National Cancer Registry Ireland **Cancer Trends**

# Primary Brain Cancer

## Cancers of central nervous system: some key facts

On average about 480 primary tumours of the brain and central nervous system (CNS) were diagnosed each year in Ireland between 1994 and 2013, representing 1.8% of all tumours registered by the National Cancer Registry (NCR). Of these, 289 or 60% were invasive tumours in the brain specifically (Table 1). In addition, approximately 10 invasive tumours were registered per year in both the meninges (the thin layer of tissue covering the brain) and in the rest of the CNS outside of the brain, mostly in the spinal cord. Many primary tumours in the CNS are non-malignant cancers, i.e. are unlikely to spread beyond their primary location. The bulk of meningeal tumours are benign of which almost 100 were diagnosed here per year. A further 6 cases per year were of uncertain malignancy. 11% of tumours located in the brain were either of uncertain malignancy or benign. In the rest of the CNS outside of the brain and meninges, 27 cases per year were found to be benign tumours (mostly affecting the cranial nerves) and 5 per year were of uncertain malignancy.

Brain and CNS tumours have a younger age-profile than for many common cancers, and represent >25% of all childhood cancers in Ireland[1]. The median age at diagnosis for all brain & CNS patients (all behaviours) was 58 years and was highest (70 years) for those with invasive tumours of the meninges. Brain tumours were more common in men than in women, although the opposite was the case for meningeal cancers. The remainder of this report focuses on malignant tumours of the brain only (i.e. those coded ICD10: C71 only).

**Table 1. Case numbers and incidence rates for primary tumours of the brain & central nervous system, 1994–2013**

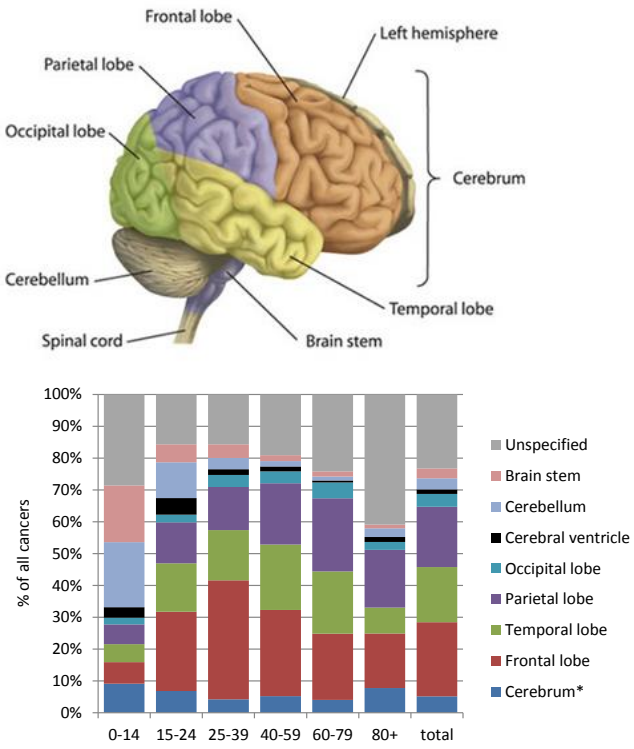
| | Invasive | Benign | Uncertain |
|---|---|---|---|
| **BRAIN** | | | |
| Annual average | 289 | 10 | 26 |
| % all registered cancers | 1.1% | <0.1% | 0.1% |
| % all invasive cancers | 1.8% | n/a | n/a |
| Male/Female ratio | 1.4 | 0.9 | 1.2 |
| Rate | 7.3 | 0.3 | 0.6 |
| Risk | 0.6% | <0.1% | <0.1% |
| Median age at diagnosis | 60 | 47 | 24 |
| **MENINGES** | | | |
| Annual average | 9 | 95 | 6 |
| % all registered cancers | <0.1% | 0.4% | <0.1% |
| % all invasive cancers | 0.1% | n/a | n/a |
| Male/Female ratio | 0.6 | 0.3 | 0.8 |
| Rate | 0.2 | 2.4 | 0.2 |
| Risk | <0.1% | 0.2% | <0.1% |
| Median age at diagnosis | 70 | 63 | 53 |
| **SPINAL CORD, CRANIAL NERVES & OTHER CNS** | | | |
| Annual average | 11 | 27 | 5 |
| % all registered cancers | <0.1% | 0.1% | <0.1% |
| % all invasive cancers | 0.1% | n/a | n/a |
| Male/Female ratio | 0.9 | 0.8 | 0.9 |
| Rate | 0.3 | 0.7 | 0.1 |
| Risk | <0.1% | <0.1% | <0.1% |
| Median age at diagnosis | 39 | 50 | 38 |

*~ rate per 100,000 per year (European age standardised)*

## Brain cancer anatomical sites and tumour types

Approximately equal proportions of malignant brain tumours were sited in the frontal, temporal and parietal lobes, with a further 20% not specific to a particular area (Figure 1). There was some variation in the distribution of anatomical sites with patient age, with tumours of the brain stem and cerebellum relatively more common in children. Over 40% of tumours in patients aged 80 and over were of unspecified site. There was no difference in the distribution of anatomical sites between males and females.

**Figure 1. Diagram showing main areas of the brain & distribution of anatomical sites of brain tumours by patient age group, 1994-2013**




** excluding lobes & ventricles*

Almost 75% of all brain cancers diagnosed during 1994-2013 were histologically verified; the remainder largely diagnosed via radiology and other imaging methods, such as MRI/MRS. There has been an increase in the proportion diagnosed histologically over time, and in 2012 a maximum of 83% were histologically verified (Figure 2). Elderly patients aged 80 and over were least likely to have a histological confirmation of their diagnosis; 9% were diagnosed histologically, 79% via radiology/scan and 13% clinically only.

**Figure 2. Trends in the method of diagnosis of brain cancers, 1994-2013**

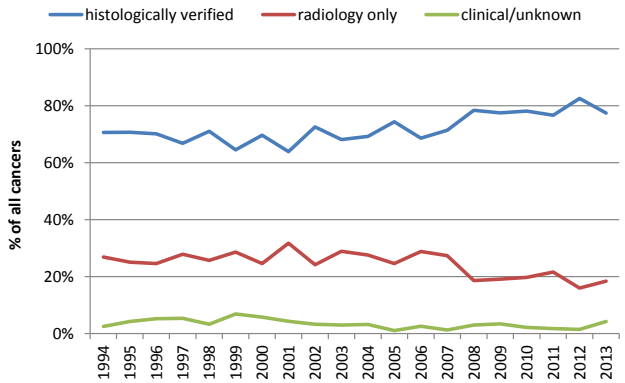




Table 2 summarises the breakdown of cases into subtypes as defined by the World Health Organisation[2]. Astrocytic tumours represented over two-thirds of all cases, most of which were glioblastoma or anaplastic astrocytomas; tumours that have a poor prognosis. Almost one-fifth of all brain cancers were of unspecified subtype, most of these tumours being diagnosed clinically or through radiology only.

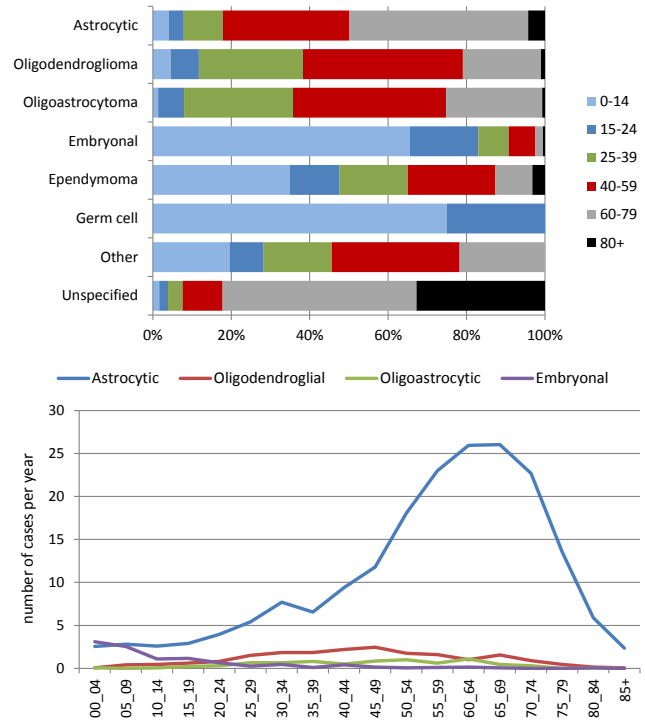
**Table 2. Histological subtypes[2] of invasive brain tumours, 1994–2013**

| | Annual average | % of all |
|---|---|---|
| **Astrocytic** | **193** | **67%** |
| *Glioblastoma* | *124* | *43%* |
| *Anaplastic astrocytoma* | *23* | *8%* |
| *Astrocytoma NOS (diffuse low grade)* | *24* | *8%* |
| *Glioma, NOS* | *16* | *6%* |
| *Other Astrocytic tumours#* | *6* | *2%* |
| **Oligodendroglioma** | **20** | **7%** |
| **Oligoastrocytoma** | **8** | **3%** |
| **Embryonal** | **9** | **3%** |
| *Medulloblastoma NOS/melanocytic* | *4* | *1%* |
| *Medulloblastoma, desmoplastic* | *1* | *<1%* |
| *Primitive neuroectodermal (pNET)* | *3* | *1%* |
| *Other Embryonal tumours* | *1* | *<1%* |
| **Ependymoma** | **5** | **2%** |
| **Germ cell tumour** | **1** | **<1%** |
| **Other subtypes*** | **1** | **<1%** |
| **Unspecified** | **52** | **18%** |
| **Total** | **289** | |

*# mainly low grade gemistocystic & fibrillary astrocytomas. * includes ganglioma, chordoma, astroblastoma, haemangiopericytoma & choroid-plexus*

Over half of all astrocytic tumours were diagnosed in patients aged 60 or over and 33% of unspecified subtypes were diagnosed in patients aged 80 or older. In contrast, embryonal tumours and ependymomas had a much younger profile and all germ cell tumours were diagnosed in children or young adults (Figure 3). Astrocytic tumours outnumbered all other subtypes, particularly in middle aged and older patients. There was no difference in the relative proportion of tumour subtypes between males and females.

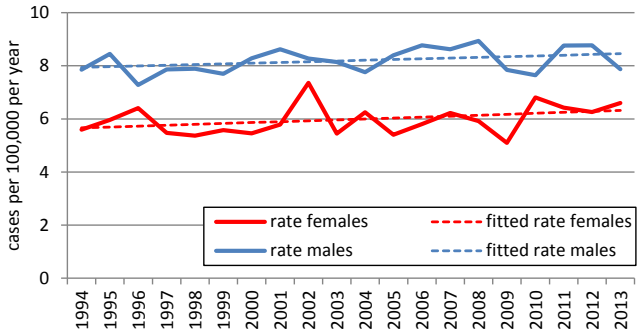
**Figure 3. Percentage age distribution of brain cancers by histological subtype[2], and the annual average number of cases of the most common subtypes by age, 1994–2013**




## *Time trends in incidence*

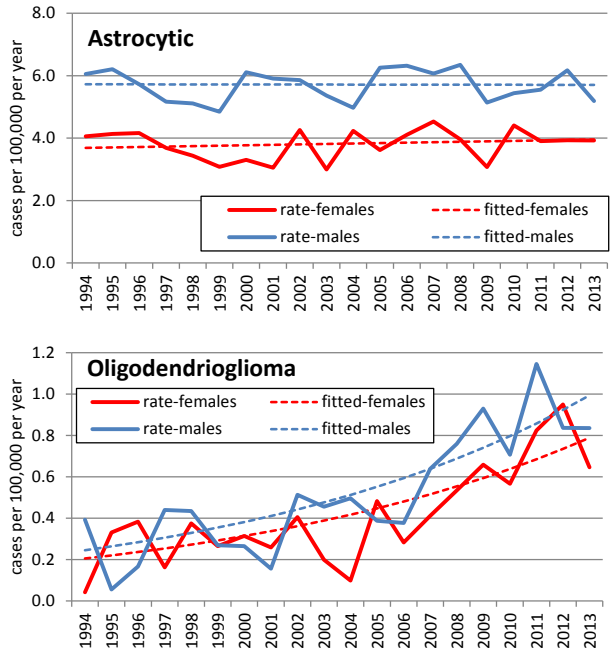
Age-standardised incidence rates for brain cancers as a whole have remained fairly stable, with (annual percentage changes (APC) averaging +0.6% (95% CI -0.2%, +1.3%) in females and +0.3% (-0.1%, +0.8%) in males (Figure 4). Case numbers increased from about 100 females and 140 males per year in the mid 1990s to 140 females and 185 males per year in 2009-2013, but this largely reflected population increase and ageing.

**Figure 4. Incidence rates for all brain cancers 1994-2013[3]**




Because of their numerical predominance, astrocytic tumours showed a similar trend in incidence to that for all brain cancers combined, and male rates in particular have remained largely unchanged over time, with non-significant APCs of +0.4% per year in females and 0.0% per years in males (Figure 5). However other subtypes, particularly oligodendrogliomas and embryonal tumours, show obvious trends, albeit with marked fluctuations from year to year (reflecting the small numbers involved) (Figure 5). Incidence of oligodendroglioma increased significantly for both sexes between 1994 and 2013 (APC females +7.3% (95% CI +4.3%, +10.4%), males +7.6% (+4.8%, +10.5%)), with case numbers increasing from 10 cases per year in the mid 1990s to 37 per year during 2009-2013.

**Figure 5. Incidence rates for brain cancer subtypes 1994-2013[3]**




Although incidence rates for embryonal cancers were more variable, there was also a significant increase of these cancers in



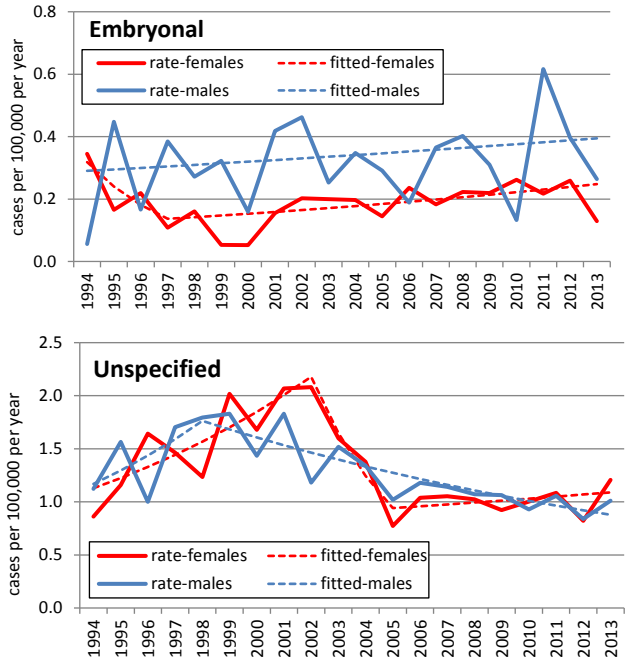
 

females after 1997 (APC +3.8% (95%CI +0.2%, +7.5%). Male rates also increased (APC +1.6%) but this was not significant.

No clear trend was evident for other specific subtypes. However, the incidence of unspecified cancers showed a clear pattern of initial increase followed by subsequent decline in both sexes. The increase in female incidence between 1994 and 2002 was significant (APC +8.6% (95%CI +2.3%, +15.2%) and, although not statistically significant, the subsequent sharp decline (2002-2005, APC -24.4%) is notable, despite a slight increase after 2005 (APC: 1.9%). In males, incidence rates of unspecified tumours declined significantly after the late 1990s (APC -4.5% (95%CI: -6.3%, -2.7%).

Although representing 18% of all brain cancers in total (Table 1), the proportion of unspecified tumours fell from a maximum of 29% of all brain cancers in 1999 to a minimum of 11% of all cases diagnosed in 2012. This trend likely reflects the increase in the histological diagnosis of cases as well as improvements in imaging techniques enabling more tumours to be more precisely defined.

**Figure 5 continued. Incidence rates for brain cancer subtypes 1994-2013[3]**

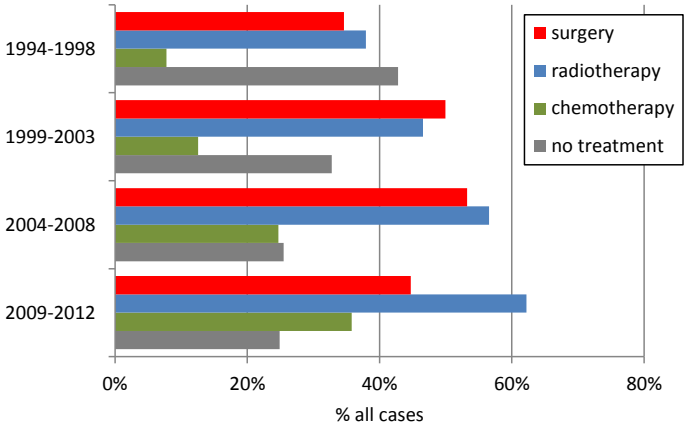



### *Treatment[4]*

Between 1994 and 2012, 46% of all patients with invasive brain cancer had tumour-directed surgery, 51% had radiotherapy, 21% had chemotherapy and 31% had no tumour-directed therapy (but may have had pain-relieving treatment or palliative care). Some changes were observed over time (Figure 6). Most notable was a decline in the proportion of patients not recorded as having any tumour-directed treatment, from 43% in 1994-1999 to 25% in 2009-2012.

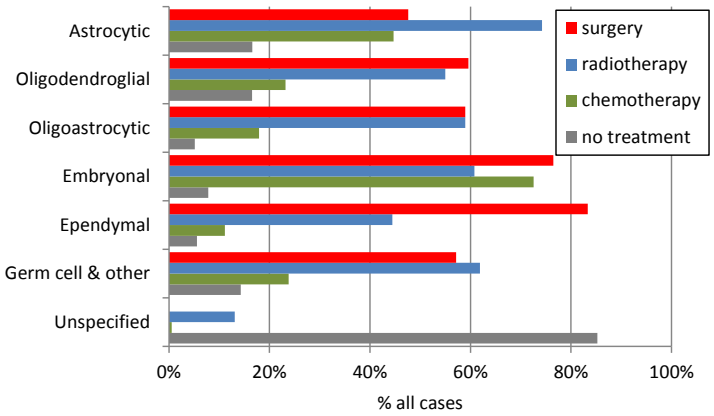
Surgery and radiotherapy (alone or in combination) represented the most common treatments. Of patients having chemotherapy, this was usually in combination with either radiotherapy or surgery. There was a clear increase in the proportion of patients having chemotherapy and radiotherapy (with or without surgery) over time.

**Figure 6. Treatment of brain cancers over time, 1994-2012[4]**




For patients diagnosed in the most recent years (2009-2012), the proportion having tumour-directed surgery varied from 48% for astrocytic tumours to 83% for ependymal cancers (Figure 7). Over half of all patients with the most common tumour types had radiotherapy, with the exception of ependymal tumours (44%). Chemotherapy was most likely for embryonal and astrocytic cancers. As expected the greatest numbers of patients not having any tumour-directed therapy were those with unspecified tumour types, where the proportion untreated was very large (85%, 150 of 176 cases). Of patients with tumours identified to subtype, more than 80% had at least one tumour-directed treatment.

**Figure 7. Treatment of brain tumours by subtype, 2009-2012[4]**




Patients aged 80 or over were the most likely to have no tumour-directed therapy and, of those that had treatment, most had radiotherapy only (Table 3). Radiotherapy was the most common treatment overall, particularly in the older age groups.

In 2012, Temozolomide was the most common chemotherapy drug administered to brain cancer patients and was taken by 135 of all 153 patients who had chemotherapy. This drug is recommended for glioblastoma and other high-grade gliomas, usually in combination with radiotherapy and after surgical resection where possible[5]. NCR figures show that 61% of all glioblastoma and 57% of anaplastic astrocytomas diagnosed in 2012 had chemotherapy (almost all in combination with radiotherapy). Of these patients, Temozolomide was administered to 97% and 85%, respectively. Avastin (Bevacizumab) was the second most common chemotherapy, with 25 out of 153 chemotherapy patients receiving this drug. The other most commonly administered chemotherapy drugs in 2012 were Vincristine (mainly for embryonal tumours), Cisplatin and Cyclophosphamide.



**Table 3. Treatment patterns for brain cancer patients by age group, 2009-2012[4]**

| | <25 | 25-39 | 40-59 | 60-79 | 80+ | All |
|---|---|---|---|---|---|---|
| Total cases | 130 | 148 | 352 | 552 | 131 | 1313 |
| | | | | | | |
| Surgery | 50% | 59% | 55% | 41% | 6% | 45% |
| Radiotherapy | 46% | 57% | 78% | 66% | 21% | 62% |
| Chemotherapy | 45% | 32% | 47% | 34% | 1% | 36% |
| | | | | | | |
| *surgery only* | *11%* | *27%* | *11%* | *6%* | *3%* | *10%* |
| *radio only* | *8%* | *14%* | *14%* | *19%* | *18%* | *16%* |
| *chemo only* | *3%* | *1%* | *1%* | *1%* | *2%* | *1%* |
| *surg & radio* | *7%* | *14%* | *17%* | *13%* | *3%* | *13%* |
| *surg & chemo* | *10%* | *1%* | *0%* | *0%* | *0%* | *1%* |
| *radio & chemo* | *9%* | *11%* | *20%* | *13%* | *1%* | *13%* |
| *all treatments* | *22%* | *18%* | *27%* | *21%* | *0%* | *21%* |
| *no treatment* | *17%* | *14%* | *11%* | *27%* | *73%* | *25%* |

**Table 4. Five-year net survival (NS) for brain cancers in adults (aged 15-99) diagnosed 1994-2013, by subtype**

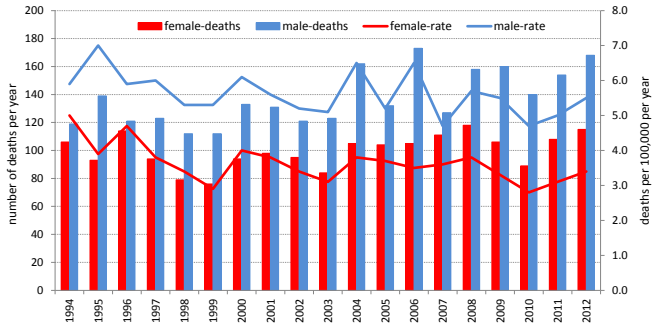
| | Total cases | NS (%) | 95%CI |
|---|---|---|---|
| **Astrocytic** | 3864 | 13.1 | 12.0, 14.2 |
| *Glioblastoma* | *2488* | *3.8* | *3.0, 4.6* |
| *Anaplastic astrocytoma* | *459* | *16.5* | *13.2, 19.9* |
| *Astrocytoma, NOS* | *479* | *44.6* | *39.6, 49.3* |
| *Glioma, NOS* | *316* | *23.7* | *18.8, 28.9* |
| *Other Astrocytic tumours** | *122* | *41.1* | *31.2, 50.5* |
| **Oligodendroglioma** | 392 | 58.6 | 52.6, 64.1 |
| **Oligoastrocytoma** | 151 | 47.5 | 38.3, 56.1 |
| **Embryonal** | 172 | 73.1 | 58.1, 83.3 |
| **Ependymoma** | 97 | 64.6 | 48.7, 76.6 |
| **Other subtypes**** | 46 | 58.9 | 37.2, 75.1 |
| **Unspecified** | 1041 | 15.6 | 13.2, 18.0 |
| **Total** | 5775 | 19.3 | 18.2, 20.4 |

** mainly gemistocystic & fibrillary astrocytomas. ** includes ganglioma, chordoma, astroblastoma, haemangiopericytoma & choroid plexus*

### *Mortality*[6]

Between 1994 and 2012, an average of 100 female and 137 male deaths from tumours of the brain and CNS occurred each year in Ireland (Figure 8). Rates have fluctuated somewhat over time, but there has been a small decline overall, by about 1.5% per year in females and almost 1% in males. Comparing data from 2007 onwards, years for which deaths for invasive brain cancers alone is available[7], almost all CNS cancer deaths (98%) were from invasive brain tumours particularly.

**Figure 8. Mortality from brain and central nervous system cancers in Ireland, 1994-2012[6]**

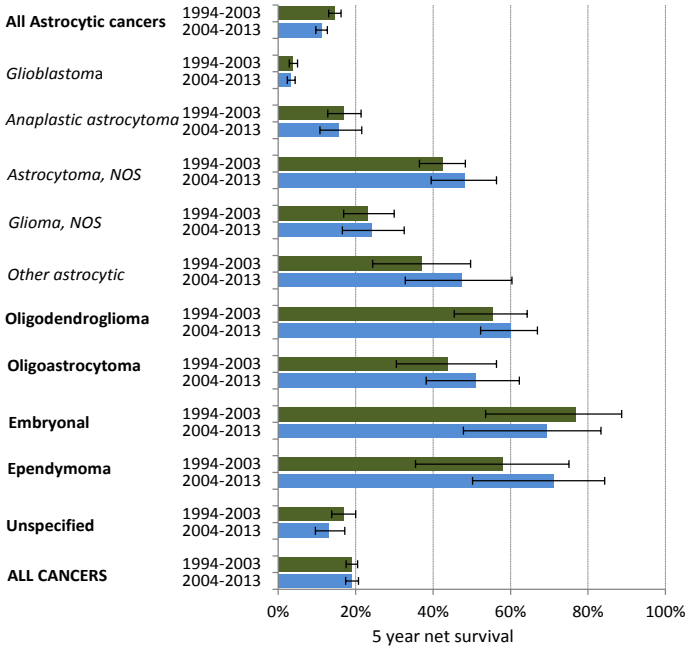



### *Survival*

Survival for patients with malignant brain cancer is poor and in Ireland, five-year net survival overall was just 19% (Table 4), similar to figures quoted for the UK[8]. Glioblastoma, which represented over 40% of all malignant brain tumours (Table 2), had by far the worst survival with just 4% of patients surviving five years. Anaplastic astrocytomas, another subtype of fast-growing tumours also had very poor survival, similar to that for patients whose cancer was not specified to subtype (five-year net survival 16%). It is possible that many of these unspecified tumours, as well as those identified as simply 'glioma NOS', may actually be high-grade astrocytomas, which would explain their poor survival, though late diagnosis of such poorly characterised cancers may also contribute. Astrocytoma NOS (or diffuse low-grade astrocytoma) which are slower growing tumours, had somewhat better survival, although still poor at 45% at five years. Embryonal tumours and ependymomas, most commonly diagnosed in young patients, had the best survival figures (over 60% at five years).

There has been little change in survival from malignant brain cancers over time and overall five-year net survival was 19% for both 1994-2003 and 2004-2013 diagnosis periods. Modest but not statistically significant improvements were observed for unspecified (low grade) astrocytomas, oligodendroglioma, oligoastrocytomas and ependymomas (Figure 9).

**Figure 9. Changes in five-year net survival for malignant brain cancer by subtype between 1994-2003 and 2004-2013 cohorts**




### *Prevalence*

Of almost 5,800 patients diagnosed with malignant brain cancer since 1994, 1,167 or 20% were known to be alive on 31/12/2013 (Table 5). Two-thirds of all patients diagnosed in 2013 were still alive at the end of that year (1-year prevalence), and just over one-third of all patients diagnosed during 2009-2013 inclusive were alive on this date (5-year prevalence). Percent prevalence was lowest for patients with glioblastoma and high grade astrocytomas. However because of their relatively large numbers, 50% of all patients alive on 31/12/2013 diagnosed since 1994 were those with astrocytic tumours, 20% with glioblastoma. A further 20% were patients with oligodendrogliomas and 10% had unspecified tumours.



**Table 5. Prevalence of brain cancer subtypes by period since diagnosis, patients diagnosed since 1994 and alive on 31/12/2013**

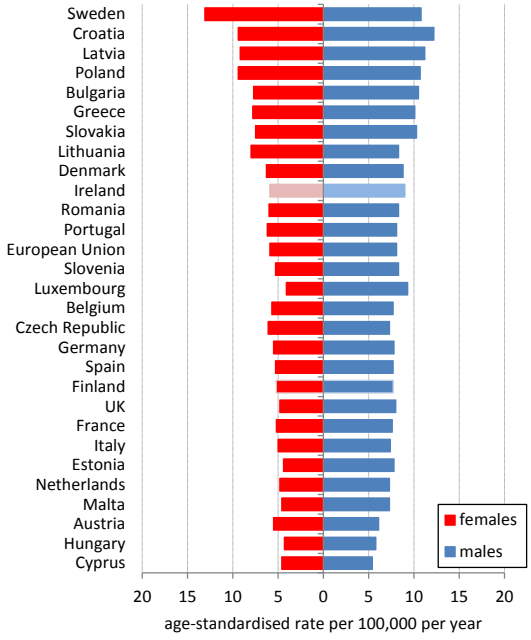
| | 1 yr | 5 yr | 20 yr |
|---|---|---|---|
| **Astrocytic** | 141 (67%) | 304 (29%) | 591 (15%) |
| *Glioblastoma* | 105 (66%) | 174 (22%) | 220 (9%) |
| *Anaplastic astrocytoma* | 11 (58%) | 29 (32%) | 69 (15%) |
| *Astrocytoma, NOS* | 14 (88%) | 52 (68%) | 181 (38%) |
| *Glioma, NOS* | 7 (70%) | 26 (44%) | 70 (22%) |
| *Other Astrocytic tumours** | 4 (67%) | 23 (66%) | 51 (42%) |
| **Oligodendroglioma** | *32 (94%)* | *131 (71%)* | *218 (56%)* |
| **Oligoastrocytoma** | *14 (93%)* | *42 (78%)* | *73 (48%)* |
| **Embryonal** | *4 (80%)* | *35 (63%)* | *88 (51%)* |
| **Ependymoma** | *8 (89%)* | *24 (89%)* | *53 (55%)* |
| **Other subtypes**** | *8 (89%)* | *19 (76%)* | *25 (54%)* |
| **Unspecified** | *12 (24%)* | *30 (13%)* | *111 (11%)* |
| **Total** | *219 (66%)* | *590 (36%)* | *1167 (20%)* |

*Figures refer to the number and proportion of all patients diagnosed within this period that were still alive on 31/12/2013 (i.e. 1 yr = diagnosed in 2013 only, 5 yr = diagnosed 2009-2013, 20 yr = diagnosed 1994-2013)*

### *International variation in incidence and mortality[9]*

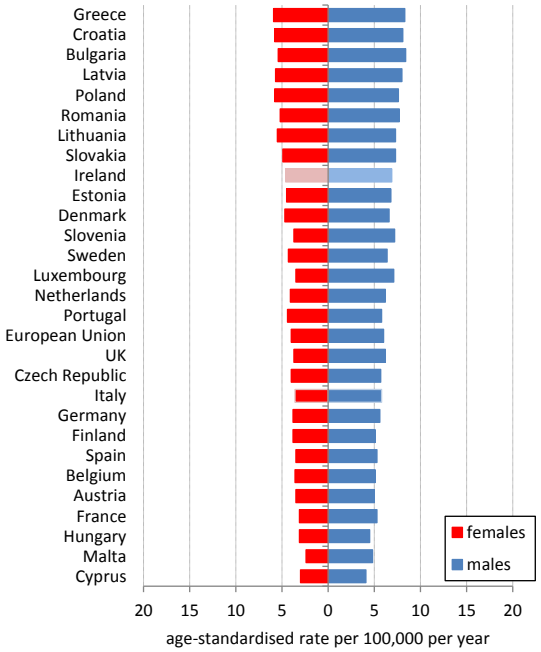
Combined brain and CNS cancer incidence in Irish males and females ranked 9th and 13th highest respectively of all 27 EU countries in 2012[8]. However rates were, in general, fairly uniform between countries and (excluding females in Sweden), rates mostly varied by less than 20% from the average EU overall rate (Figure 10). Incidence rates for Irish females were the same as the EU average and male rates were 11% higher.

**Figure 10. Estimated incidence of cancer of the brain & central nervous system, all EU countries 2012[9]**




Rankings of Irish mortality rates were similar to those for incidence with Irish males ranked 11th and Irish females 15th of 27 countries (Figure 11). Mortality rates for both sexes in Ireland were 15% higher than the EU average. Mortality/incidence ratios in Ireland (0.8 for females, 1.1 for males) were similar to the EU average (0.7 for females, 1.0 for males).

**Figure 11. Estimated mortality from cancer of the brain & central nervous system, all EU countries 2012[9]**




### *A brief note on metastatic brain tumours*

This report describes trends in primary invasive brain cancer only. However many brain tumours are secondary (metastatic), i.e. have originated elsewhere and have spread to the brain. The NCR records all notified metastatic tumours (linked to primary site) but, partly due to the difficulty in assessing the completeness of this information, it is not possible to present data on metastatic cancers in the same format as for primary cancer. However it is worth noting that between 1994 and 2013 just over 7700 patients were registered as having had cancer metastatic to the brain, 5725 of which were diagnosed within one year of the patients' primary cancer. These figures indicate that secondary brain cancer is more common than primary disease. These tumours were most commonly registered from patients that had primary lung cancer (60%) or unspecified primary disease (15%). Other sites included female breast (12%), melanoma and primary cancers of the digestive and urinary systems (4-6%).

### *References and notes*


1. National Cancer Registry. 2014. Childhood Cancer. Cancer Trends No. 23.
2. Louis DN et al. (Eds) 2007. WHO classification of tumours of the central nervous system, 4th edition. IARC, Lyon
3. All rates standardised to the European (1976) standard population.
4. Treatment data not complete for 2013 cases so treatment data for this year is not included. Only treatments administered within 1 year of diagnosis are included. Details of chemotherapy drugs provided for 2012 only.
5. Ahmed R et al 2014. Malignant gliomas: current perspectives in diagnosis, treatment, and early response assessment using advanced quantitative imaging methods. Cancer Manag Res. 6: 149–170
6. Data extracted from the WHO database (http://www-dep.iarc.fr/WHOdb/WHOdb.htm). Note, rates standardised to the world standard population.
7. Central Statistics Office. Deaths by cause and year of occurrence http://www.cso.ie/en/databases/
8. Cancer Research UK. Brain Cancer (C71), Age-Standardised 1-, 5- & 10-year net survival, adults (aged 15-99), England & Wales, 2010-2011, Data provided by London School of Hygiene & Tropical Medicine. http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/brain-tumours/survival#heading-Zero
9. Source: European Cancer Observatory (ECO), EUCAN database. Rates standardised to the European (1976) standard population. http://eco.iarc.fr/EUCAN/Cancer.aspx?Cancer=34

