resections performed in each hospital is presented for each diagnostic period in Table 8.

The bulk of tumour resection surgery (>95% of cases) was confined to eight hospitals.

St James's Hospital dealt with 40% of cases who underwent surgery over the period 2004-2008. Other hospitals with greater than 5% of cases nationally during the period 2004-2008 were: Mater MUH (12%), St Vincent's UH (12%), Cork UH (11%), Beaumont Hospital (8%), St Vincent's Private Hospital (6%), Mater Private Hospital (4%) and UCH Galway (3%).

Of the larger hospitals, only St James's Hospital showed an increase in the number of surgical cases over time. Beaumont Hospital showed a decrease in the percentage of cases over time (14% in 1996-1999, 8% in 2004-2008).

Table 9
HSE-area of surgery relative to HSE area of residence:
Diagnostic periods 1996-2003 & 2004-2008

HSE area of residence	HSE AREA OF SURGERY			
	(1996-2003)			
	DNML	DNNE	South	West
DNML	87%	13%	-	-
DNNE	18%	82%	-	-
South	28%	5%	67%	-
West	53%	18%	9%	20%
	(2004-2008)			
DNML	94%	6%	-	-
DNNE	29%	71%	-	-
South	38%	4%	58%	-
West	70%	10%	5%	15%

The proportion of cases who attended for tumour directed resective surgery[f] in HSE areas outside their HSE area of residence is presented in Table 9.

All cases originating in the eastern HSE areas received their surgery within one of the eastern HSE areas.

A substantial proportion of cases originating in HSE West (and to a lesser extent in HSE South) travelled to DNML (and DNNE) for their surgery. The reasons for this are not known. It is suggested that it was because specialist surgery may not have been available locally.

[e] Mater MUH, DN: Mater Misericordiae University Hospital, Dublin
[f] Appendix II: Treatment definitions: surgery

4.3 Radiotherapy caseload: Hospitals

Table 10
Lung cancer radiotherapy caseload by hospital:
Diagnostic periods: 1996-1999, 2000-2003, 2004-2008

Diagnostic period	1996-99 cases/yr	%	2000-03 cases/yr	%	2004-08 cases/yr	%
Total	**584**	**100%**	**656**	**100%**	**770**	**100%**
St Luke's Hospital, DN	405	69%	445	68%	418	54%
Cork University Hospital (UH), CK	103	18%	126	19%	135	17%
University College Hospital (UCH), GY	-	-	2	<1%	78	10%
Mater Private Hospital, DN	39	7%	48	7%	50	7%
Mid-Western Regional Hospital (RH), LK	-	-	-	-	25	3%
Whitfield Clinic, WD	-	-	-	-	23	3%
St Vincent's Private Hospital, DN	36	6%	34	5%	20	3%
The Galway Clinic, GY	-	-	-	-	16	2%
Beacon Clinic, DN	-	-	-	-	3	<1%
Centres: Unknown	2	<1%	2	<1%	4	<1%

The annual average number of cases who underwent at least one radiotherapy session at each centre is presented in Table 10.

Radiotherapy services for lung cancer were provided by nine facilities over 2004-2008.

St Luke's Hospital provided treatment for most cases, albeit the share for St Luke's Hospital fell from 69% in 1996-1999 to 54% in 2004-2008. This fall may be accounted for by the introduction of radiotherapy at UCH Galway (10%), the MWRH Limerick (3%) and the Whitfield Clinic (3%) during the period 2004-2008. The Galway Clinic and Beacon Clinic also introduced radiotherapy services during the period 2004-2008 (2% and <1% respectively).

4.4 Chemotherapy caseload: Hospitals

Table 11
Lung cancer chemotherapy caseload by hospital:
Diagnostic periods: 1996-1999, 2000-2003, 2004-2008

Diagnostic period	1996-99 cases/yr	%	2000-03 cases/yr	%	2004-08 cases/yr	%
Totals	**245**	**100%**	**366**	**100%**	**635**	**100%**
St James's Hospital, DN	36	15%	37	10%	81	13%
Beaumont Hospital, DN	19	8%	50	14%	53	8%
Tallaght Regional Hospital (RH), DN	1	<1%	3	1%	47	7%
Waterford Regional Hospital (RH), WD	5	2%	16	4%	43	7%
St Vincent's Hospital, DN	25	10%	31	8%	39	6%
Cork University Hospital (UH), CK	16	6%	29	8%	39	6%
Mercy University Hospital (UH), CK	11	4%	20	5%	33	5%
Mater MUH, DN	22	9%	26	7%	31	5%
Tullamore General Hospital (GH), OY	-	-	8	2%	30	5%
University College Hospital (UCH), GY	11	4%	7	2%	28	4%
St Luke's Hospital, DN	22	9%	18	5%	21	3%
Letterkenny General Hospital (GH), DL	-	-	5	1%	20	3%
Mid-Western Regional Hospital (RH), LK	1	<1%	12	3%	19	3%
Sligo General Hospital (GH), SO	1	<1%	9	2%	18	3%
St Vincent's Private Hospital, DN	19	8%	17	5%	16	3%
Bon Secours Hospital, CK	5	2%	9	2%	15	2%
Merlin Park Hospital, Galway	23	9%	23	6%	14	2%
Hospital: Other or unknown	31	13%	50	14%	89	14%

The annual average number of cases who underwent at least one chemotherapy treatment at each centre is presented in Table 11.

In 2004-2008, St James's Hospital dealt with the largest number of cases (13%) followed by Beaumont Hospital (8%) and Tallaght RH (7%).

Other hospitals with significant caseloads in 2004-2008 were: Waterford RH (7%), St Vincent's Hospital (6%), Cork UH (6%), Mercy UH Cork (5%), Mater MUH (5%), Tullamore GH (5%), UCH Galway (4%), St Luke's Hospital (3%), Letterkenny GH (3%) and MWRH Limerick (3%). Some of the larger hospitals showed decreased caseloads in 2004-2008 compared to earlier periods: St Vincent's Hospital (6%, down from 10% in 1996-1999), Mater MUH (5%, down from 9% in 1996-1999) and St Luke's Hospital (3% down from 9% in 1996-1999).

The bulk of chemotherapy services (>85%) was provided by 17 hospitals during 2004-2008. Overall, it appeared that some regional/general hospitals such as Tallaght RH, MWRH Limerick, Letterkenny GH and Tullamore GH took some of the caseload from the larger Dublin hospitals, perhaps to allow greater accessibility for patients.

4.5 Factors associated with treatment receipt

Table 12
Factors associated with receipt of tumour directed treatment by case and tumour characteristics

Variable	category	cases	(%) treat -ed	Risk Ratio RR	95% CI	
gender	male	13,841	57%	1.00		
	female	8,758	56%	1.01	0.97	1.04
age	15-44 yr	420	88%	1.00		
	45-54 yr	1,676	81%	**0.85**	0.75	0.95
	55-64 yr	4,642	75%	**0.76**	0.68	0.85
	65-74 yr	7,809	61%	**0.65**	0.59	0.73
	75 yr +	8,052	34%	**0.41**	0.37	0.46
stage	I	3,094	68%	1.00		
	II	1,519	71%	0.99	0.92	1.06
	III	5,327	65%	**0.92**	0.87	0.97
	IV	7,435	58%	**0.84**	0.80	0.89
	Stage unknown	5,224	34%	**0.65**	0.61	0.69
morphology	squamous	5,821	72%	1.00		
	adenocarcinoma	4,176	70%	**0.91**	0.87	0.96
	SCLC	3,028	70%	0.95	0.90	1.00
	large undiff cell	551	70%	0.93	0.84	1.03
	Other/Unknown	9,023	35%	**0.58**	0.55	0.61
smoking	non smoker	2,041	55%	1.00		
	ex smoker	5,574	63%	1.06	0.99	1.14
	smoker	11,133	61%	0.96	0.90	1.03
	unknown	3,851	35%	**0.75**	0.70	0.82
deprivation	1 Least	3,766	60%	1.00		
	2	2,531	56%	**0.92**	0.86	0.98
	3	2,536	56%	0.95	0.88	1.01
	4	3,633	56%	**0.93**	0.88	0.99
	5 Most	8,286	56%	**0.89**	0.85	0.94
	Unknown	1,847	53%	**0.92**	0.85	0.99
period	1996-1999	6,309	52%	1.00		
	2000-2003	6,790	54%	1.05	1.00	1.10
	2004-2008	9,500	61%	**1.15**	1.10	1.20
HSE area	DNML	6,722	60%	1.00		
	DNNE	5,241	57%	0.98	0.93	1.02
	South	5,497	56%	**0.93**	0.89	0.98
	West	5,139	51%	**0.89**	0.84	0.93
	Total	**22,599**	**56%**			
	RR in bold are significantly different from baseline (1.0)					

The patient and tumour factors associated with tumour directed treatment were identified and are presented in Table 12. *Treatment* was defined as receipt of any: resection, chemotherapy or radiotherapy, undertaken or commenced at any time during the course of disease.[g] A *risk ratio* less than 1.0 indicates a lesser likelihood of treatment relative to the baseline level of a variable (1.0).[h] Similarly, a risk ratio greater than 1.0 indicates a greater likelihood of treatment after adjusting for the other variables in the model.

Overall, 56% of cases received some form of tumour directed treatment during the course of disease. There was no difference between men and women in the proportions in receipt of treatment.

Patient age at diagnosis was significantly associated with treatment receipt. While 88% of cases between the ages of 15-44yr received treatment within one year, only 81%, 75%, 61% and 34% of cases received treatment in the age categories 45-54yr, 55-64yr, 65-74yr and 75 yr+ respectively.

Cases diagnosed at stage III and IV were significantly less likely to receive treatment (65% and 58% respectively) compared to stage I cases (68%).

After adjusting for other factors in the model, cases with adenocarcinoma (70%) and small cell carcinoma (70%) were less likely to receive treatment relative to squamous cell cases (72%). Only 35% of cases with 'other' or 'unknown' morphologies received some form of tumour directed treatment.

Smoking status had little influence on the likelihood of treatment receipt, except for those cases with unknown smoking status, who were less likely to receive treatment (35% compared to 55% for non smokers). Cases in the more deprived quintiles were less likely to receive treatment (56%) relative to cases in the least deprived quintile (60%).

Cases originating in the diagnostic period (2004-2008) were significantly more likely to receive treatment (61%) in comparison to those cases originating in the earliest diagnostic period (52%, 1996-1999).

Cases originating in HSE West (51%) and HSE South (56%) were significantly less likely to receive treatment compared to cases originating in Dublin Mid Leinster (60%).

[g] Appendix II: Treatment definitions
[h] Appendix II: Statistical methods

5. SURVIVAL

5.1 Relative survival

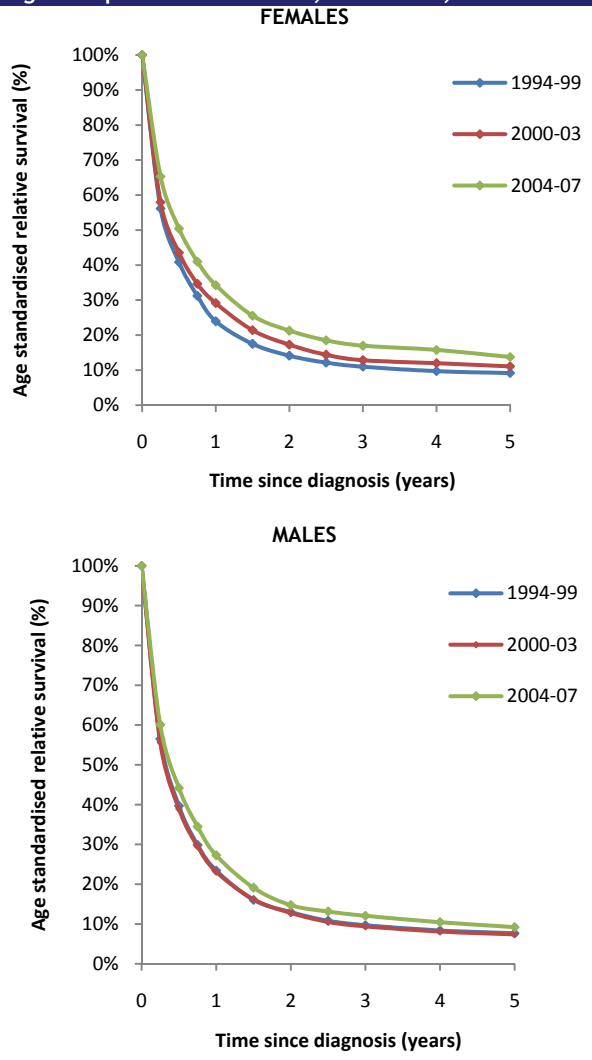
Table 13
Age-standardised relative survival for lung cancer by gender: Diagnostic periods‡ 1994-1999, 2000-2003, 2004-2007

	Age standardised relative survival & 95% confidence intervals						
	Period	1-year	95% CI		5-year	95% CI	
All persons	1994-99	23.6%	(22.7%,	24.5%)	8.1%	(7.5%,	8.7%)
	2000-03	25.4%	(24.3%,	26.5%)	8.7%	(8.0%,	9.5%)
	2004-07	30.1%	(29.0%,	31.3%)	11.2%	(10.4%,	12.2%)
Males	1994-99	23.4%	(22.3%,	24.6%)	7.6%	(6.8%,	8.3%)
	2000-03	23.1%	(21.8%,	24.5%)	7.3%	(6.5%,	8.3%)
	2004-07	27.3%	(25.9%,	28.7%)	9.6%	(8.5%,	10.7%)
Females	1994-99	24.0%	(22.4%,	25.5%)	9.1%	(8.0%,	10.2%)
	2000-03	29.2%	(27.3%,	31.1%)	11.0%	(9.7%,	12.4%)
	2004-07	34.3%	(32.5%,	36.1%)	13.6%	(12.2%,	15.2%)

Relative survival is the ratio of the observed survival for a given group of cancer cases to the expected survival of a group of individuals of the same age, gender and country.

Relative survival is used by most cancer registries in place of *cause specific survival* because the actual cause of death in any given cancer case is not always known. Relative survival also facilitates international comparison.

Figure 13
Age-standardised relative survival for lung cancer by gender
Diagnostic periods: 1994-1999, 2000-2003, 2004-2007



Relative survival was derived using age and sex specific life tables for Ireland.

Relative survival estimates at 1 year and 5 years post-diagnosis are presented for males and female lung cancer cases in Ireland across three periods: 1994-1999, 2000-2003 and 2004-2007 in (Table 13, Figure 13)

There was a steady improvement in female survival at one (24%, 29% and 34%) and five years (9%, 11% and 14%) across the three diagnostic periods.

For males, relative survival also improved at 1 year (23%, 23% and 27%) and five years (7.6%, 7.3% and 9.6%) across the three diagnostic periods respectively.

Table 14
Age-standardised relative survival for lung cancer patients by age group: Diagnostic periods: 1994-1999, 2000-2003, 2004-2007

	Age standardised relative survival & 95% confidence intervals						
‡Age group	Period	1-year	95%CI		5-year	95%CI	
15-44yr	1994-99	45.1%	(37.3%,	52.6%)	27.9%	(21.3%,	35.0%)
	2000-03	48.9%	(39.8%,	57.3%)	26.6%	(19.1%,	34.5%)
	2004-07	55.9%	(47.5%,	63.6%)	30.5%	(22.0%,	39.4%)
45-54yr	1994-99	32.5%	(29.1%,	36.1%)	11.8%	(9.5%,	14.4%)
	2000-03	35.1%	(30.8%,	39.5%)	12.0%	(9.2%,	15.1%)
	2004-07	43.2%	(38.9%,	47.3%)	15.6%	(12.3%,	19.3%)
55-64yr	1994-99	26.9%	(24.8%,	29.0%)	9.6%	(8.2%,	11.2%)
	2000-03	31.5%	(28.9%,	34.0%)	11.4%	(9.7%,	13.3%)
	2004-07	38.8%	(36.3%,	41.2%)	13.8%	(11.9%,	15.9%)
65-74yr	1994-99	24.6%	(23.1%,	26.1%)	8.5%	(7.5%,	9.5%)
	2000-03	25.3%	(23.4%,	27.2%)	8.7%	(7.5%,	10.0%)
	2004-07	30.1%	(28.2%,	32.0%)	11.2%	(9.7%,	12.8%)
75+yr	1994-99	17.6%	(16.1%,	19.1%)	5.2%	(4.3%,	6.4%)
	2000-03	18.7%	(17.0%,	20.5%)	5.8%	(4.6%,	7.1%)
	2004-07	19.9%	(18.2%,	21.7%)	7.8%	(6.4%,	9.3%)

Relative survival was calculated at one year and five years post-diagnosis by age group (Table 14).

As might be expected, there was a steady decrease in survival with each increment in age group.

In the most recent period, 2004-2007, 1 year relative survival fell from 56% in the 15-44 year age group to 20% in those aged 75 years and over.

There was a steady improvement in survival over time for all age groups across the diagnostic periods. Taking the age group with the highest incidence (65-74 years), the 1 year relative survival increased from 25% to 30% from 1994-1999 to 2004-2007. In the youngest age group (15-44 years) the 1 year relative survival increased from 45% to 56% from 1994-1999 to 2004-2007.

Table 15
Age-standardised relative survival for lung cancer patients by diagnostic method: Diagnostic period: 1994-1999, 2000-2003, 2004-2007

	Age standardised relative survival &95% confidence intervals						
	Period	1 year	95%CI		5-year	95%CI	
Microscopic	1994-99	26.5%	(25.4%,	27.6%)	9.0%	(8.3%,	9.8%)
	2000-03	28.6%	(27.3%,	29.9%)	10.2%	(9.3%,	11.1%)
	2004-07	33.4%	(32.1%,	34.6%)	12.6%	(11.6%,	13.7%)
Clinical	1994-99	14.9%	(13.4%,	16.5%)	5.3%	(4.3%,	6.5%)
	2000-03	15.8%	(13.9%,	17.8%)	4.3%	(3.2%,	5.6%)
	2004-07	16.7%	(14.7%,	18.9%)	5.6%	(4.2%,	7.4%)

Relative survival was calculated at one year and five years post diagnosis by method of verification, microscopic or clinical (Table 15).

In the most recent period, 2004-2007, cases with microscopic verification showed much better survival at one year (33%) compared to that of cases with clinical verification only (17%). Similarly, 5-year survival was also better (13%) for cases with microscopic verification compared to clinical verification only (6%).

The microscopic diagnosis of lung cancer was made by bronchoscopy and biopsy, which was generally performed by cardiothoracic surgeons or respiratory physicians. The data shows that cases who had microscopic verification survived longer than cases diagnosed clinically.

Cases that were not diagnosed microscopically tended to be older (and may have had other serious co morbidities). The fact that they did not have a biopsy may have been appropriate and consistent with their poor prognosis and lack of suitability for more intensive treatment.

Table 16
Age-standardised relative survival for lung cancer patients by morphology of tumour: Diagnostic period: 1994-1999, 2000-2003, 2004-2007

	Age standardised relative survival & 95% confidence intervals						
	Period	1-year	95%CI		5-year	95%CI	
Squamous cell	1994-99	29.3%	(27.6%,	31.1%)	10.1%	(8.9%,	11.3%)
	2000-03	31.7%	(29.4%,	34.1%)	11.7%	(10.0%,	13.4%)
	2004-07	37.5%	(35.1%,	39.8%)	14.6%	(12.7%,	16.7%)
Adenocarcinoma	1994-99	30.0%	(27.4%,	32.5%)	10.4%	(8.7%,	12.2%)
	2000-03	33.7%	(30.9%,	36.6%)	11.6%	(9.7%,	13.7%)
	2004-07	39.7%	(37.1%,	42.3%)	16.1%	(13.8%,	18.4%)
Small cell (SCLC)	1994-99	22.4%	(20.1%,	24.9%)	5.2%	(4.0%,	6.7%)
	2000-03	21.1%	(18.4%,	24.0%)	4.6%	(3.2%,	6.3%)
	2004-07	25.7%	(23.0%,	28.5%)	5.4%	(4.0%,	7.1%)
Other	1994-99	17.4%	(16.1%,	18.7%)	6.7%	(5.9%,	7.7%)
	2000-03	19.5%	(17.9%,	21.0%)	7.0%	(6.0%,	8.1%)
	2004-07	21.8%	(20.2%,	23.4%)	8.8%	(7.5%,	10.2%)

Relative survival was calculated at one year and five years post diagnosis by morphology of tumour (Table 16).

In the most recent period 2004-2007, cases with small cell tumours (SCLC) had significantly lower 1 year survival (26%) relative to cases with squamous (38%) and adenocarcinoma (40%).

Table 17
Age-standardised relative survival for lung cancer patients by stage: Diagnostic period: 1994-1999, 2000-2003, 2004-2007

	Age standardised relative survival & 95% confidence intervals						
	Period	1-year	95%CI		5-year	95%CI	
Stage I	1994-99	46.5%	(49.1%,	43.8%)	20.8%	(23.2%,	18.5%)
	2000-03	56.6%	(59.9%,	53.1%)	26.6%	(29.9%,	23.4%)
	2004-07	64.7%	(67.9%,	61.3%)	34.1%	(38.1%,	30.2%)
Stage II	1994-99	37.0%	(40.5%,	33.5%)	11.7%	(14.3%,	9.4%)
	2000-03	43.9%	(48.7%,	39.0%)	14.8%	(18.6%,	11.4%)
	2004-07	54.1%	(58.9%,	49.0%)	25.8%	(31.2%,	20.7%)
Stage III	1994-99	22.8%	(24.8%,	20.8%)	5.3%	(6.6%,	4.2%)
	2000-03	26.6%	(28.9%,	24.4%)	5.8%	(7.1%,	4.6%)
	2004-07	30.7%	(32.9%,	28.6%)	8.2%	(9.7%,	6.8%)
Stage IV	1994-99	9.4%	(10.7%,	8.2%)	2.6%	(3.4%,	2.0%)
	2000-03	9.3%	(10.6%,	8.1%)	1.9%	(2.6%,	1.3%)
	2004-07	14.5%	(15.9%,	13.2%)	3.3%	(4.2%,	2.6%)

Relative survival was calculated at one year and five years post diagnosis by stage of disease (Table 17).

The proportion surviving longer than 1 and 5 years decreased with each increment in stage.

In the most recent period 2004-2007, relative survival at 1 year was 65% for cases with stage I tumours compared to 31% and 15% for cases with stage III and IV tumours respectively.

In the period 2004-2007 relative survival at five years was only 8% and 3% for cases with stage III and IV tumours respectively, compared to 34% and 26% for those with stage I and stage II respectively

Table 18
Age-standardised relative survival for lung cancer patients by smoking status: Diagnostic periods: 1994-1999, 2000-2003, 2004-2007

	Age standardised relative survival & 95% confidence intervals						
	Period	1-year	95%CI		5-year	95%CI	
Non smoker	1994-99	25.8%	(22.7%,	29.0%)	11.9%	(9.6%,	14.5%)
	2000-03	30.3%	(26.6%,	34.0%)	10.3%	(8.0%,	13.1%)
	2004-07	36.4%	(32.5%,	40.4%)	14.8%	(11.6%,	18.4%)
Ex smoker	1994-99	27.3%	(25.3%,	29.3%)	9.9%	(8.5%,	11.4%)
	2000-03	26.2%	(24.1%,	28.5%)	9.0%	(7.6%,	10.6%)
	2004-07	31.0%	(28.8%,	33.1%)	12.5%	(10.8%,	14.4%)
Current smoker	1994-99	22.9%	(21.7%,	24.1%)	7.2%	(6.4%,	7.9%)
	2000-03	24.9%	(23.4%,	26.5%)	8.3%	(7.3%,	9.4%)
	2004-07	29.9%	(28.3%,	31.5%)	10.1%	(9.0%,	11.4%)
Unknown	1994-99	18.0%	(15.7%,	20.4%)	6.3%	(4.8%,	8.0%)
	2000-03	21.2%	(18.4%,	24.1%)	8.2%	(6.4%,	10.4%)
	2004-07	24.4%	(21.5%,	27.3%)	10.3%	(8.0%,	12.9%)

Relative survival was calculated at one year and five years post diagnosis by smoking status (Table 18).

In the most recent period 2004-2007, relative survival at 1 year was 36% in non smokers compared to 30% in current smokers.

At five years, relative survival was 15% in non smokers compared to 10% in current smokers.

Table 19
Age-standardised observed survival for lung cancer patients by deprivation* quintiles: Diagnostic period: 1994-1999, 2000-2003, 2004-2007

Deprivation	Observed survival & 95% confidence intervals						
	Period	1-year	95%CI		5-year	95%CI	
1 Least	1994-99	24.30%	(22.0%,	26.6%)	8.30%	(7.0%,	9.9%)
	2000-03	27.00%	(24.4%,	29.8%)	9.50%	(7.8%,	11.3%)
	2004-07	31.40%	(28.7%,	34.1%)	11.20%	(9.2%,	13.3%)
2	1994-99	24.60%	(22.0%,	27.4%)	6.80%	(5.3%,	8.5%)
	2000-03	25.10%	(22.0%,	28.3%)	7.00%	(5.3%,	9.0%)
	2004-07	31.90%	(28.7%,	35.3%)	10.20%	(8.0%,	12.8%)
3	1994-99	25.50%	(22.8%,	28.3%)	7.50%	(6.0%,	9.3%)
	2000-03	24.90%	(21.8%,	28.1%)	7.70%	(5.9%,	9.8%)
	2004-07	25.90%	(22.7%,	29.2%)	8.20%	(6.1%,	10.6%)
4	1994-99	22.00%	(19.9%,	24.2%)	7.20%	(5.9%,	8.7%)
	2000-03	24.90%	(22.2%,	27.6%)	8.30%	(6.7%,	10.1%)
	2004-07	28.60%	(25.9%,	31.3%)	10.10%	(8.2%,	12.3%)
5 Most	1994-99	21.60%	(20.3%,	23.1%)	6.60%	(5.8%,	7.4%)
	2000-03	23.40%	(21.7%,	25.2%)	6.80%	(5.8%,	7.9%)
	2004-07	28.70%	(27.0%,	30.5%)	9.40%	(8.2%,	10.7%)

As life tables for Ireland are not available for socio-economic status, *observed survival* (rather than *relative survival*) is presented for one year and five years post-diagnosis by quintiles of deprivation score (Table 19).

Survival decreased consistently with increasing deprivation at 1-year and 5-years post diagnosis. For example, in the most recent period 2004-2007, 1-year survival in the most deprived quintile (29%) was significantly lower than that of the least deprived quintile (31%).

Similarly, 5-year survival in the most deprived quintile (9%) was significantly lower than that of the least deprived quintile (11%).

5.2 Factors associated with observed survival

Table 20
Factors associated with survival in patients with lung cancer: Diagnostic period: 1994-1999, 2000-2003, 2004-2007. Cox proportional hazards regression model: *Observed survival*

Variable	Category	cases	alive^ %	Hazard Ratio*	95% CI	
Age‡	15-44	432	29%	1.00		
	45-54	1,675	14%	**1.50**	1.33	1.70
	55-64	4,459	12%	**1.69**	1.50	1.90
	65-74	7,785	8%	**2.06**	1.83	2.31
	75+	7,143	4%	**2.73**	2.43	3.06
Sex	Male	13,377	7%	1.00		
	Female	8,117	11%	**0.88**	0.85	0.90
Stage	I	3,087	22%	1.00		
	II	1,561	14%	**1.40**	1.31	1.49
	III	5,059	6%	**2.03**	1.93	2.13
	IV	7,124	3%	**3.07**	2.92	3.22
	unknown	4,663	8%	**1.67**	1.59	1.76
Morphology	Squamous	5,950	10%	1.00		
	Adenocarcinoma	3,761	12%	0.96	0.92	1.00
	SCLC	3,011	5%	**1.21**	1.15	1.26
	Large undiff	616	8%	**1.21**	1.11	1.32
	other/unknown	8,156	7%	1.04	0.99	1.09
Diagnosis	Microscopic	16,529	10%	1.00		
	Clinical	4,965	4%	1.00	0.95	1.05
Smoking	Non smoker	1,985	11%	1.00		
	Ex smoker	5,443	10%	**1.13**	1.07	1.20
	Current smoker	11,335	8%	**1.20**	1.14	1.26
	Unknown	2,731	7%	**1.23**	1.15	1.31
Treatment	None	9,132	4%	1.00		
	Treated†	12,362	12%	**0.44**	0.43	0.46
HSE area of residence	DNML	6,310	9%	1.00		
	DNNE	5,015	9%	0.99	0.95	1.03
	South	5,278	7%	**1.06**	1.02	1.10
	West	4,891	9%	**0.90**	0.87	0.94
Period of diagnosis	1994-1999	8,711	5%	1.00		
	2000-2003	6,110	7%	**0.94**	0.91	0.98
	2004-2007	6,673	15%	**0.83**	0.80	0.86
Deprivation	1 Least	3,561	10%	1.00		
	2	2,444	8%	1.01	0.95	1.06
	3	2,382	8%	0.99	0.93	1.04
	4	3,470	8%	1.02	0.97	1.07
	5 Most	8,071	8%	**1.09**	1.04	1.13
	Unknown	1,566	10%	1.00	0.94	1.06
	Total	**21,494**	**8%**			

Hazard ratios in bold are significantly different from baseline (1.0)
^ Alive at censoring date: 31/12/2008 (end of follow-up)
‡Model was stratified by age group
*HR was adjusted for all other variables in the model
†Cases received some form of tumour directed treatment
(surgery, chemo, radiotherapy or combinations thereof)

Survival analysis was performed on cases accrued over three diagnostic periods 1994-99, 2000-03 and 2004-07. Cases were followed up until date of death or censoring date.[i] A multivariate model is presented in Table 20.

Hazard ratios (HR) greater than 1.0 indicate relatively shorter survival. Conversely, HR's less than 1.0 indicate longer survival relative to the baseline level of a variable (1.0)

As might be expected, survival time decreased with increasing age. At the end of follow-up, only 4% of cases in the 75 year+ age category were alive compared to 29% in the 15-44 year age category.

Female survival was greater than males. By the end of follow-up, 11% of females were alive compared to 7% of males.

Higher stage of disease at diagnosis was associated with reduced survival time. By the end of follow-up, only 3% of cases with stage IV disease were alive compared to 22% of stage I cases.

Small cell tumours were associated with shorter survival time compared to squamous cell and adenocarcinoma tumour types. By the end of follow-up, only 5% of small cell cases were alive compared to 10% of squamous cell cases and 12% of adenocarcinoma cases.

Cases with clinical verification of tumour had shorter survival time relative to cases with microscopic verification of tumour. By the end of follow-up, only 4% of clinically verified cases were alive compared to 10% of cases who had microscopic verification.

A history of smoking was associated with shorter survival time. At the end of follow-up, 11% of non smokers were alive compared to 10% of ex smokers, 8% of current smokers and 7% of cases with unknown smoking status.

Cases who received no treatment showed significantly poorer survival. By the end of follow-up, only 4% of these cases were alive compared to 12% of cases who received any kind of tumour directed treatment.

[i] Cases were followed up until 31/12/2008 (censoring date)

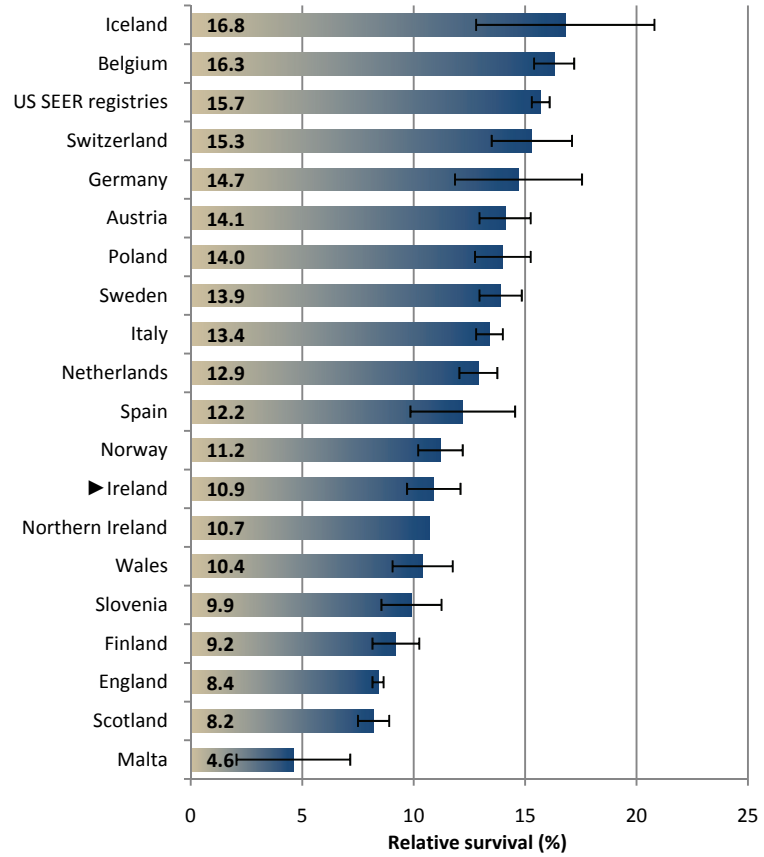
Cases originating in HSE South showed poorer survival relative to cases from DNML. By the end of follow-up, 7% of cases in HSE South were alive compared to 9% in DNML. Conversely, cases originating in HSE West showed better survival times relative to cases in DNML (HR=0.90, 95%CI 0.87, 0.94).

Belonging to the most socially deprived quintiles was associated with shorter survival time. By censoring date, 8% of such cases were alive compared to 10% in the most affluent quintile.

There was a significant improvement in survival over time (HR=0.83, 95%CI 0.80, 0.86). By the end of follow-up, 5% of cases diagnosed during 1994-1999 were alive compared to 7% of cases diagnosed in 2000-2003 and 15% of cases diagnosed in 2004-2007.

5.3 International comparison of relative survival

Figure 14
Age adjusted 5-year relative survival of lung cancer: Diagnosis period 2000-2002



(Eurocare-4. Verdecchia A, et al., 2007) [13]

A comparison of 5-year relative survival for the years 2000-2002 is presented in Figure 14 for lung cancer in males and females combined.[13]

5-year survival for cases in Ireland (RoI) was similar to that of the Eurocare average (10.9%).

Relative survival in Ireland was marginally higher relative to our nearest neighbours England (8.4%), Scotland (8.2%) and Wales (10.4%) and Northern Ireland (10.7%). However, it was apparent that 5-year relative survival in Ireland was substantially poorer compared to other European countries with national cancer registries such as Germany (14.7%), Poland (14.0%), Sweden (13.9%) and the Netherlands (12.9%).

Pooled 5-year survival derived from 13 SEER registries in the United States was 15.7% which was significantly higher than 5-year survival for similar cases in Ireland (10.7%) and the majority of European countries.

6. MORTALITY

Lung cancer was the leading cause of male cancer death in Ireland during 1994-2007 and the second leading cause of death among women behind breast cancer, making up a quarter of all male and approximately one sixth of all female cancer deaths.

Table 21
Incidence of lung cancer deaths by gender: 1994-2007

	MORTALITY			
	MALE		FEMALE	
YEAR	Cases	EASMR	Cases	EASMR
1994	1,031	68.0	519	27.7
1995	1,035	66.9	539	27.9
1996	960	61.7	507	25.4
1997	889	56.7	497	24.7
1998	979	60.9	549	27.7
1999	916	56.5	532	25.8
2000	981	59.4	587	28.7
2001	933	56.1	545	25.4
2002	922	53.9	542	25.5
2003	980	55.8	594	27.2
2004	984	54.9	625	28.4
2005	934	50.3	653	28.7
2006	964	50.9	659	28.6
2007	1,020	52.6	648	27.7
Total	**13,528**		**7,996**	
APC	**-0.1%**	**-2.0%**	**2.1%**	**0.5%**
95%CI(APC)	(-0.8, 0.6%)	(-2.5, -1.4%)	(1.4, 2.8%)	(-0.2, 1.2%)

6.1 Mortality trends

Mortality data for the period 1994-2007 are presented in Table 21.

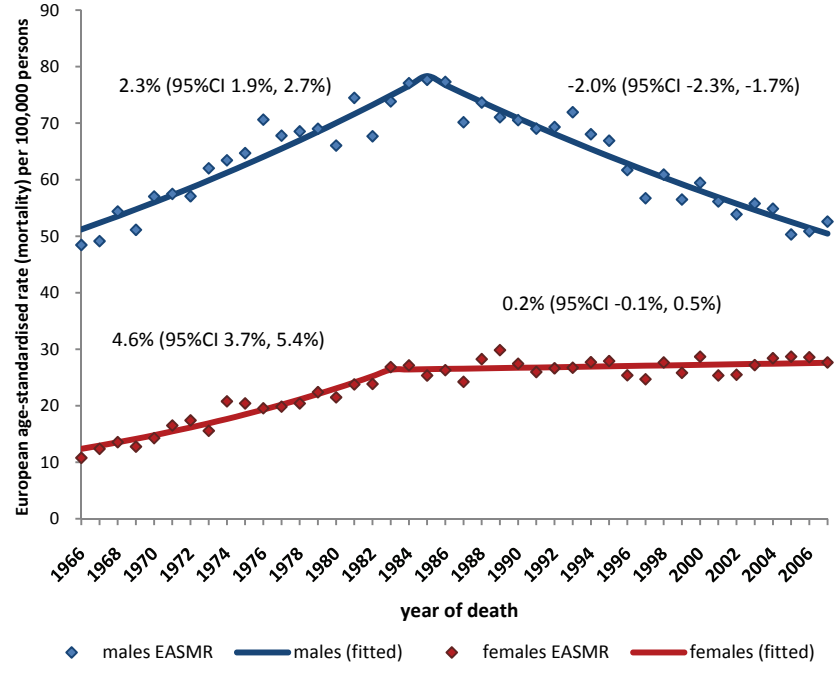
There were on average 966 male deaths and 571 female deaths annually between 1994 and 2007.

For males, the European age standardised mortality rate (EASMR) declined from 68/100,000 in 1994 to 53/100,000 in 2007, a significant annual reduction in deaths of 2% per year.

For females, the EASMR ranged from 25/100,000 in 1996 to 28/100,000 in 2007, an annual increase of 0.5% between 1994 and 2007.

6.2 Long term mortality trend

Figure 15
Long term trends in lung cancer mortality rates in the Republic of Ireland: 1966-2007
Observed and fitted EASMR and annual percentage change (APC)



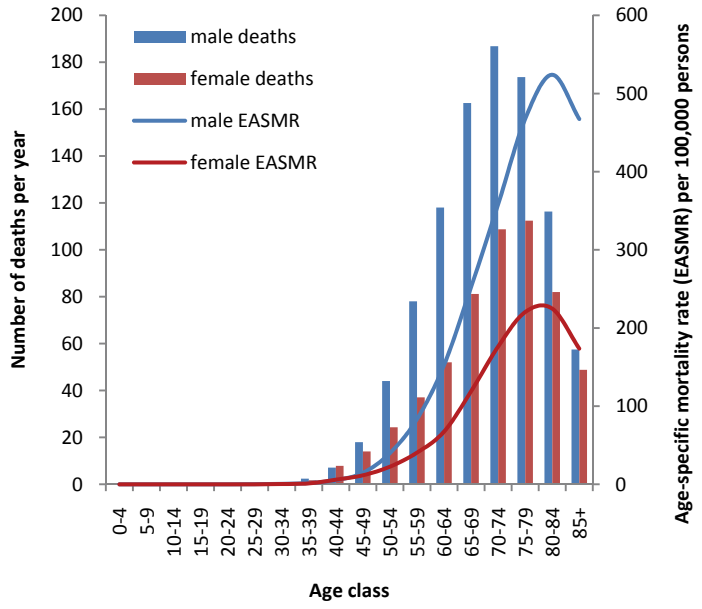
European age standardised mortality rates (EASMR) for the period 1966-2007 are presented in Figure 15. [21]

A significant 2.3% annual percentage increase in mortality was observed from 1966 to 1984 for males. Thereafter, there was a significant 2% annual decrease in mortality from 1985 to 2007.

For females, there was a significant 4.6% annual percentage increase in mortality from 1966 to 1983. Thereafter, from 1983 to 2007, the annual percentage change has been close to zero, at 0.2% per year. Therefore, the reduction in male mortality observed since the mid 1980's in Ireland (RoI) has not materialised for females, which is of some concern.

6.3 Age distribution of mortality

Figure 16
Number of deaths per year from lung cancer by gender and age with age-specific mortality rate (EASMR) per 100,000 persons: period 1994-2007



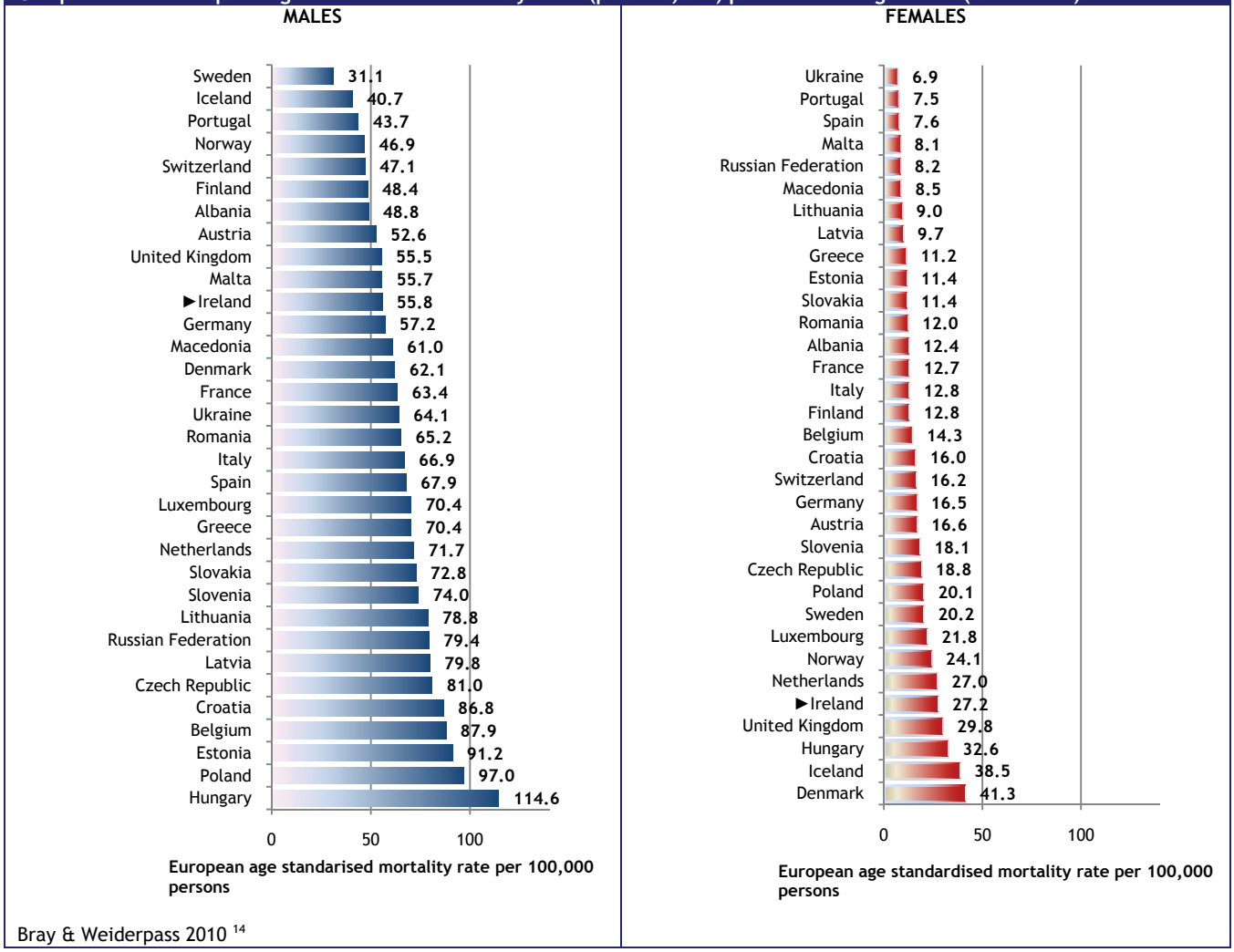
The number of lung cancer deaths per year by age group over the period 1994-2007 is presented in Figure 16.

The number of deaths per year peaked in the 70-74 year age category for males and the 75-79 year age category for females with 187 and 112 deaths per year respectively. These totals represented 19% of both male and female lung cancer deaths.

Age specific mortality rates climbed steadily to a maximum of 524/100,000 in males and 225/100,000 in females in the 80-84 year age group.

6.4 International comparisons of mortality

Figure 17
Comparisons of European age standardised mortality rates (per 100,000) persons for lung cancer (*circa* 2003)



Bray & Weiderpass 2010 [14]

An international comparison of mortality rates for Europe is presented for men and women in Figure 17. [14]

For males, there was a general tendency for the Scandinavian countries to have lower mortality rates, whereas eastern and southern European counties tended to have higher mortality rates. Ireland (RoI) ranked 11th (from lowest to highest mortality rate) of 33 countries surveyed with a standardised mortality rate of 56/100,000 behind Sweden (1st, 31/100,000), Iceland (2nd, 41/100,000), Portugal (3rd, 44/100,000), Norway (4th, 47/100,000), Switzerland (5th, 47/100,000) and Finland (6th, 48/100,000). Ireland's mortality rate was similar to that of the UK (55/100,000). The three countries with the highest recorded male mortality rates up to 2007 were: Hungary (115/100,000), Poland (97/100,000) and Estonia (91/100,000).

For females, the mortality rate was relatively high in comparison with other European countries (27/100,000). Ireland ranked 5th highest out of 33 countries surveyed. Ireland's mortality rate was similar to that of the UK (30/100,000). The countries with higher female mortality rates than Ireland (RoI) were: Denmark (1st, 41/100,000), Iceland (2nd, 39/100,000), Hungary (3rd, 33/100,000) and UK (4th, 30/100,000).

APPENDIX I

Lung cancer: Data sources and dataset for the Republic of Ireland

Since 1st January 1994, all newly diagnosed cancers in Ireland (RoI) have been registered by the NCR. The process is highly effective, with over 96% of cancers being identified.[16] Prior to 1994, there was no national cancer registration and therefore no reliable information on cancer incidence.

The dataset used in this report consisted of all primary invasive lung cancers (ICD-10 code C34) registered by the National Cancer Registry (NCR) with a date of diagnosis from 1 January 1994 to 31 December 2008.

For analysis of incidence and treatment patterns, the dataset was divided into three diagnostic periods: 1996-1999, 2000-2003 and 2004-2008.

For survival analysis, the dataset was divided into three separate diagnostic periods; 1994-1999, 2000-2003, 2004-2007. Survival time was censored at 31 December 2008 to ensure that all cases had follow-up for at least one year. Only first primary invasive tumours of the lung were included in the dataset.

Lung cancers were included in survival analyses only if they were not preceded by another cancer. Following convention, cases where the sole evidence of cancer was diagnosed from a death certificate or at autopsy were excluded from survival analysis.

Table 22
Cases of lung cancer 1994-2008

All registered lung tumours (1994-2008)	25,848
Exclusions before incidence & treatment analysis‡	180
Final incidence (1994-2008)	25,668
Further exclusions before survival analysis*	4,174
Final survival dataset 1994-2007	21,494

‡In-situ and tumours of uncertain behaviour

* Autopsy-only cases & DCO cases & lung cancers preceded by another malignancy

APPENDIX II

Variable definitions and methods of analysis

Demographic variables

Age

This was the age at diagnosis; the difference between date of birth and date of diagnosis. This variable was available for all patients. The EUROCARE convention for age categories in lung cancer was used: 15-44 years, 45-54 years, 55-64 years, 65-74 years and 75+ years. [18]

Smoking status

Lung cancer cases were classified as 'non smokers' if they had never smoked, 'ex-smokers' if they had ever smoked but had not smoked for a year prior to diagnosis. Current smokers were classified as 'smokers'.

Marital status

Lung cancer cases were classified as 'ever married' if they were married, widowed, divorced or separated and 'never married' if they had never been married.

Date of incidence

The NCR subscribes to the European network of cancer registries (ENCR) guidance for this data item.[24] Date of incidence was taken to be the date of histological confirmation (or date of clinical diagnosis if there was no histological confirmation).

Date of death

For survival calculations, the last day of follow-up was taken to be 31 December 2008 (censoring date). The date of death was taken to be that recorded on the death certificate if available, otherwise the date of death was that observed in the case hospital notes.

HSE area of residence

All patients in the dataset were allocated to a HSE administrative area according to their main address at the time of diagnosis: Dublin Mid Leinster (DNML), Dublin North East (DNNE), West (W) and South (S).

Deprivation

Quintiles of deprivation were derived from data in the 1996 census at electoral division (ED) level, and applied to individual patients by linkage of address.[17] The score consisted of 1 (least deprived) through to 5 (most deprived).

Tumour characteristics

TNM

TNM category of tumour was described in the medical record. Where a pathological T (primary tumour), N (regional nodes) or M (distant metastasis) category was given, this was used; otherwise the clinical diagnosis was used. Version 5 of the TNM AJCC manual was used for cases after 2000.[19] Cases in the earlier period (1994-1999) were staged using version 4 of the manual. However, there were no changes in the guidelines for lung cancer between version 4 and version 5. Cases where the metastasis was coded as 'MX' (unknown) were re-coded to 'M0' (i.e. assumed that metastasis had not occurred).

Table 23
Stage grouping: Lung Cancer

	T	N	M
Stage 0 (excluded)	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
Stage IIA	T1	N1	M0
Stage IIB	T2	N1	M0
	T3	N0	M0
Stage IIIA	T1, T2	N2	M0
	T3	N1, N2	M0
Stage IIIB	Any T	N3	M0
	T4	Any N	M0
Stage IV	Any T	Any N	M1

Summary stage

Summary stage was derived by algorithm from TNM categories and collapsed from the published categories of stage IA, IB, IIA, IIB, IIIA, IIIB, IV to the simpler breakdown of stage I, II, III and IV.[19]

Grade

Tumour grade was transcribed from pathology reports and listed as 1 (well differentiated), 2 (moderately differentiated), 3 (poorly differentiated), 4 (undifferentiated) or unknown.

Morphology

Three broad categories of tumour histology were derived as follows: Non Small Cell Lung cancer (NSCLC) and Small Cell Lung Cancer (SCLC) and others/unknown/NOS. For analysis, a more detailed breakdown of morphology designations was used according to Devesa et al (2005):[10] (1) squamous cell carcinoma (ICD-0 codes 8050-8076); (2) adenocarcinoma (8140, 8211, 8230-8231, 8250-8260, 8323, 8480-8490, 8550-8560, 8570-8572); (3) small cell carcinoma (8040-8045); (4) large/undifferentiated cell carcinoma (8012-8031, 8310); (5) other specified carcinoma (8082, 8120-8123, 8141-8143, 8190, 8200-8201, 8240-8241, 8244-8246, 8290, 8320, 8430, 8470- 8471, 8500, 8510, 8562); (6) unspecified carcinoma (8010-8011, 8032-8034); (7) other specified morphology (8580, 8693, 8720, 8730, 8800-8811, 8830, 8840-8920, 8933, 8940, 8963, 8972, 8980-8981, 8990-8991, 9040-9044, 9050-9053, 9064, 9070, 9080, 9085, 9110, 9120-9134, 9140, 9150, 9220, 9240, 9251, 9260, 9364, 9473, 9503, 9540-9581); and (8) unspecified morphology (8000-8004).

Basis of diagnosis

Cases were classified as *microscopically verified* if the tumour had been confirmed by histological or cytological methods. Cases were classified as *clinically verified* if diagnosed by radiology, ultrasound or by autopsy.

Treatment definitions

The focus was on *tumour-directed treatment*. This was interpreted as treatment aimed at removing, reducing, destroying or preventing further growth of tumour. No distinction was made between 'curative' and 'palliative' treatment. For the purposes of this report, five treatment scenarios (a-e) were defined as follows:

a) *Surgery*

A case was considered to have undergone *surgery* if at least one tumour resection was recorded. Endoscopic procedures were excluded.

b) *Chemotherapy*

A case was considered to have undergone *chemotherapy* if at least one chemotherapeutic agent was administered (including conventional, hormonal or biological agents).

c) *Radiotherapy*

A case was considered to have undergone *radiotherapy* if least one radiotherapy session was recorded.

d) *Treated*

A case was considered to have been *treated* if at least one treatment was recorded for that case (i.e. treatment as defined in a-c above).

e) *Not treated*

A case was considered as *not treated* if there was no treatment recorded for that case as defined in a-c above. However, many cases had other types of medical and surgical interventions not covered in a-c above.

Statistical methods

Patient, tumour and treatment variables were tabulated across three diagnostic periods: 1996-1999, 2000-2003, and 2004-2008. European age standardised rates (EASR) and annual percentage change (APC) of incidence and mortality over time were calculated using the Joinpoint statistical program.[15] Joinpoint regression was also used to test for *linear trend* over time for select variables in sections 3 (incidence) and 4 (treatment).

Standardised rate ratios (SRR) were calculated for the period 2004-2008. The EASIR is the index of cases in a given population weighted by the European age structure. Rather than consider the most recent year (2008), the numbers of cases occurring during 2004-2008 in Ireland were summed and divided by the sum of persons at risk in the RoI (summed for 2004-2008) using intercensal population estimates.[25] The EASIR for 2004-2008 was calculated for each county in a similar fashion. The ratio of county EASIR over country EASIR gives the standardised rate ratio (SRR). The 95% CI of the SRR ratio was also calculated.[23] A county was considered to have a significantly higher (or lower) incidence of cases than the national average if the 95% confidence interval of the SRR did not include unity.

Odds ratios (OR) were calculated using logistic regression to identify factors associated with 'receipt of treatment'. However, as treatment was common, the odds ratio overestimated the risk of treatment when it was more than 1 or underestimated the risk when it was less than 1.[28] To overcome this problem, odds ratio were converted to the risk ratio (RR) according to the formula $RR=[OR]/[(1-P_0)+(OR \times P_0)]$, where P_0 in this instance was the proportion untreated at each level of a categorical variable.[28] Looking at tables of adjusted RR's leads to the same conclusions as adjusted OR's; except that the RR can be conveniently interpreted as the proportion who received treatment relative to the baseline level of a variable.

Survival data is presented as *relative survival* (RS); the ratio of observed survival among a group of cases to the expected survival among the general population of the same age, sex and country. Relative survival was calculated using the '*strs*' command in STATA 11.0.[20] RS was derived for each level of the variables: age, sex, stage, morphology, smoking status, diagnostic period, treatment receipt, method of diagnosis and HSE area. As the life tables (for RoI) used to calculate relative survival do not take into account of deprivation quintiles, *observed survival* for each quintile of the deprivation score was calculated using the Kaplan-Meier method. Factors associated with observed survival were determined using a Cox proportional hazards regression model.

CONTRIBUTORS

The information in this report is based on the data held by the National Cancer Registry, and has been collected, processed and analysed since 1994 by dedicated and skilled Registry staff. The registry, in turn, is dependent on the help and support of hospital staff throughout the country. The CSO and General Register Office provided the death certificate data. Most of the data analysis was carried out by the writing group; Dr Paul M Walsh extracted the lung cancer dataset and provided the *relative survival* figures. Mr Neil McCluskey provided map graphics in section 3 (variation in incidence at county level).
The writing group for this report was: Dr Joe McDevitt, Dr Linda Sharp and Dr Harry Comber.

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