

Chapter 09:

Liver cancer (c22)

KEY FINDINGS

- INCIDENCE AND MORTALITY

- Between 2000 and 2004 there were on average 111 males and 68 females diagnosed in Ireland each year.
- Incidence rates increased between 1994 and 2004 by 4.8% per year for males and 4.3% per year for females.
- Males and females had higher than expected incidence rates in Belfast while males also had higher levels than expected in Dublin, Cork and Waterford.
- Incidence rates in Ireland were among some of the lowest found in developed countries.
- During 2000-2004 there was on average 132 male and 105 female liver cancer deaths per year.
- There was no significant trend in mortality rates in Ireland for either males or females between 1994 and 2004.

- SURVIVAL AND PREVALENCE

- Relative survival from the disease was very poor with five-year relative survival estimated to be 10.9% for males and 12.8% for females.
- There was no significant change in relative survival between those diagnosed in 1994-1996 and 1997-1999 for either males or females or in Northern Ireland or Republic of Ireland.
- At the end of 2004 there were 214 people living in Ireland who had been diagnosed with the disease in 1994-2004.

- NORTH/SOUTH COMPARISONS

- Incidence rates of liver cancer were similar in Northern Ireland and Republic of Ireland for both sexes during 2000-2004.
 - Increases in incidence rates were apparent in Republic of Ireland (6.9% for males, 8.9% for females) but not in Northern Ireland.
 - There was no significant difference in five-year (age-standardised) relative survival between Northern Ireland and Republic of Ireland.
 - There was no significant variation in mortality rates between Northern Ireland and Republic of Ireland during 2000-2004.
 - Female mortality rates in Republic of Ireland rose by 3.6% each year, while there was no significant change in Northern Ireland.
 - At the end of 2004 the number of people living with liver cancer diagnosed within the previous five years per 100,000 persons was 11.8% greater in Republic of Ireland than Northern Ireland.
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9.1: Incidence

The liver is often a site of secondary spread of cancer, however both cancer registries in Ireland carefully check each liver cancer to exclude secondary cancers and thus only records primary tumours. Between 2000 and 2004 there were 111 males and 68 females diagnosed each year with a primary liver cancer. It was one of the less common cancers contributing 1.0% of male and 0.6% of female cancers (excluding NMSC) during the period making it the sixteenth most common male and eighteenth most common female cancer. The risk of a member of the population developing the disease before the age of 75 was small but not negligible (0.3% for males and 0.2% for females). (Tab. 9.1)

The difference between males and females increased when incidence rates were adjusted for the different age distribution of the two sexes with male European age standardised incidence rates (EASIR) double those of females ($p < 0.001$). Incidence rates were however similar in Northern Ireland and the Republic of Ireland for both sexes during 2000-2004. (Tab. 9.1)

Table 9.1: Summary statistics for incidence of liver cancer: 2000-2004

	Northern Ireland			Republic of Ireland			Ireland		
	Male	Female	All persons	Male	Female	All persons	Male	Female	All persons
Number of cases per year	36	24	60	76	44	119	111	68	179
% of all cancer cases (ex. NMSC)	1.1%	0.7%	0.9%	1.0%	0.6%	0.8%	1.0%	0.6%	0.8%
Rank (ex. NMSC)	16	18	20	16	18	20	16	18	20
Median age at diagnosis	69	72	71	68.5	70	69	69	71	69
Cumulative risk (Aged 0 to 74)	0.3%	0.2%	0.3%	0.3%	0.2%	0.3%	0.3%	0.2%	0.3%
Crude rate per 100,000 persons	4.3	2.8	3.5	3.9	2.2	3.0	4.0	2.4	3.2
EASIR \pm 95% CI	4.4 \pm 0.6	2.2 \pm 0.4	3.2 \pm 0.4	4.4 \pm 0.4	2.1 \pm 0.3	3.2 \pm 0.3	4.4 \pm 0.4	2.2 \pm 0.2	3.2 \pm 0.2
% difference (NI vs ROI) \pm 95% CI (+ NI higher, - NI lower)							0.2% \pm 18.1	5.3% \pm 24.7	0.0% \pm 14.2

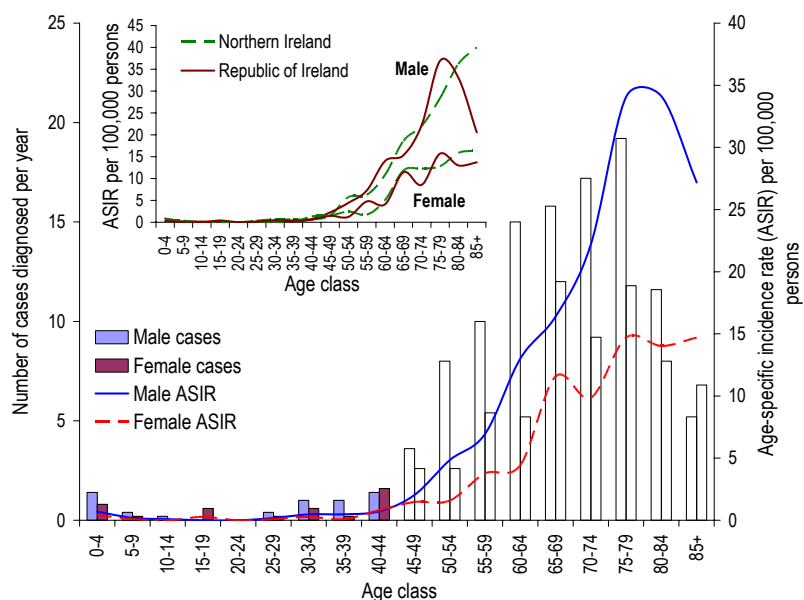
EASIR: European age-standardised incidence rate per 100,000 persons; CI: Confidence interval

9.1.1: Age distribution

Like most cancers liver cancer is a disease found mostly in the elderly with a median age at diagnosis during 2000-2004 of 69 years. However there was an average of 2 boys and 1 girl (aged 0-14) diagnosed each year during 2000-2004. (Tab. 9.1)

For males diagnoses of liver cancer peaked in the 75-79 age class with 19 cases per year (17.2% of male cases) while for females the 65-69 age class had the highest number of cases with 12 per year (17.7% of female cases). Age-specific incidence rates (ASIR) however were highest for males aged 80-84 and females aged 85 and over. This pattern varied by country with male ASIRs for those aged 85+ lower in Republic of Ireland than in Northern Ireland. (Fig. 9.1)

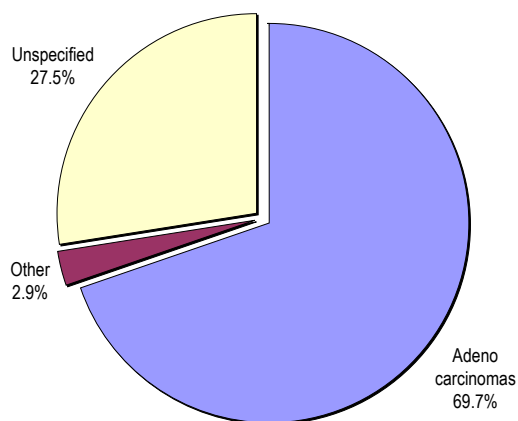
Figure 9.1: Number of cases of liver cancer diagnosed per year by sex and age with age-specific incidence rate (ASIR) per 100,000 persons: 2000-2004



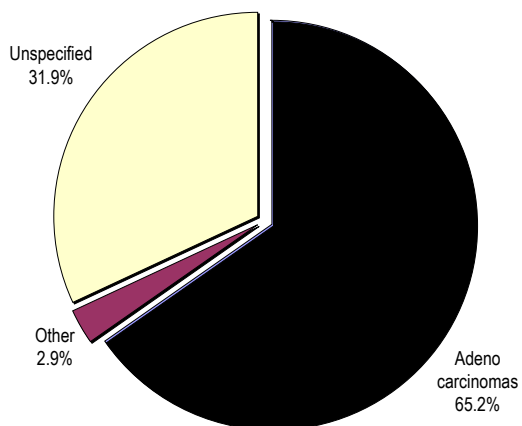
9.1.2: Cell type

Adenocarcinomas were the most common form of liver cancer diagnosed in Ireland during 2000-2004 making up 68.0% of the 179 liver cancers diagnosed per year with a further 29.1% of an unspecified cell type. These proportions varied slightly by sex but larger differences occurred between countries with 10.4% of cases having an unspecified cell type in Northern Ireland compared to 38.5% in Republic of Ireland. The majority of childhood liver cancers were complex mixed and stromal neoplasms. (Fig. 9.2)

Figure 9.2: Types of liver cancer diagnosed in Ireland: 2000-2004
(a) Male



(b) Female

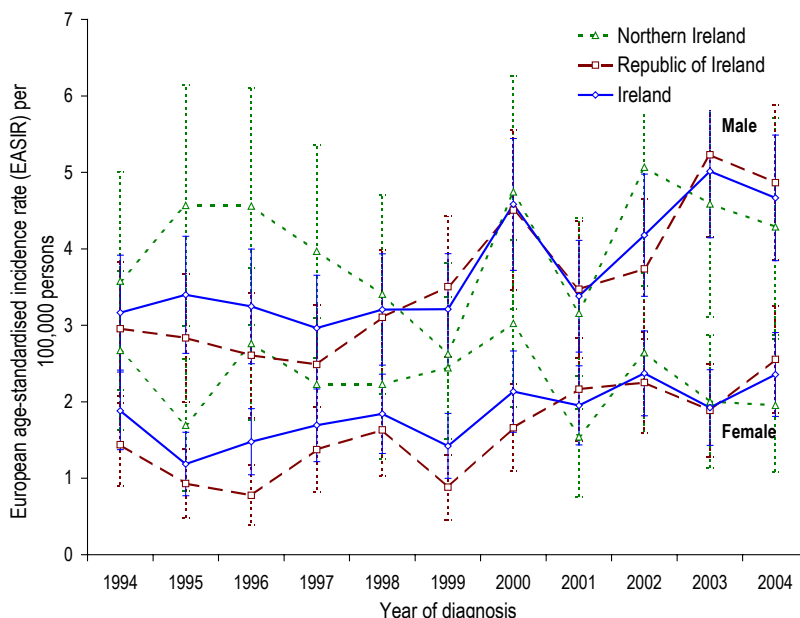


9.1.3: Trends

European age-standardised incidence rates (EASIR) for liver cancer increased between 1994 and 2004 by 4.8% (p=0.003) per year for males and 4.3% (p=0.018) per year for females. This corresponded to an annual increase of 5.8 male and 2.8 female cases per year. (Fig. 9.3, Tab. 9.2)

The significant increase in rates was not observed in Northern Ireland but was apparent in Republic of Ireland where EASIRs increased by 6.9% (p<0.001) per year for males and 8.9% (p=0.004) per year for females. (Fig. 9.3, Tab. 9.2)

Figure 9.3: Trends in European age-standardised incidence rates (EASIR) for liver cancer by sex and country: 1994-2004



9.1.4: Geographic variations

Belfast had higher than expected levels of liver cancer diagnosed in 2000-2004 for both males and females. Males also had higher than expected levels of liver cancer in Dublin, Cork and Waterford. Eleven counties/councils had lower than expected levels of the disease among males while six had lower levels among females. The majority of these areas were in Republic of Ireland. (Fig. 9.4)

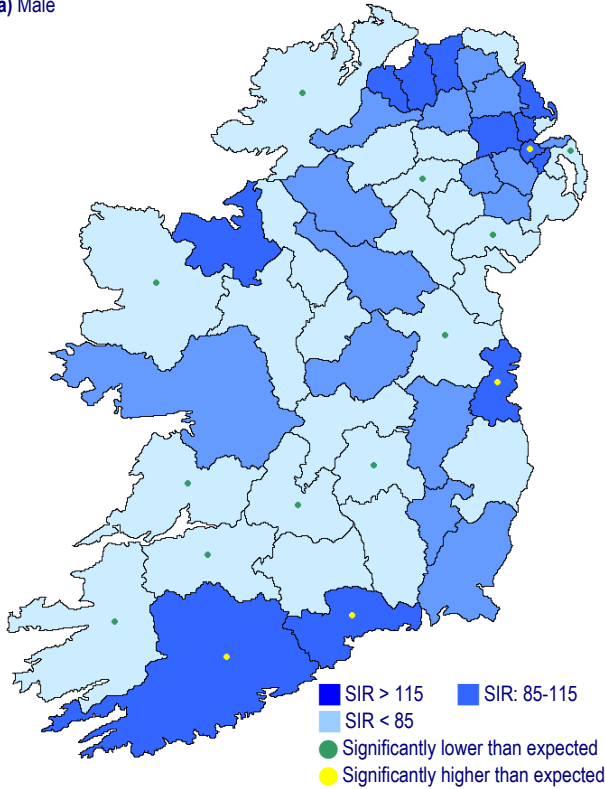
Table 9.2: Number of cases and European age-standardised incidence rates (EASIR) for liver cancer by year of diagnosis, sex and country: 1994-2004

Year	Male						Female					
	Northern Ireland		Republic of Ireland		Ireland		Northern Ireland		Republic of Ireland		Ireland	
	Cases	EASIR	Cases	EASIR	Cases	EASIR	Cases	EASIR	Cases	EASIR	Cases	EASIR
1994	25	3.6 ±1.4	46	3.0 ±0.9	71	3.2 ±0.8	29	2.7 ±1.0	29	1.4 ±0.5	58	1.9 ±0.5
1995	33	4.6 ±1.6	45	2.8 ±0.8	78	3.4 ±0.8	16	1.7 ±0.9	18	0.9 ±0.4	34	1.2 ±0.4
1996	34	4.6 ±1.6	40	2.6 ±0.8	74	3.2 ±0.7	32	2.8 ±1.0	16	0.8 ±0.4	48	1.5 ±0.4
1997	32	4.0 ±1.4	40	2.5 ±0.8	72	3.0 ±0.7	29	2.2 ±0.9	25	1.4 ±0.6	54	1.7 ±0.5
1998	27	3.4 ±1.3	49	3.1 ±0.9	76	3.2 ±0.7	22	2.2 ±1.0	30	1.6 ±0.6	52	1.8 ±0.5
1999	19	2.6 ±1.2	57	3.5 ±0.9	76	3.2 ±0.7	29	2.4 ±0.9	18	0.9 ±0.4	47	1.4 ±0.4
2000	38	4.7 ±1.5	72	4.5 ±1.0	110	4.6 ±0.9	32	3.0 ±1.1	35	1.7 ±0.6	67	2.1 ±0.5
2001	25	3.2 ±1.3	59	3.5 ±0.9	84	3.4 ±0.7	16	1.5 ±0.8	42	2.2 ±0.7	58	2.0 ±0.5
2002	42	5.1 ±1.6	65	3.7 ±0.9	107	4.2 ±0.8	27	2.6 ±1.0	49	2.3 ±0.7	76	2.4 ±0.6
2003	38	4.6 ±1.5	92	5.2 ±1.1	130	5.0 ±0.9	23	2.0 ±0.9	39	1.9 ±0.6	62	1.9 ±0.5
2004	36	4.3 ±1.4	90	4.9 ±1.0	126	4.7 ±0.8	22	2.0 ±0.9	54	2.6 ±0.7	76	2.4 ±0.5

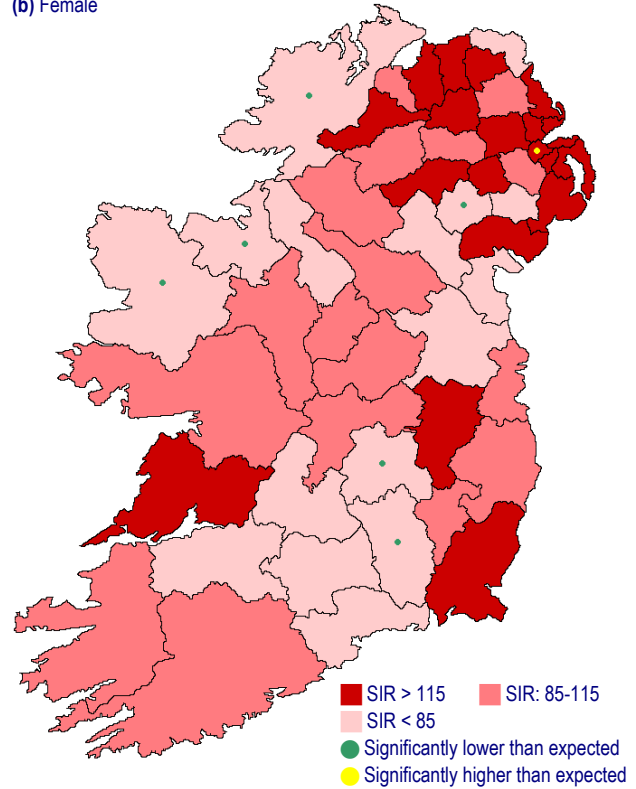
EASIR: European age-standardised incidence rate per 100,000 persons with 95% confidence interval

Figure 9.4: Significant differences in county/council standardised incidence ratios for liver cancer compared to Ireland as a whole: 1994-2004

(a) Male



(b) Female

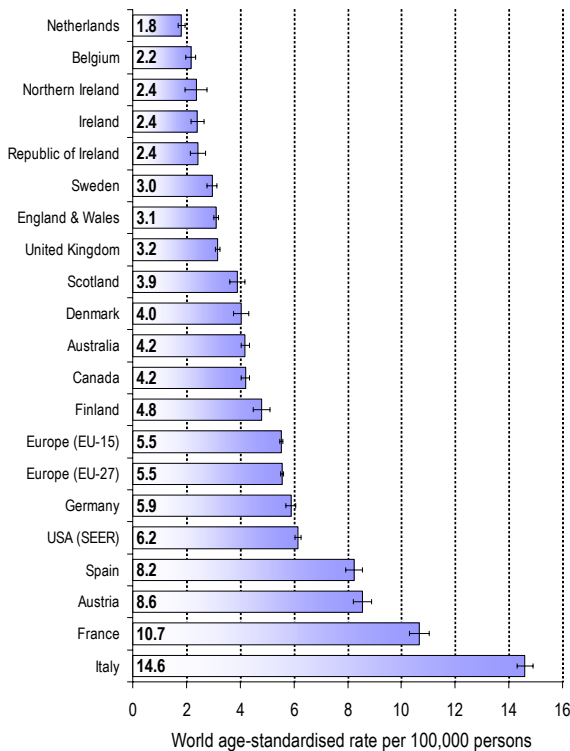


9.1.5: International comparisons

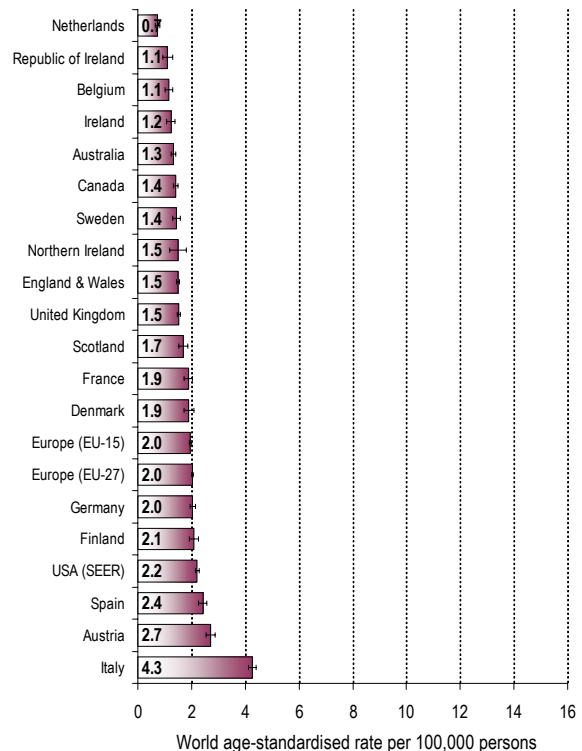
Internationally Ireland had some of the lowest incidence rates of liver cancer among developed countries with only the Netherlands having significantly lower rates. In particular incidence rates were below those of the European Union and USA for both males and females and than UK, Canada and Australia for males. Incidence rates were also lower in Republic of Ireland than in Canada and the UK for females. These variations however may be related to the inclusion of secondary liver cancers in other countries (Fig. 9.5)

Figure 9.5: International comparisons of world age-standardised incidence rates for liver cancer: 1998-2000

(a) Male



(b) Female



Source: IARC⁶⁶

9.2: Survival

Relative survival (age-standardised) from liver cancer was very poor with an estimated 26.6% of patients diagnosed in 2000-2004 surviving one-year and 11.2% surviving five-years. (Fig. 9.6, Tab. 9.3)

These values did not vary significantly by sex or country despite female five-year (age-standardised) relative survival

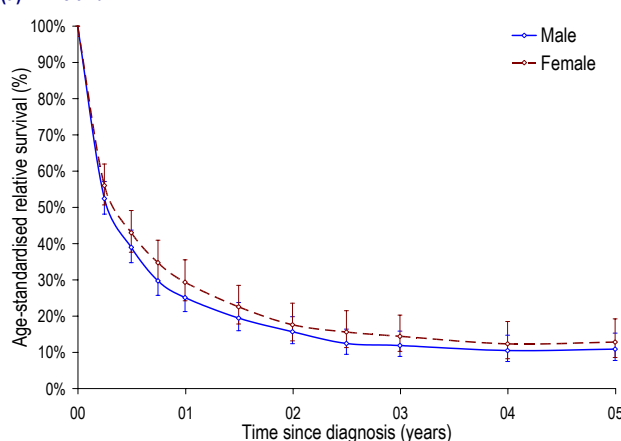
appearing 11.4% ($p=0.058$) higher in Republic of Ireland compared to Northern Ireland. This difference was likely an artefact of the small number of liver cancer patients in Northern Ireland, particularly the number surviving five years. (Fig. 9.6, Tab. 9.3)

Table 9.3: Age-standardised relative survival for liver cancer patients by country and sex: 2000-2004 period analysis estimates

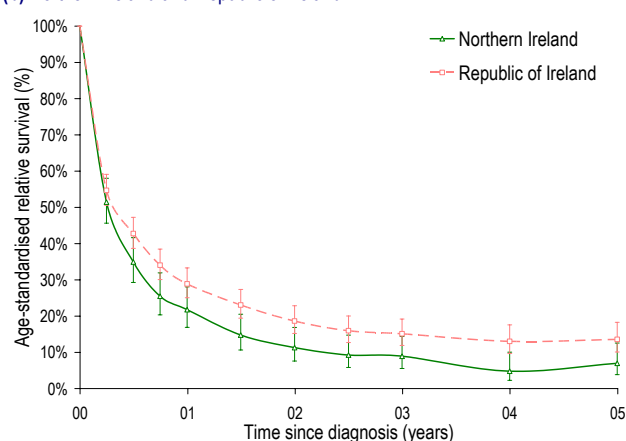
		Age-standardised relative survival (95% CI)		
		Male	Female	All
1-year	Northern Ireland	20.1% (14.4%, 28.1%)	25.5% (17.7%, 36.6%)	21.8% (16.9%, 28.1%)
	Republic of Ireland	27.5% (22.8%, 33.2%)	30.6% (24.5%, 38.2%)	28.9% (25.1%, 33.3%)
	Ireland	25.1% (21.3%, 29.6%)	29.3% (24.2%, 35.5%)	26.6% (23.5%, 30.1%)
5-year	Northern Ireland	6.3% (2.9%, 13.5%)	4.3% (1.4%, 13.3%)	7.0% (3.9%, 12.6%)
	Republic of Ireland	11.7% (8.0%, 17.1%)	15.7% (10.1%, 24.5%)	13.6% (10.1%, 18.3%)
	Ireland	10.9% (7.7%, 15.3%)	12.8% (8.6%, 19.2%)	11.2% (8.5%, 14.8%)

Figure 9.6: Age-standardised relative survival for liver cancer patients by country and sex: 2000-2004 period analysis estimates

(a) All Ireland



(b) Northern Ireland and Republic of Ireland



Despite poor survival among adults, children with liver cancer usually have a different cell type affected and their survival experience was much better, with five-year relative survival for children (aged 0-14) with liver cancer diagnosed in 2000-2004 estimated to be 91.9% (95% CI: 77.5%, 109.0%). It should be stressed however that this conclusion is based on a small number of cases.

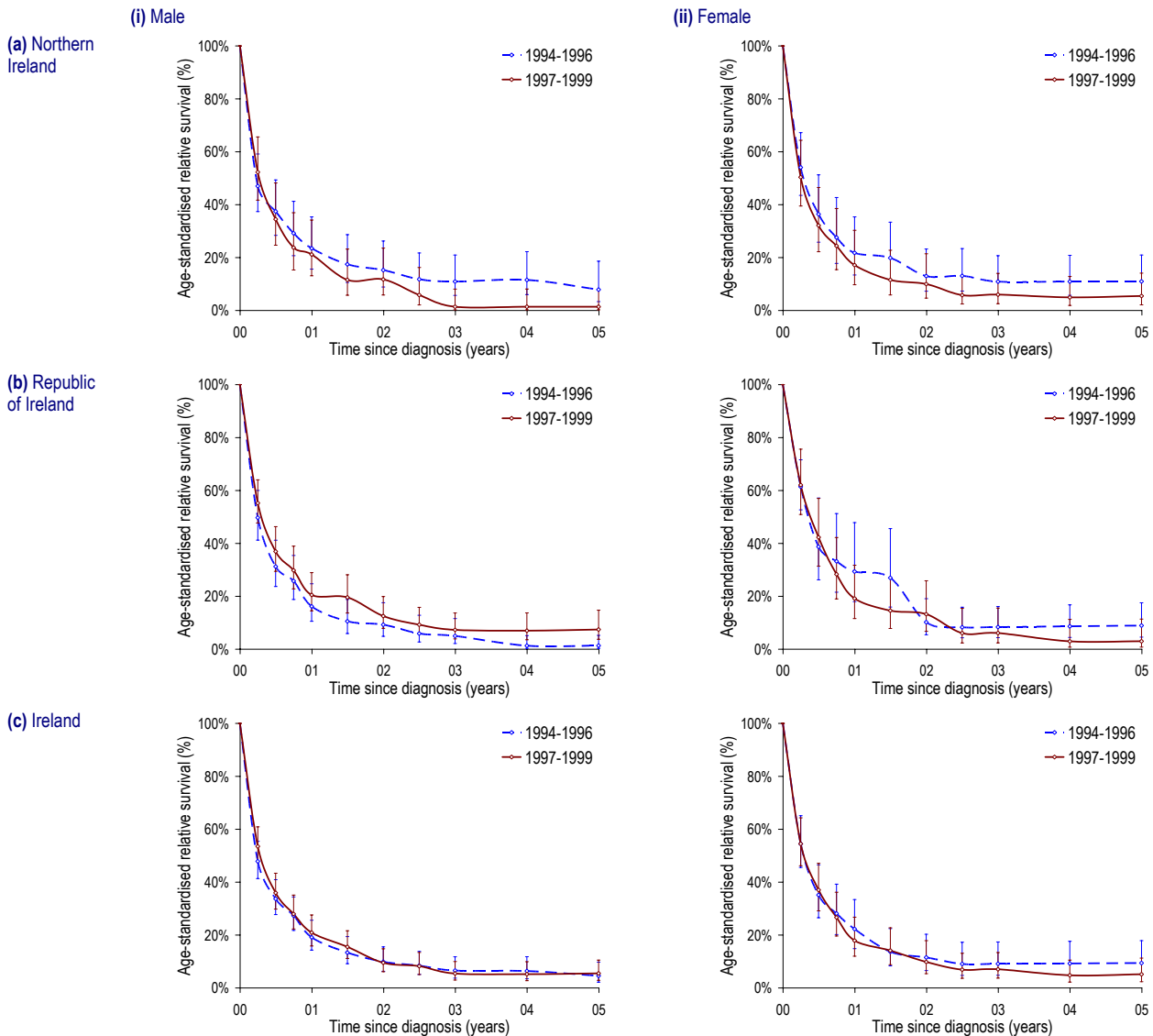
9.2.1: Changes in survival over time

There was no significant variation in (age-standardised) relative survival for males or females between those diagnosed in 1994-1996 and 1997-1999. This was apparent in Northern Ireland and Republic of Ireland as well as Ireland as a whole. (Fig. 9.7, Tab. 9.4)

Table 9.4: Age-standardised relative survival for liver cancer patients by sex, country and period of diagnosis: 1994-1999

		Age-standardised relative survival (95% CI)			
		1-year		5-year	
		1994-1996	1997-1999	1994-1996	1997-1999
All persons	Northern Ireland	21.7% (15.6%, 30.2%)	18.7% (12.9%, 27.0%)	7.0% (3.4%, 14.4%)	4.4% (1.9%, 10.3%)
	Republic of Ireland	17.5% (12.6%, 24.3%)	20.4% (15.3%, 27.3%)	4.1% (2.1%, 8.3%)	6.2% (3.3%, 11.5%)
	Ireland	19.4% (15.4%, 24.4%)	20.0% (16.0%, 25.0%)	5.6% (3.4%, 9.1%)	5.7% (3.5%, 9.4%)
Male	Northern Ireland	23.5% (15.6%, 35.4%)	21.2% (13.1%, 34.2%)	7.9% (3.4%, 18.6%)	1.4% (0.2%, 8.1%)
	Republic of Ireland	16.2% (10.6%, 24.8%)	20.5% (14.5%, 29.0%)	1.4% (0.4%, 5.3%)	7.5% (3.8%, 14.7%)
	Ireland	19.1% (14.3%, 25.6%)	20.9% (15.9%, 27.6%)	4.6% (2.2%, 9.8%)	5.5% (2.9%, 10.5%)
Female	Northern Ireland	21.8% (13.4%, 35.4%)	17.2% (9.7%, 30.3%)	11.0% (5.8%, 21.0%)	5.5% (2.1%, 14.1%)
	Republic of Ireland	29.4% (18.0%, 47.9%)	19.2% (11.6%, 31.8%)	8.9% (4.6%, 17.6%)	3.0% (0.8%, 11.4%)
	Ireland	22.3% (14.9%, 33.4%)	17.9% (12.0%, 26.8%)	9.4% (5.0%, 17.9%)	5.2% (2.4%, 11.3%)

Figure 9.7: Age-standardised relative survival for liver cancer patients by sex, country and period of diagnosis: 1994-1999



9.2.2: Observed survival

One-year observed survival (which includes causes of death other than cancer) was 20.0% for males and 16.4% for females diagnosed in 1997-1999. Five-year observed survival was also very poor for those diagnosed in this time period at 4.4% for males and 4.5% for females. The variations by sex were not statistically significant, nor were any variations in observed survival between Northern Ireland and Republic of Ireland. Analysis of differences in observed survival over time did not reveal any significant change between 1994-1996 and 1997-1999. (Tab. 9.5)

Table 9.5: Observed survival for liver cancer patients by sex, country and period of diagnosis: 1994-1999

		Observed survival (95% CI)			
		1-year		5-year	
		1994-1996	1997-1999	1994-1996	1997-1999
All persons	Northern Ireland	18.5% (13.3%, 25.9%)	17.7% (12.4%, 25.3%)	4.6% (2.2%, 9.6%)	3.5% (1.5%, 8.4%)
	Republic of Ireland	16.4% (11.8%, 22.7%)	19.2% (14.4%, 25.5%)	4.4% (2.2%, 8.6%)	5.1% (2.8%, 9.2%)
	Ireland	17.4% (13.7%, 21.9%)	18.6% (14.9%, 23.2%)	4.5% (2.7%, 7.4%)	4.4% (2.7%, 7.3%)
Male	Northern Ireland	22.2% (14.8%, 33.4%)	20.0% (12.5%, 32.0%)	6.2% (2.6%, 14.4%)	1.4% (0.2%, 10.0%)
	Republic of Ireland	14.9% (9.7%, 22.8%)	20.0% (14.3%, 28.0%)	1.7% (0.4%, 6.5%)	5.9% (3.0%, 11.6%)
	Ireland	17.8% (13.3%, 24.0%)	20.0% (15.2%, 26.3%)	3.5% (1.7%, 7.2%)	4.4% (2.3%, 8.3%)
Female	Northern Ireland	14.3% (8.0%, 25.4%)	15.5% (9.0%, 26.7%)	2.9% (0.7%, 11.2%)	5.6% (2.2%, 14.6%)
	Republic of Ireland	19.4% (11.6%, 32.2%)	17.5% (10.2%, 29.9%)	9.7% (4.5%, 20.7%)	3.2% (0.8%, 12.4%)
	Ireland	16.7% (11.4%, 24.4%)	16.4% (11.2%, 24.1%)	6.1% (3.1%, 11.9%)	4.5% (2.0%, 9.8%)

9.3: Mortality

Liver cancer was the thirteenth commonest form of cancer death among males during 2000-2004 and was the eleventh most common cause of female cancer death. With 132 male deaths per year it made up 2.2% of male cancer deaths (excluding NMSC) with a cumulative risk of death from this disease before age 75 of 0.4%. Among females there were 105 deaths per year thereby contributing 2.0% of female cancer deaths (excluding NMSC) with a cumulative risk of 0.2% of death from this disease before age 75. (Tab. 9.6)

The number of deaths per year was higher among males than females by 25.7% with European age-standardised mortality rates (EASMR) higher among males by 67.7% ($p < 0.001$). There was however no significant difference in EASMRs between Northern Ireland and Republic of Ireland during 2000-2004. (Tab. 9.6)

In both countries the average number of deaths each year from liver cancer between 2000 and 2004 exceeded the number of cases diagnosed. This was probably a result of deaths classified as being the result of liver cancer including secondary liver cancer which has spread from a different part of the body to the liver.

Table 9.6: Summary statistics for deaths from liver cancer: 2000-2004

	Northern Ireland			Republic of Ireland			Ireland		
	Male	Female	All persons	Male	Female	All persons	Male	Female	All persons
Number of deaths per year	39	34	73	93	70	164	132	105	237
% of all cancer deaths (ex. NMSC)	2.1%	1.9%	2.0%	2.3%	2.0%	2.2%	2.2%	2.0%	2.1%
Rank (ex. NMSC)	13	12	15	13	12	14	13	11	15
Median age at death	73	74	73	72	76	74	72	75	74
Cumulative risk (Aged 0 to 74)	0.3%	0.2%	0.3%	0.4%	0.2%	0.3%	0.4%	0.2%	0.3%
Crude rate per 100,000 persons	4.7	4.0	4.3	4.8	3.6	4.2	4.8	3.7	4.2
EASMR \pm 95% CI	4.7 \pm 0.7	3.0 \pm 0.5	3.7 \pm 0.4	5.4 \pm 0.5	3.1 \pm 0.3	4.1 \pm 0.3	5.2 \pm 0.4	3.1 \pm 0.3	4.0 \pm 0.2
% difference (NI vs ROI) \pm 95% CI (+ NI higher, - NI lower)							-13.9% \pm 14.7	-3.8% \pm 18.6	-10.6% \pm 11.3

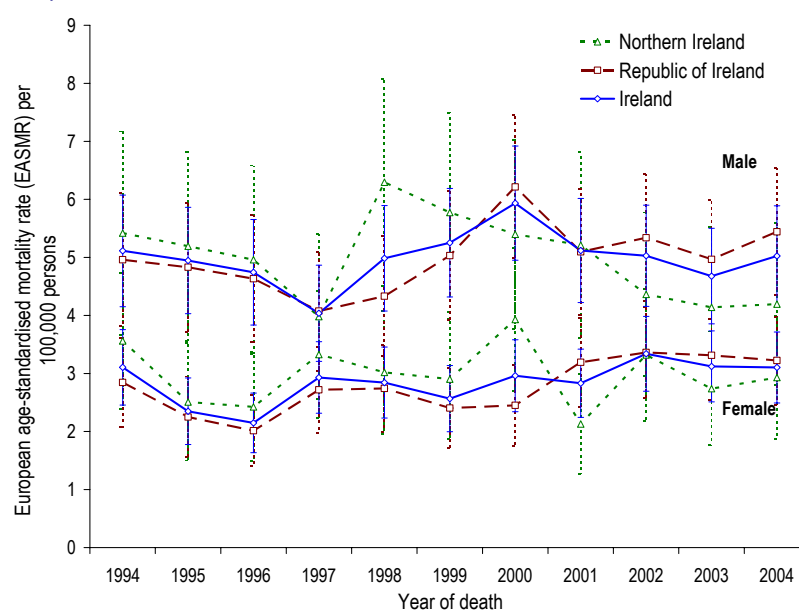
EASMR: European age-standardised mortality rate per 100,000 persons; CI: Confidence interval

9.3.1: Trends

Between 1994 and 2004 there was no significant trend in European age-standardised mortality rates (EASMR) for liver cancer in Ireland for either males or females. However the actual number of deaths rose by 2.8 male and 3.1 female deaths per year as a result of growth and ageing of the population. All of the increase in deaths was due to increases observed in Republic of Ireland with the number of deaths per year in Northern Ireland remaining static between 1994 and 2004. (Fig. 9.8)

While the differing trend in the absolute number of deaths between countries was reflected in the annual percentage change in EASMRs for each country, the only significant trend established was in Republic of Ireland where female EASMRs rose by 3.6% ($p = 0.015$) each year between 1994 and 2004. (Fig. 9.8)

Figure 9.8: Trends in European age-standardised mortality rates (EASMR) for liver cancer by sex and country: 1994-2004



9.4: Prevalence

Between 1994 and 2004 there were 1,636 people diagnosed with liver cancer. Of these 13.7% (224 people) were still alive at the end of 2004. The majority of these (195 people) were diagnosed in the 2000-2004 period, which was 21.8% of all those diagnosed within these five years. (Tab. 9.7)

The majority of those alive at the end of 2004 having been diagnosed within

the previous five years were male (124 males compared to 71 females) while 53 survivors were resident in Northern Ireland compared to 142 in Republic of Ireland. At the end of 2004 the number of people living with liver cancer diagnosed within the previous five years per 100,000 persons was 11.8% greater in Republic of Ireland than Northern Ireland. (Tab. 9.7)

Table 9.7: Prevalence of liver cancer in Ireland at the end of 2004 by country, sex and period of diagnosis

		Diagnosed 1994-2004		Diagnosed 2000-2004	
		Prevalence	% of cases diagnosed during period	Prevalence	% of cases diagnosed during period
Northern Ireland	Male	40	11.5%	33	18.4%
	Female	23	8.3%	20	16.7%
	All persons	63	10.1%	53	17.7%
Republic of Ireland	Male	101	15.4%	91	24.1%
	Female	60	16.9%	51	23.3%
	All persons	161	15.9%	142	23.8%
Ireland	Male	141	14.0%	124	22.3%
	Female	83	13.1%	71	20.9%
	All persons	224	13.7%	195	21.8%

9.5: Discussion

The liver performs many of the body's chemical functions ranging from the production of bile for digestive purposes to helping the blood clot in the event of an injury. It is the second largest organ in the body and is located behind the right lung. Symptoms of the disease include significant loss of weight (more than 10%) and/or appetite, dark coloured urine with light coloured faeces and/or a swollen or painful abdomen.⁶⁷ Cirrhosis is the strongest predisposing risk factor of liver cancer, which may be caused by alcohol⁶⁸ or infection with hepatitis B or hepatitis C viruses.^{69,70} Further established and likely risk factors include diabetes,⁷¹ exposure to Aflatoxin B¹⁷⁰ or vinyl chloride or in tropical countries from liver fluke infection.⁶⁸

Worldwide there are approximately 560,000 cases of liver cancer diagnosed annually; however it is a disease more common in developing countries, particularly in Asia and central Africa due to its relationship to hepatitis B. In developing countries such as Ireland however it is liver cirrhosis caused by alcohol abuse that is the major causal factor.

Treatment options for this cancer are limited as liver cancer is largely resistant to radiotherapy. While both chemotherapy and surgery are used the former has limited impact on survival and while the latter can prove an effective treatment it is only applicable at an early stage and in the absence of other liver disease. The difficulty in treating the disease means that survival for patients diagnosed with liver cancer is typically very poor.

Due to the poor survival control of this disease in Ireland will most likely be achieved through prevention programmes with efforts continuously ongoing to reduce alcohol consumption by changing public attitudes towards levels of alcohol intake. Additionally as a result of increases in the numbers of people diagnosed with the hepatitis C virus in Republic of Ireland careful monitoring of those affected is also undertaken and good diagnostic procedures for the virus are in place.

Incidence rates of liver cancer have shown an increase over recent years in Republic of Ireland and have remained static in Northern Ireland. This however is not necessarily an indication of a failure on the part of the programmes in place to reduce alcohol consumption, nor has it been directly connected to increases in hepatitis C (although this cannot be completely ruled out as a possible explanation). Given that immigration from other countries in the European Union has been partly responsible for the large increase in the population of Republic of Ireland over the last ten years, it is likely that immigration has also contributed to the increases in liver cancer in Republic of Ireland as a result of higher incidence rates of liver cancer in European countries, particularly Italy and Spain, which immigrants originally resided in. The degree to which immigration should lead to an expectation of liver cancer increase in Ireland is however difficult to quantify due to the different treatment of secondary liver cancers by different cancer registries.