National Cancer Registry Ireland **Cancer Trends**

Hodgkin's lymphoma

Case numbers and histological types

An average of 101 cases of Hodgkin's lymphoma (HL) was diagnosed per year in Ireland between 1994 and 2011, equating to an incidence rate of 2.5 cases per 100,000 per year (Table 1). Representing 16% of all lymphomas (626 cases in total, 525 of which were non-Hodgkin's lymphoma), or just 0.7% of all invasive cancers combined, it ranks as the 23rd most common invasive cancer overall. Incidence in males was slightly higher than in females with 20% more males than females diagnosed.

The WHO has classified HL into 2 main types; classical HL (of which there are 4 subtypes) and nodular lymphocyte predominant HL.[1] Almost all cases diagnosed between 1994 and 2011 were microscopically confirmed although almost 20% of cases were of unspecified subtype (Table 1). Most cases were nodular sclerosis subtypes, followed by mixed cellularity HL, and there was some difference in the relative proportion of subtypes between males and females. Only 3% of all cases diagnosed were nodular lymphocyte predominant.

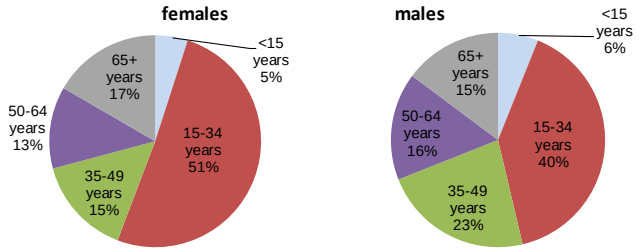
Table 1. Annual average number and percentage composition of histological subtypes of Hodgkin's lymphoma, 1994–2011

	females	males	total
annual average	46	55	101
incidence rate (cases per 100,000 per year)	2.2	2.7	2.5
% all lymphomas	16%	16%	16%
% all cancers	0.6%	0.7%	0.7%
subtypes:			
classical HL: nodular sclerosis	64%	50%	56%
classical HL: mixed cellularity	13%	18%	16%
classical HL: lymphocyte-rich	3%	5%	4%
classical HL: lymphocyte-depletion	2%	2%	2%
nodular lymphocyte predominant	1%	5%	3%
unspecified	18%	20%	19%

Age profile

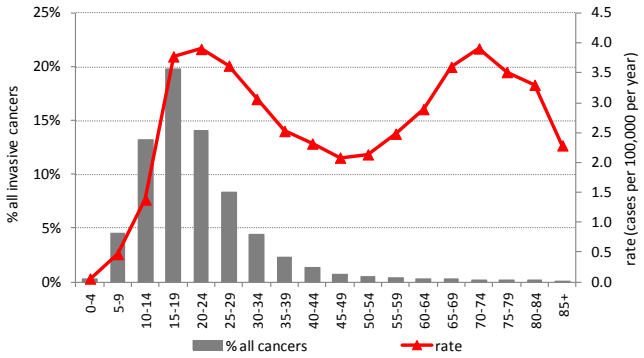
Approximately half of all HL patients were under 35 years when diagnosed, with males and females having a similar age distribution (Figure 1). Only 16% of all HL patients were aged 65 or older.

Figure 1. Age distribution of Hodgkin's lymphoma 1994–2011



Typically HL has a bi-modal age-specific incidence pattern[2], and this was observed in Irish patients, with a peak in incidence in patients aged 15-34 and another, later peak in patients aged 65-84 (Figure 2). Although incidence rates in these 2 groups were similar, it is important to note that HL represented a much greater proportion of all cancers in the younger patients compared to the older group. HL ranked as the 4th most common cancer in patients aged 15-34 (after testicular cancer, melanoma and breast cancer) and represented 9% of all cancers in this age group (or almost 20% of all cancers in 15-19 year old patients alone). However HL represented only 0.2% of all cancers in patients aged over 65.

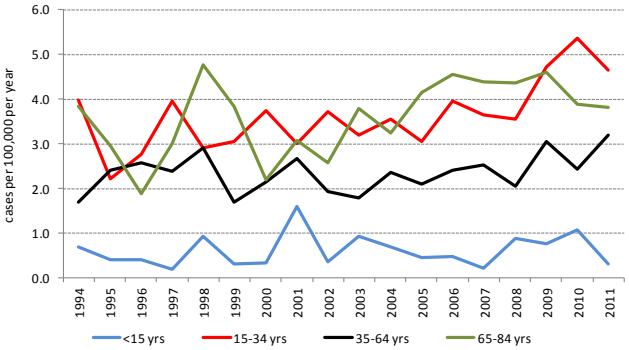
Figure 2. Incidence of Hodgkin's lymphoma by age, 1994–2011



Time trends in incidence

Age-standardised incidence rates for HL (all ages) increased from 2.3 to 3.0 cases per 100,000 per year between 1994 and 2011, an overall annual percentage change (APC) of 1.9% (Figure 3). Rates in children aged under 15 remained more or less constant and the greatest increase in incidence was observed in 15-34 year old patients where there was an APC of 2.6% between 1994 and 2011. There was very little change in the relative composition of HL subtypes over the 18 year period.

Figure 3. Trends in incidence of Hodgkin's lymphoma, 1994–2011



Geographical distribution

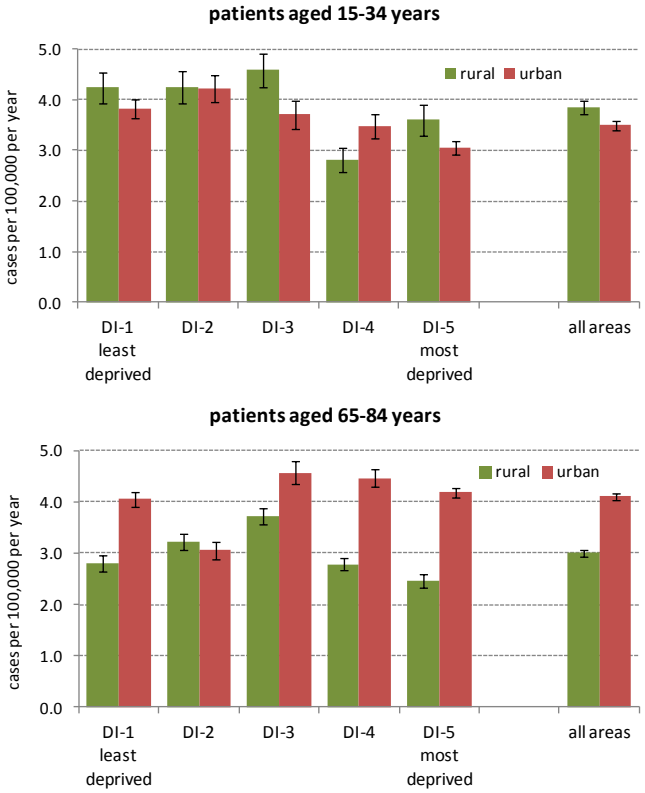
There was little obvious geographic variation in HL incidence in Ireland; rates were highest in the HSE Dublin & Mid-Leinster region and lowest in the HSE West, although regional rates were not statistically significantly different from each other or from national rates (Table 2).

Table 2. Incidence rates (cases per 100,000 per year) by HSE region, Hodgkin's lymphoma, 1994–2011

	rate	95%CI
Dublin & Mid Leinster	2.68	2.46 – 2.90
Dublin & North East	2.35	2.11 – 2.59
South	2.47	2.24 – 2.69
West	2.26	2.04 – 2.49
Ireland overall	2.45	2.34 – 2.56

A positive association between HL incidence and socio-economic status has been frequently reported in the literature, where an elevated risk of HL in young adulthood has been associated with the postponement of common childhood infections.[3] Analysis of HL incidence rates by deprivation index or by urban or rural area of residence in Ireland showed variable results (Figure 3). Although incidence rates in adolescents and young adults (aged 15-34 years) were significantly higher in rural compared to urban areas, the opposite was true for older patients (aged 65-84). Incidence was highest in areas of low to moderate deprivation (deprivation index 1-3 in both urban and rural areas) for young (15-34 year old) patients. However for older patients, highest incidence rates were found for those living in the most deprived urban areas.

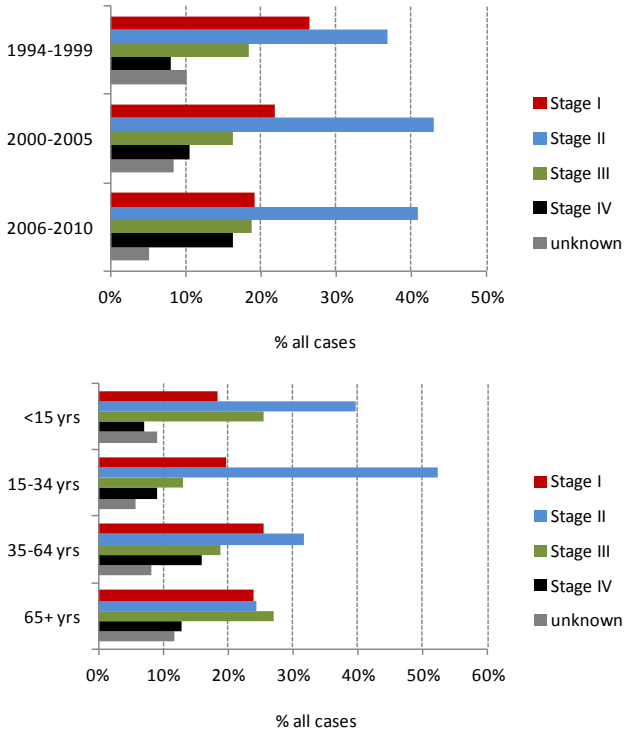
Figure 3. Incidence of Hodgkin's lymphoma and variation with deprivation index (DI)[4] and urban/rural area of residence, 1994–2011 *(rural areas defined by population density <1 person per hectare)*



Stage at diagnosis

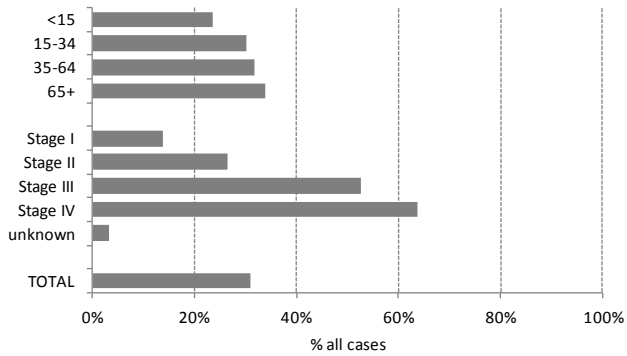
Greatest numbers of patients (40%) were diagnosed with stage II disease; approximately 20% were each diagnosed with stage I and stage III cancer, 12% were stage IV and 8% were of unknown stage, with little change in stage distribution over time (Figure 4). Young patients (aged under 35) were generally diagnosed at an earlier stage than older patients. The proportion of patients with unstaged disease was also highest in those aged over 65 years.

Figure 4. Distribution of Hodgkin's lymphoma stage (a) by time period and (b) by age group, 1994–2010[5]



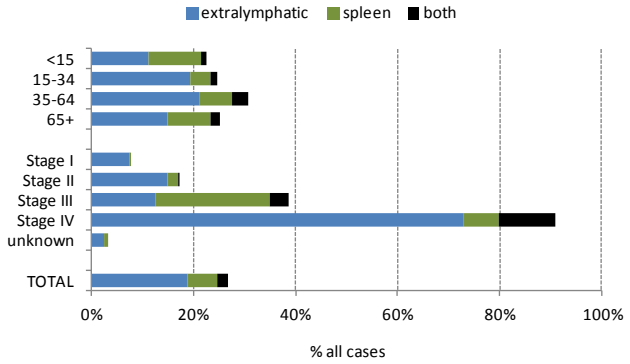
The presence or absence of defined systemic symptoms (weight loss, fever, night sweats) as well as the involvement or not of the spleen and other extralymphatic sites at diagnosis are important elements in staging Hodgkin's lymphoma.[6] One third of all cases presented with systemic symptoms (Figure 5). The proportion of patients with these symptoms varied little according to age but as expected there was a clear increase in the frequency of these symptoms with advancing tumour stage.

Figure 5. Proportion of Hodgkin's lymphoma patients presenting with systemic symptoms[6], by age and stage: 2004–2010[5]



In all, 27% of patients had involvement of either or both the spleen and other extralymphatic organs or sites (Figure 6). As with systemic symptoms, there was little variation with age, and 22% to 31% of patients in each age group presented with these features. Over 70% of patients with stage IV disease had extralymphatic involvement and a further 18% had either spleen involvement only or both extralymphatic and spleen involvement. One fifth of all patients with stage III HL also had disease present in the spleen.

Figure 6. Proportion of Hodgkin's lymphoma patients that had extralymphatic or spleen involvement or both: 2004–2010[5]



Treatment

Chemotherapy is the principal treatment for Hodgkin's lymphoma; 81% of all patients in Ireland had chemotherapy, either alone (48%) or in combination with radiotherapy (22%), surgery (7%) or with both radiotherapy and surgery (4%) (Table 3). In all, 35% of patients had radiotherapy. Surgical treatment is comparatively rare and only 14% of all patients had surgery, either on its own or with other therapies.

Almost one-quarter of all patients aged 65 or over had no tumour directed treatment. However as this group represented just 16% of all cases, the proportion of untreated patients overall was low (8%). Treatment varied little by age, although those aged under 35 were more likely than older patients to have combined chemo- and radio-therapy.

Table 3. Combinations of the main categories of treatment for Hodgkin's lymphoma patients by age group, 1994-2010[5]

	All cases	<35 years	35-64 years	65+ years
chemotherapy only	48%	47%	51%	46%
radiotherapy only	8%	7%	8%	11%
chemo & radio only	22%	29%	19%	7%
surgery & chemo only	7%	7%	9%	6%
surgery & radio only	1%	1%	2%	2%
chemo & radio & surgery	4%	4%	3%	2%
surgery only	2%	2%	2%	3%
no treatment	8%	4%	6%	24%
Total cases	1670	852	555	263

88% of patients with late stage disease had chemotherapy, 67% of whom had no other treatment (Figure 7). Patients with early stage HL were more likely to have combination therapy and although 80% had chemotherapy, half of these also had some other treatment (radiotherapy or surgery). The majority of patients that had no tumour directed therapy were of unknown stage.

Figure 8 shows the variation in treatment over time. Between 1994-1999 and 2006-2010 the percentage of all patients having had chemotherapy, either on its own or in combination with other treatments, increased from 74% to 86%. In contrast the number of patients having radiotherapy decreased from almost half of all patients in 1994-1999 to just 25% in 2006-2010. Approximately two-thirds of all patients having radiotherapy were treated in combination with either chemotherapy or surgery or both. The decline in the proportion of patients having radiotherapy over time was evident in the case of radiotherapy alone as well as in combination with chemotherapy.

Figure 7. Variation in treatment for Hodgkin's lymphoma patients by disease stage, 1994-2010[5]

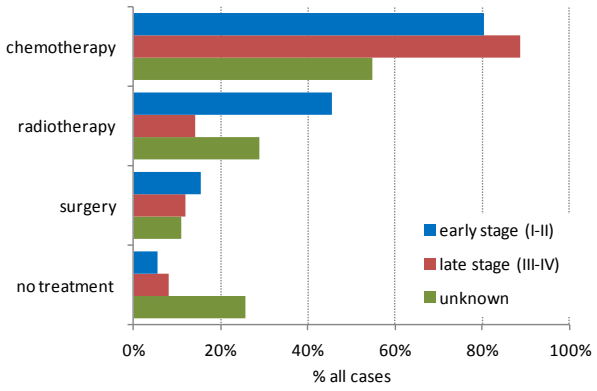
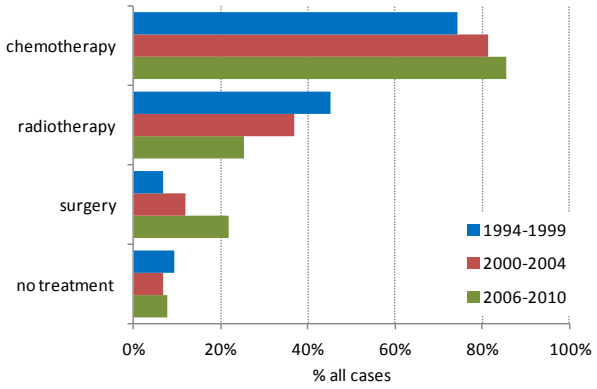


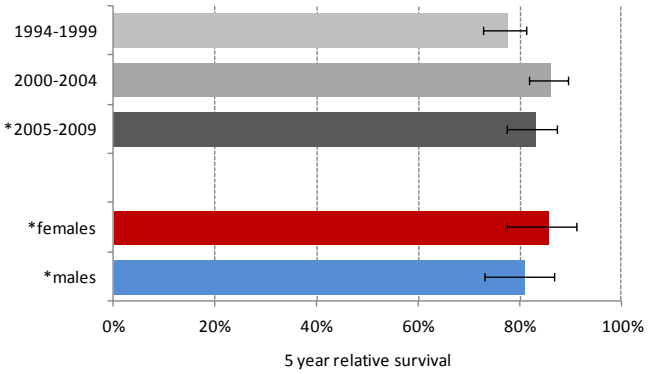
Figure 8. Variation in treatment for Hodgkin's lymphoma patients over time, 1994-2010[5]



Survival[7]

Survival rates for Hodgkin's lymphoma are amongst the highest for all invasive cancers and most recent estimates indicate a 5 year survival of over 80%, with rates for females slightly higher than for males (Figure 9). Between 1994-1999 and 2000-2004 there was a statistically significant improvement in overall relative survival from 77% to 86%. Subsequently survival rates have fallen slightly, to 83%, although this was not statistically significant.

Figure 9. Five year relative survival by time period (with 95% confidence intervals) and sex, Hodgkin's lymphoma, 1994-2009[7]



**females and males RS for 2005-2009 period only*

Long term trends in Irish mortality rates

There has been a pronounced decline in mortality from Hodgkin's lymphoma in recent years with mortality rates falling for both males and females (Figure 10). Mortality rates were highest from the late 1950's and during the 1960's when an average of 51 deaths was recorded per year, with deaths in males outnumbering females by a factor of 2 approximately (Table 4). However in recent years, mortality rates between the sexes have almost equalized and currently fewer than 20 deaths from HL are recorded per year.

Figure 10. Age-standardised mortality rate (world standard population) for Hodgkin's lymphoma in Ireland 1955–2010[8]

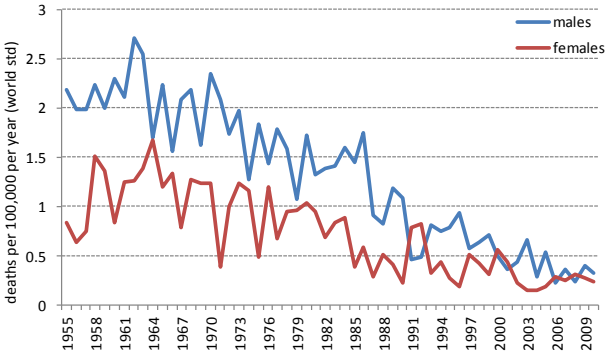


Table 4. Annual average number of deaths from Hodgkin's lymphoma each decade from the 1950's to 2010[8]

	females	males	total
late 1950's	15	32	47
1960's	18	32	51
1970's	16	29	45
1980's	14	25	40
1990's	10	15	25
2000's	9	11	19

International variation in incidence and mortality[9]

Estimates of Irish incidence rates for HL in 2012 were the 5th highest in Europe, after Switzerland, France, Belgium and Portugal (Figure 11). Rates in Ireland were 12% higher than the EU average for males and 19% higher in the case of females. Romania and Hungary were ranked lowest with incidence rates almost 40% lower than the EU average.

Mortality rates in Ireland were similar to the EU average for both males and females (Figure 12). Irish males ranked 9th and females 7th highest in Europe but had similar rates to several other countries, e.g. France, Netherlands and Portugal. The highest mortality rates and the highest mortality/incidence ratios were estimated for Greece and a number of other eastern and south-eastern European countries. Ireland's mortality/incidence ratios for males (0.2) and females (0.1) were similar to the EU average and close to values found in several other European countries.

Figure 11. Incidence of Hodgkin's lymphoma in Europe, 2012[9]

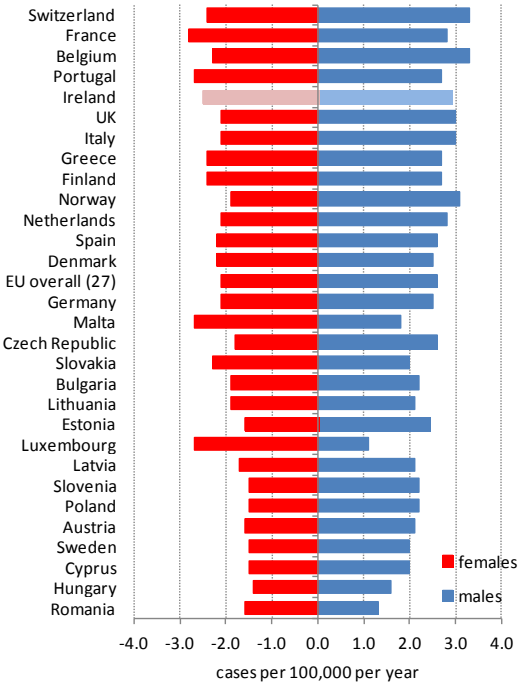
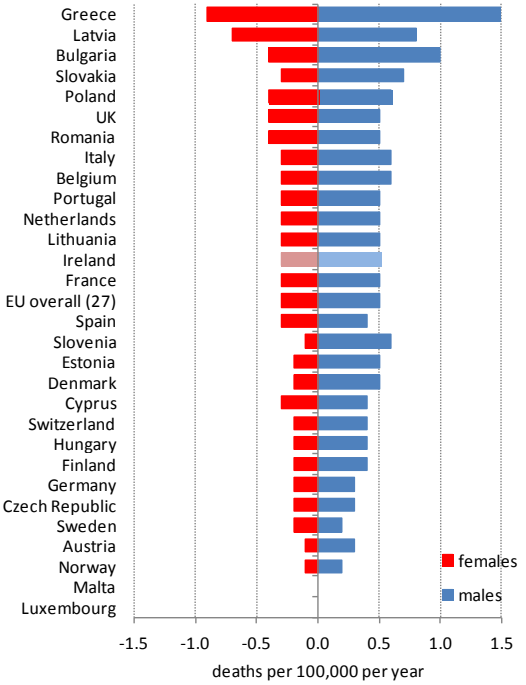


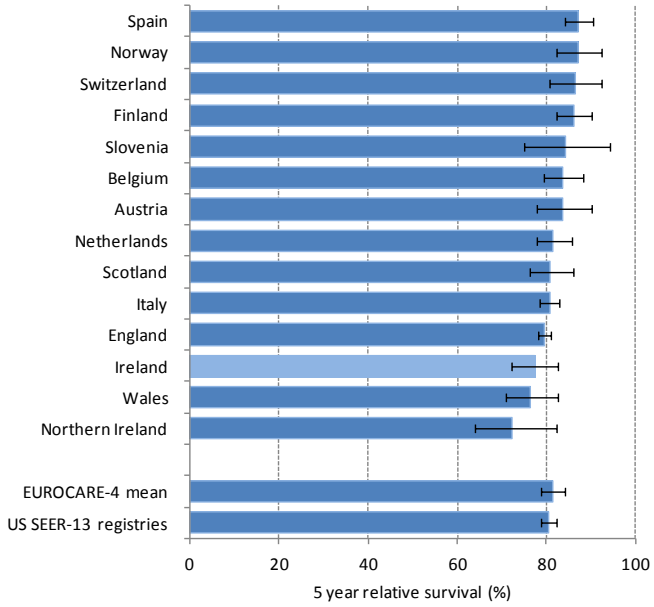
Figure 12. Mortality from Hodgkin's lymphoma in Europe, 2012[9]



International variation in survival[10]

Period survival analysis for 2000-2002 indicated a five year relative survival estimate of 81% for both Europe overall and in the US (Figure 13). Irish estimates, at 77%, rank 12th out of 14 European countries, although variation between countries was low and the only country with a survival rate statistically significantly higher than Ireland was Spain. Survival estimates for Ireland were lower than, but close to, values for England and slightly higher than rates in Wales and Northern Ireland. The highest relative survival rates in Europe were found in Spain, Norway, Switzerland and Finland.

Figure 13. Five year relative survival for Hodgkin's lymphoma (period analysis 2000-2002[10])



References and notes

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