National Cancer Registry Ireland **Cancer Trends**

non-Hodgkin's lymphoma (NHL)

Case numbers and histological types

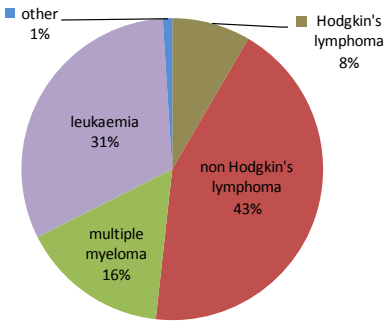
An average of 660 cases of non Hodgkin's lymphoma (NHL) was diagnosed per year in Ireland between 2007 and 2011 (Table 1). Incidence rates were slightly higher in males than in females where NHL was the 5th and 8th most common cancer diagnosed respectively. Overall lifetime risk of diagnosis of NHL was 1 in 83.

Table 1. Annual average number and incidence rate of all non Hodgkin's lymphoma diagnosed in Ireland, 2007-2011

	females	males	total
cases per year	304	356	660
incidence rate	13.0	17.1	14.9
cumulative lifetime risk	1.1%	1.3%	1.2%
% of all cancers	3%	4%	4%
ranking of most common cancers	8th	5th	6th

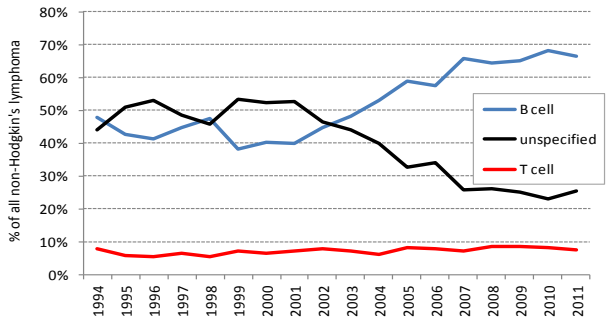
Although NHL comprised just 4% of all cancers overall, it represented 43% of cancers of the blood and lymph system (Figure 1). Hodgkin's lymphoma represented just 8% of these cancers. Leukaemia and multiple myeloma comprised 31% and 16% respectively.

Figure 1. Composition of blood & lymphatic cancers, 2007-2011



NHL represents a diverse group of lymphomas, the classification and coding of which have changed considerably in recent years, a result of major advancements in diagnostic techniques[1]. The proportion of unspecified cancers has fallen from over half of all NHL during the 1990's to approximately 25% in recent years. This is reflected in a corresponding increase in the proportion of B cell tumours (Figure 2).

Figure 2. Variation in the proportions of NHL classified to a specific subtype, 1994-2011



B cell tumours represented approximately two-thirds of all NHL diagnosed between 2007 and 2011, with T cell tumours making up just 8% (Table 2). Although 25% of NHL remained unspecified, only 9% were due of a lack of detailed diagnostic information (ICD-03: M-9590); the other 16% representing tumours where the histological descriptions were detailed but did not fall clearly into one of the specific subgroups listed by the WHO[1] or under ICD-03[2] (ICD-03: M-9591). Large B cell diffuse tumours made up the majority of all NHL (31%) with follicular NHL representing a further 19%. Cutaneous lymphomas represented the bulk of T cell subtypes, although these were comparatively few in number overall.

Table 2. Annual average number of NHL by histological subtype, 2007-2011

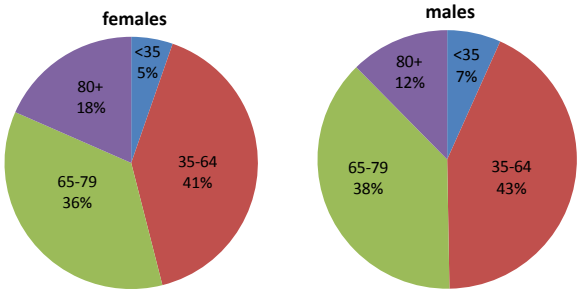
	females	males	total	% all NHL
B cell				
large B cell diffuse	94	112	206	31%
follicular	62	63	126	19%
CLL/SLL*	14	21	35	5%
mantle cell	7	20	27	4%
MALT	16	11	27	4%
Burkitt's lymphoma	4	8	12	2%
other marginal zone	2	1	3	<1%
mediastinal	<1	0	<1	<1%
total B cell	*199*	*237*	*436*	*66%*
T cell				
mycosis fungoides	5	11	16	2%
anaplastic large cell	5	5	10	2%
cutaneous, NOS	4	5	9	1%
peripheral, NOS	4	5	9	1%
angioimmunoblastic	1	2	3	<1%
enteropathy type, intestinal	<1	2	2	<1%
extranodal NK/T nasal type	<1	1	1	<1%
other cutaneous T cell	1	1	2	<1%
total T cell	*20*	*33*	*53*	*8%*
precursor cell, NOS	2	3	6	1%
NHL unclassifiable (M-9591)	52	54	107	16%
lymphoma, NOS (M-9590)	29	29	59	9%
TOTAL NHL	304	356	660	

** B-cell chronic lymphocytic leukaemia /small lymphocytic lymphoma*

Age profile

Unlike Hodgkin's lymphoma, where approximately half of all patients were under 35 when first diagnosed[3], less than 10% of NHL patients were in this age category (Figure 3). The average age at diagnosis was 63 for females and 64 for males. Similar proportions of patients were aged 35-64 and 65-79 and although females had a greater proportion of elderly patients aged over 80, the overall age distributions of males and females were fairly similar.

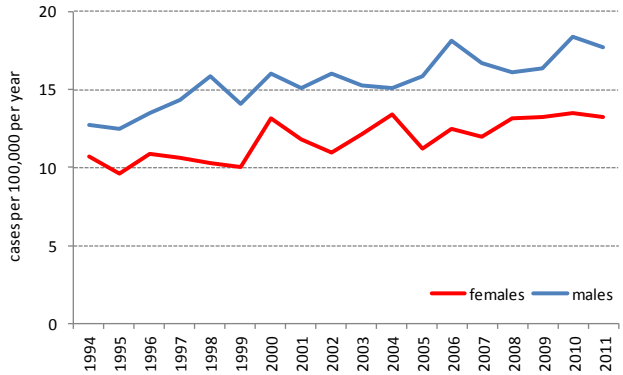
Figure 3. Age distribution of NHL patients, 2007-2011



Time trends in incidence and mortality

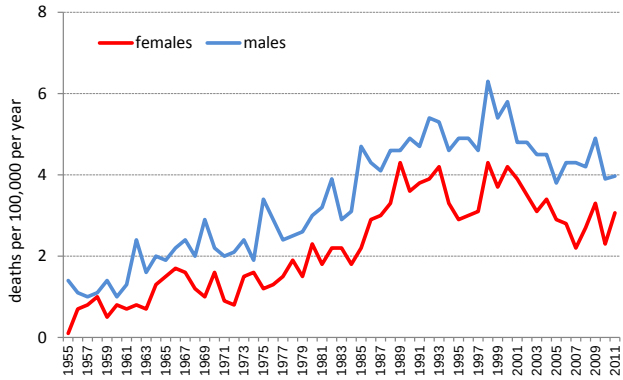
The number of cases of NHL diagnosed per year in Ireland has increased from 381 in 1994 to 721 in 2011, with incidence rates in both sexes have increasing annually by 1.7% in females and 1.8% in males (Figure 4). An increase in NHL incidence has been noted in many countries, with improvements in diagnostic techniques, particularly for extra nodal lymphomas, suggested as an important contributing factor.[4]

Figure 4. Trends in NHL incidence, 1994–2011



Mortality rates for NHL in Ireland increased considerably from the mid 1950's to the late 1990's, likely influenced by more precise diagnostic methods and coding of death certificates (Figure 5). While less than 50 deaths from NHL were recorded during the late 1950's and early 1960's, an average of 253 deaths per year have been recorded in the late 2000's. However mortality rates have declined substantially over the last decade and mortality rates are now equivalent to those observed in the 1980's.

Figure 5. Trends in mortality from non-Hodgkin's lymphoma, 1955–2011 [5, 6]

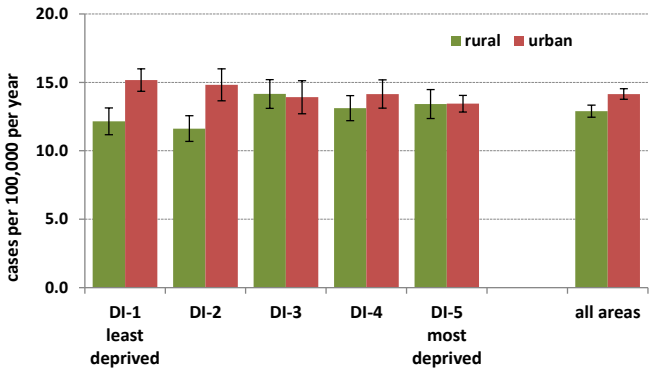


Geographical distribution

Similar to observations made for Hodgkin's lymphoma[3], there was little difference in incidence rates for NHL between the 4 HSE areas in Ireland and rates for the entire 18 year period 1994-2011 varied less than 3% higher or lower than the national average of 13.6 cases per 100,000 per year.

Unlike Hodgkin's lymphoma, there is little evidence of socio-economic status being a risk factor for a diagnosis of NHL and equal proportions of patients from all SES strata have been reported in a number of studies.[7,8] In Ireland, incidence was somewhat higher in the least deprived/most affluent urban areas compared to the most deprived urban areas. In rural areas by contrast, incidence was statistically significantly low in the least deprived compared to moderately and most deprived areas (Figure 6). Overall, incidence was statistically significantly higher in urban compared to rural areas.

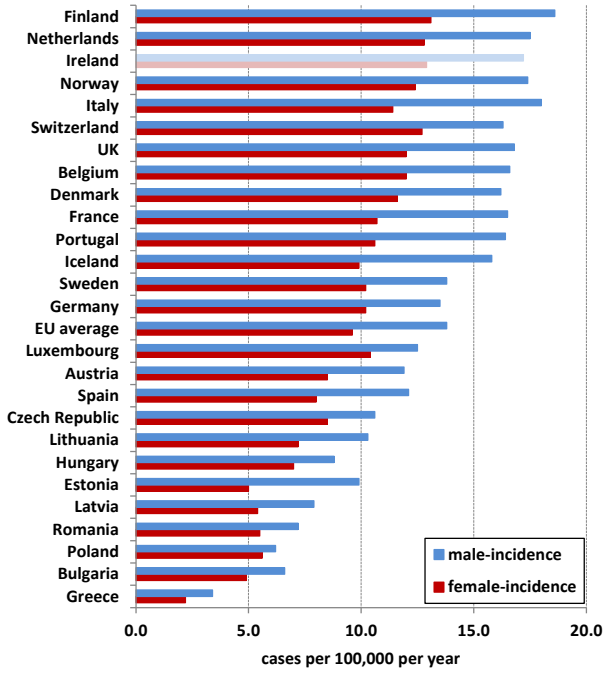
Figure 6. Incidence of non-Hodgkin's lymphoma and variation with deprivation index (DI)[9] and urban/rural area of residence, 1994–2011 *(rural areas defined by population density <1 person per hectare)*



International variation in incidence and mortality

Compared to 26 other European countries, estimated NHL incidence in Ireland in 2012 ranked 2nd highest for females, and 5th highest for males (Figure 7). Incidence in Irish females was 34% higher than the European average, second only to Finland; and incidence in Irish males was 25% higher - ranked behind Finland, Italy, Netherlands and Norway. Lowest incidence rates were found in eastern European countries and in Greece.

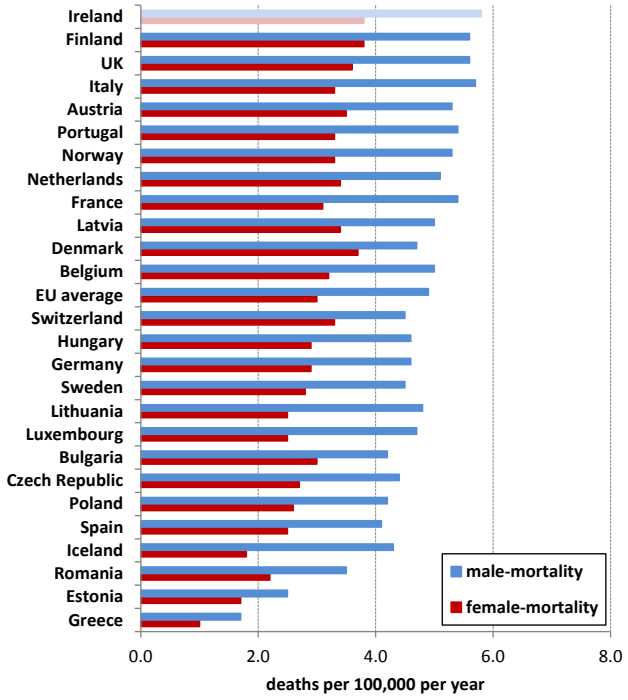
Figure 7. Incidence of non-Hodgkin's lymphoma in Europe, 2012[10]



Mortality from NHL in Ireland was ranked highest in Europe for both sexes although Irish rates were fairly close to those estimated for Finland and the UK (Figure 8). Irish female mortality rates were 27%

higher than the EU average while rates in males were 18% higher than the overall EU rate. Similar to incidence figures, lowest mortality was recorded in eastern Europe and in Greece.

Figure 8. Mortality from non-Hodgkin's lymphoma in Europe, 2012[10]

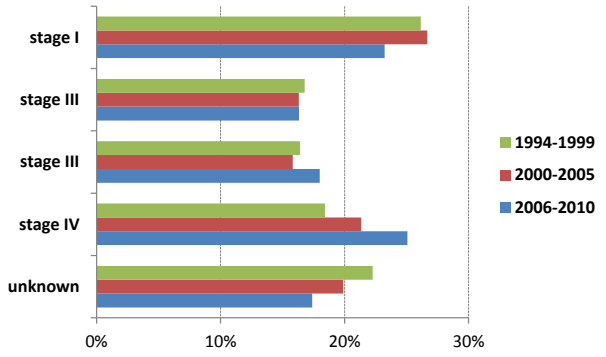


Stage at diagnosis

3

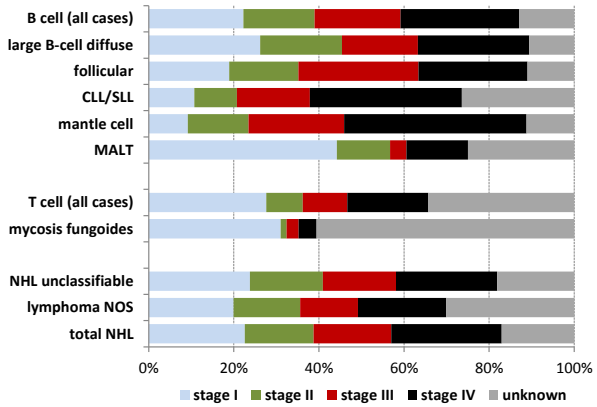
For NHL overall, there has been a decline in the relative proportion of early stage (Stage I) and an increase in the percentage of late (Stage IV) disease over time (Figure 9). However variation in the distribution of cancer stage over time is likely to be strongly affected by the large changes in disease classification and coding in recent years.[1] The reduction in the proportion of unstaged cancers may be influenced by the decline in unspecified cancers over time, as illustrated in Figure 1.

Figure 9. Variation in the distribution of all non-Hodgkin's lymphomas by stage over time[11]



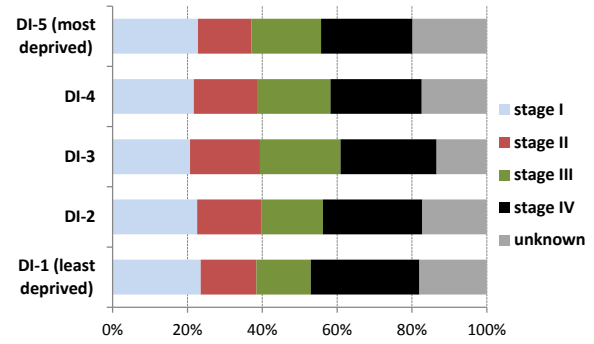
Between 2007 and 2010, almost half of B-cell lymphomas were at late stage when diagnosed (stage III-IV) (Figure 10) and only 13% of were unstaged. 36% of CLL/SLL and 43% of mantle cell subtypes were stage IV at diagnosis while 44% of MALT lymphomas were stage I. A much greater proportion (34%) of T-cell tumours were unstaged compared to B-cell subtypes. Over 60% of mycosis fungoides were unstaged but the majority of those tumours that were staged were stage I.

Figure 10. Percentage of non-Hodgkin's lymphomas by stage for most common subtypes, 2007-2010[11]



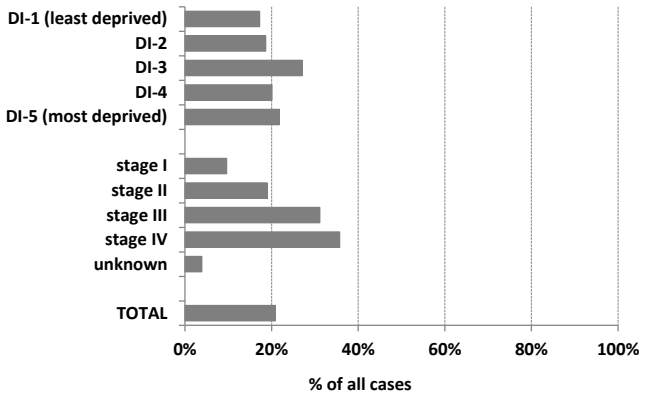
Socio-economic inequalities in prognostic indicators and treatment for NHL patients in Denmark have been reported, with those from poorer educational backgrounds more likely to present with late stage disease[8]. There is no indication that NHL disease stage varied by deprivation level in Ireland, and stage was fairly uniform across all deprivation levels (Figure 11). In contrast to many other cancers, the distribution of disease stage for NHL varied little by patient sex or age at diagnosis.

Figure 11. Percentage of non-Hodgkin's lymphomas by stage for areas of varying deprivation status, 2007-2010[11]



Only 1 in 5 cases of NHL diagnosed between 2007 and 2010 presented with systemic symptoms and, similar to the pattern observed for Hodgkin's lymphoma, this proportion increased with increasing disease stage (Figure 12). A slightly higher proportion of patients from moderate to most deprived areas presented with systemic symptoms compared to those from least deprived areas.

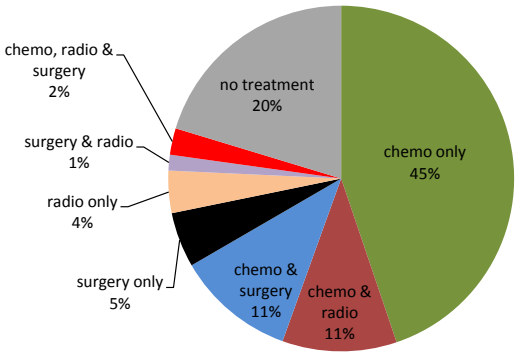
Figure 12. Proportion of non-Hodgkin's lymphoma patients presenting with systemic symptoms[6], by age and stage: 2007–2010[11]



Treatment

Almost half of all NHL patients were treated with chemotherapy alone, a further 22% had a combination of chemotherapy with either radiotherapy or surgery and one in 5 patients did not receive any tumour directed therapy (Figure 13).

Figure 13. Percentage composition of treatments for all NHL patients, 2007-2011[11]



Histological subtype is an important determinant of treatment for NHL and the percentage of patients receiving each treatment combination varied largely between subtypes (Table 3).

Table 3. Combinations of the main categories of treatment for NHL patients by histological subtype, 2007-2010[11]

	chemo only	chemo & radio	chemo & surg	surg only
B cell				
large B cell diffuse	51%	15%	12%	2%
follicular	45%	7%	14%	7%
CLL/SLL*	48%	3%	5%	9%
mantle cell	57%	10%	13%	2%
MALT	36%	3%	9%	11%
Burkitt's lymphoma	57%	12%	10%	6%
total B cell	49%	10%	12%	5%
T cell				
mycosis fungoides	8%	6%	0%	10%
anaplastic large cell	56%	13%	8%	8%
cutaneous, NOS	16%	5%	8%	22%
peripheral, NOS	41%	4%	19%	11%
total T cell	27%	7%	10%	11%
NHL unclassifiable	44%	16%	12%	4%
Lymphoma unspecified	34%	8%	7%	5%
TOTAL NHL	45%	11%	11%	5%

Table 3 continued. Combinations of the main categories of treatment for NHL patients by histological subtype, 2007-2010[11]

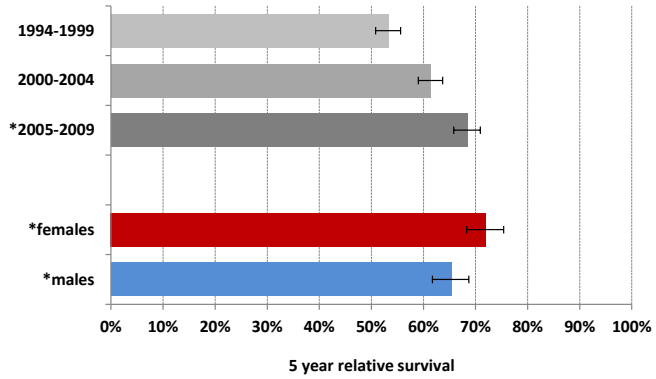
	radio only	surg & radio	chemo, radio & surg	No treatment
B cell				
large B cell diffuse	3%	1%	4%	14%
follicular	5%	3%	1%	19%
CLL/SLL*	4%	2%	1%	29%
mantle cell	3%	1%	2%	11%
MALT	13%	4%	0%	25%
Burkitt's lymphoma	2%	0%	4%	10%
total B cell	4%	2%	2%	17%
T cell				
mycosis fungoides	4%	1%	3%	68%
anaplastic large cell	3%	0%	3%	10%
cutaneous, NOS	14%	3%	5%	27%
peripheral, NOS	0%	4%	0%	22%
total T cell	5%	1%	4%	35%
NHL unclassifiable	2%	1%	4%	18%
Lymphoma unspecified	5%	1%	0%	39%
TOTAL NHL	4%	1%	2%	20%

** B-cell chronic lymphocytic leukaemia /small lymphocytic lymphoma*

Survival[12]

Survival from NHL has improved considerably and significantly over time; with 5 year relative survival of 53% recorded for patients diagnosed in the 1990's to over 68% in more recent years (Figure 14). Between 2005 and 2009, female survival rates (72%) were higher than male rates (65%) although this was not statistically significant.

Figure 14. Five year relative survival (with 95% confidence intervals) for NHL patients[12]

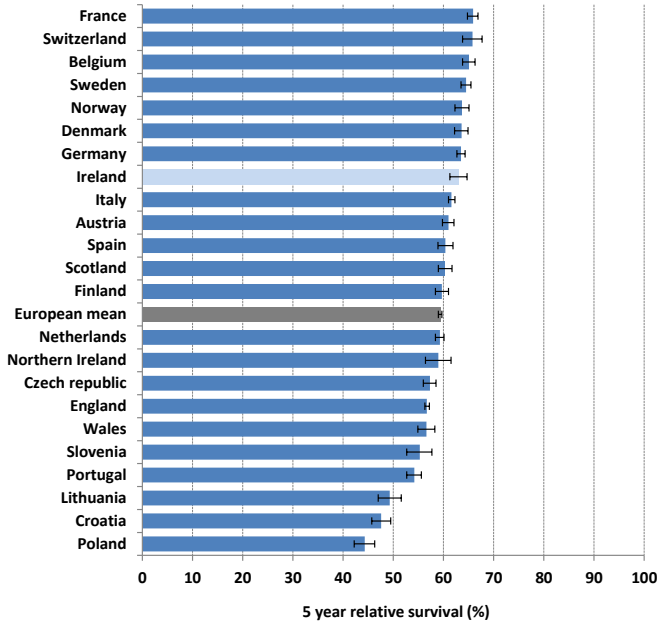


**females and males RS for 2005-2009 period only*

International variation in survival[13]

Figure 15 illustrates recently published 5 year survival rates for 23 northern, central, southern and eastern European countries. Ireland ranks amongst those countries with the highest survival rates. 5 year relative survival in Ireland was close to that found in Germany, Denmark and Norway and was estimated to be 6% higher than the European average and 11% higher than England. Of those countries shown, poorest survival was observed in Poland, Croatia and Lithuania.

Figure 15. Five year relative survival for NHL in Europe, patients diagnosed 1999-2007[13]



References and notes

1. Swerdlow SH et al (eds), 2008. WHO classification of tumours of haematopoietic and lymphoid tissues. IARC, Lyon
2. Fritz, A et al (eds) 2000. International classification of diseases for oncology, 3rd ed. WHO, Geneva
3. Hodgkin's lymphoma. Cancer Trends No. 19. NCRI www.ncri.ie/sites/ncri/files/pubs/
4. P. Boffetta, P. 2011. Epidemiology of adult non-Hodgkin lymphoma. Annals of Oncology 22 (Supplement 4): iv27–iv31
5. WHO mortality database. www-dep.iarc.fr/WHOdb/WHOdb.htm
6. CSO mortality http://www.cso.ie/px/pxeirestat/Statire/SelectVarVal/ Define.asp?maintable=VSA08&PLanguage=0
7. Wang, M et al 2008. Ethnic variations in diagnosis, treatment, socio- economic status, & survival in a large population-based cohort of elderly patients with non-Hodgkin's lymphoma. Cancer 113 (11): 3231-324
8. Fredericksen, BL et al 2011. Socioeconomic inequalities in prognostic markers of non-Hodgkin lymphoma: analysis of a national clinical database. Eur J Cancer 47(6): 910-917
9. Deprivation Index as per 2002 census. SAHRU (www.sahru.tcd.ie)
10. Non-Hodgkin's lymphoma, estimated incidence and mortality, 2012. EUCAN factsheet. http://eco.iarc.fr/EUCAN/Cancer.aspx?Cancer=38
11. Complete data on stage and treatment available to 2010 only
12. All patients were followed up to end 2011
13. Cancer survival in Europe, 1999-2007 by country and age: results of EUROCARE-5 a population-based study. De Angelis R, et al; Lancet Oncol. 2013, published online Dec 5th, 2013. http://www.thelancet.com/ journals/lanonc/article/PIIS1470-2045(13)70546-1/fulltext

