Changing incidence and improved survival of gliomas

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Abstract  Background: Tumours of the central nervous system (CNS) represent a relatively rare but serious health burden. This study provides insight into the incidence and survival patterns of gliomas in the Netherlands diagnosed in adult patients during the time period 1989–2010, with a focus on glioblastoma and low-grade gliomas.

Methods: Data on 21,085 gliomas (excluding grade I tumours) were obtained from the Netherlands Cancer Registry, including tumours of the CNS without pathological confirmation. We calculated the age-standardised incidence rates and the estimated annual percentage change (EAPC) for all glioma subtypes. Crude and relative survival rates were estimated using information on the vital status obtained from the Dutch Municipal Personal Records Database.

Results: Incidence of gliomas in adults increased over time, from 4.9 per 100,000 in 1989 to 5.9 in 2010 (EAPC 0.7%, \( p < 0.001 \)). Two thirds were astrocytoma, 10% oligodendroglioma/oligoastrocytoma, 3% ependymoma and 21% were unspecified. Within the group of astrocytic tumours, the proportion of glioblastoma rose, while the proportion of anaplastic and unspecified astrocytoma decreased. Unspecified neoplasms also decreased, but this was significant only after 2005. Over the course of the study period, glioblastoma patients more often received multimodality treatment with chemotherapy concomitant and adjuvant to radiotherapy. The crude two-year survival rate of glioblastoma patients improved significantly, from 5% in the time period 1989–1994 to 15% in 2006–2010, with median survival increasing from 5.5 to 9 months. The incidence of low-grade gliomas did not change over time. Survival rates for low-grade oligodendroglial and mixed tumours show a modest improvement.

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Conclusions: The incidence rate for the total group of gliomas slightly increased, with a decrease of anaplastic and unspecified tumours and an increase of glioblastoma. Following the introduction of combined chemoradiation, two-year survival rates for glioblastoma significantly improved. Survival improved for low-grade gliomas except for low-grade astrocytic tumours.

1. Introduction

Gliomas form a heterogeneous group of tumours of neuroepithelial tissue which comprise the majority of malignancies of the central nervous system (CNS) [1–3]. On the basis of their histopathology, gliomas are classified into astrocytoma, oligodendroglioma, oligoastrocytoma (or ‘mixed’ glioma) and ependymoma, and subdivided into grade I–IV according to the World Health Organisation (WHO) grading system [4]. Gliomas represent a relatively rare but serious health burden in terms of morbidity and mortality. Despite significant advances in diagnostics and therapeutics over the past decades, prognosis for patients with high-grade gliomas (WHO grade III and IV tumours) remains dismal, with disease generally recurring even after optimal initial treatment. For instance, addition of the alkylating agent temozolomide to the therapeutic arsenal against glioblastoma (WHO grade IV astrocytoma) increased median survival of patients by a mere 2.5 months [5], or 4.6 months in those having undergone complete resection [6].

Notwithstanding their more favourable characteristics, low-grade gliomas (WHO grade I and II tumours) may eventually cause a variety of neurological symptoms including epilepsy and cognitive disorders [7], and some have a marked potential for malignant progression. Unfortunately, complete surgical removal is commonly unfeasible due to diffuse brain infiltration [8], and procedures carry the risk of causing impairment themselves. Optimal treatment strategies have long been subject of debate [9,10]. While some advocate active surveillance until progression as a reasonable option [11,12], notably in (younger) patients who experience seizures as the only symptoms of disease [13,14], recent guidelines recommend a more active approach, with surgical tumour debulking as the preferred first course of action in most cases [15,16].

On several occasions, population-based surveys have reported rising incidence of brain tumours including gliomas in adults [17,18]. These trends should, in retrospect, be largely attributed to improved detection, in particular of low-grade tumours following introduction of computed tomography (CT) and magnetic resonance imaging (MRI) [19,20], and increased efforts to obtain histopathological diagnosis [21,22]. Indeed, the observed increase did not coincide with sudden increases in mortality rates [23]. Recent years show a stabilising or even declining incidence [2,24–26]. Some caution is warranted in interpreting these findings, however, since trends are sensitive not only to developments in diagnostic and therapeutic practices, but may also be impacted on by changes in histologic criteria and revisions in classification schemes [27,28].

The present report describes the incidence and survival of CNS gliomas in adults diagnosed in the Netherlands during the time period 1989–2010. In addition, we show survival patterns for the major histological groups of glioma, thereby focusing on glioblastoma and low-grade gliomas.

2. Materials and methods

2.1. Data sources

Electronic patient records were derived from the Netherlands Cancer Registry (NCR), which covers a nation with approximately 16.6 million inhabitants. Newly diagnosed cancer patients are notified to the registry by the Dutch Pathology Network (PALGA), to which pathology departments submit their reports on histological, cytological and autopsy examinations. Additional information on patient and tumour characteristics, diagnostics and therapy is collected from hospital records by trained registry personnel of the NCR. Topography and morphology are coded according to the International Classification of Diseases for Oncology (ICD-O). Additional cases as well as case ascertainment are provided by the national hospital discharge database. The NCR lacks information on patients who are seen only by outpatient departments, and this underregistration has previously been estimated to be less than 2% [29], with missing cases mostly being elderly patients with digestive tract tumours [30].

We obtained follow-up information on vital status for all cases through linkage with the Municipal Personal Records Database (GBA). No data were available on disease progression or recurrence. The study design, data abstraction process and storage protocols were approved by the national supervisory committee of the NCR.

2.2. Selection of cases

From the NCR, we selected adult patients (≥18 years of age) with a glioma in the brain or spinal cord (topography codes C71.0–C72.9) diagnosed during
the time period 1989–2010, thereby excluding WHO grade I tumours. We defined histology subgroups by clustering ICD-O-morphology codes into the WHO classification scheme (see Table 1) [4,31]. Not otherwise specified astrocytomas (M9400) were subdivided by histological grade, and the same was done with oligoastrocytic gliomas (M9382). As 98% of all pathologically confirmed brain tumours in adults were glioma, we also included clinically diagnosed brain tumours without histopathological confirmation. The latter were grouped with gliomas with unspecified histology (M9380).

Treatment was classified as follows: biopsy only; resection only; resection + radiotherapy (RT); biopsy + RT; resection + RT + chemotherapy (CT), and biopsy + RT + CT. We lacked information on whether chemotherapy was provided concomitantly with or adjuvantly to radiotherapy.

2.3. Statistical analyses

For overall incidence of gliomas, we calculated annual rates per 100,000 person-years using the average annual population as provided by Statistics Netherlands (CBS). The rates were age adjusted through standardisation to the European standard population (European Standardised Rates, ESR), and tabulated by histology and by gender. We estimated trends in incidence by calculating the estimated annual percentage change (EAPC).

Crude survival was calculated from time of diagnosis by the Kaplan–Meier method, and we applied log-rank tests to assess differences in survival rates. For the evaluation of survival according to treatment, we excluded patients who died within 1 month following diagnosis to account for immortal time bias, as determination of treatment status involves a delay during which follow-up time is accrued [32]. For low-grade gliomas, we calculated relative five-year survival rates as the ratio of observed survival and the expected survival in the general population of corresponding sex and quinquennial age group. All statistical analyses were two-sided, with a $p$-value $< 0.05$ being considered significant. Analyses were performed using software package Stata version 12.0 (StataCorp, College Station, Texas).

3. Results

3.1. Incidence

Between 1989 and 2010, a total of 21,085 gliomas were registered in the Netherlands, with males comprising the majority across astrocytic and unspecified tumours (Table 2). Overall, the median age at diagnosis was 59 years: while this was 61 years for glioblastoma patients and 71 years for those in whom the disease was not histologically confirmed, median ages for other histologic subtypes were substantially lower. A total of 13,829 patients (66%) presented with an astrocytic tumour and of these, 9504 (69%) were diagnosed with glioblastoma. Oligodendroglial, oligoastrocytic and ependymal tumours accounted for 1519 (7%), 710 (3%) and 669 (3%) cases, respectively. Over one-fifth of brain tumours ($n = 4358$; 21%) remained unspecified, the majority of which (92%) concerned patients who did not undergo neurosurgical resection or biopsy.

The incidence rate of glioma increased from 4.9 per 100,000 inhabitants in 1989 to 5.9 in 2010 (EAPC $0.7\%$, $p < 0.001$). Within the group of astrocytic tumours, the increasing proportion of glioblastoma was accompanied by a decreasing proportion of diffuse, diffuse.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Classification for tumours in the brain and other parts of the central nervous system (CNS) based on the International Classification of Diseases for Oncology (ICD-O-3) and World Health Organisation (WHO) grade.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glioma subtype</td>
<td>Morphology code</td>
</tr>
<tr>
<td>Astrocytic tumours</td>
<td>9400–9442</td>
</tr>
<tr>
<td>Pleiomorphic xanthoastrocytoma</td>
<td>9424</td>
</tr>
<tr>
<td>Diffuse astrocytoma</td>
<td>9400/32, 9410/32–9411/32, 9420/32</td>
</tr>
<tr>
<td>Anaplastic astrocytoma</td>
<td>9401, 9400/33, 9410/33–9411/33, 9420/33</td>
</tr>
<tr>
<td>Glioblastoma</td>
<td>9400/34, 9440–9442, 9481</td>
</tr>
<tr>
<td>Gliomatosis cerebri</td>
<td>9381</td>
</tr>
<tr>
<td>Astrocytoma, not otherwise specified (NOS)</td>
<td>9400/39</td>
</tr>
<tr>
<td>Oligodendrogial tumours</td>
<td>9450–9451</td>
</tr>
<tr>
<td>Oligodendroglial glioma</td>
<td>9450</td>
</tr>
<tr>
<td>Anaplastic oligodendroglioma</td>
<td>9451</td>
</tr>
<tr>
<td>Oligoastrocytic tumours</td>
<td>9382</td>
</tr>
<tr>
<td>Oligoastrocytoma</td>
<td>9382/31–9382/32, 9382/39</td>
</tr>
<tr>
<td>Anaplastic oligoastrocytoma</td>
<td>9382/33–9382/34</td>
</tr>
<tr>
<td>Ependymal tumours</td>
<td>9391–9393</td>
</tr>
<tr>
<td>Ependymoma</td>
<td>9391, 9393</td>
</tr>
<tr>
<td>Anaplastic ependymoma</td>
<td>9392</td>
</tr>
<tr>
<td>Unspecified tumours</td>
<td>9380, 8000–8004</td>
</tr>
<tr>
<td>Glioma malignant, NOS</td>
<td>9380</td>
</tr>
<tr>
<td>Unspecified neoplasms of the brain</td>
<td>8000–8004</td>
</tr>
</tbody>
</table>
anaplastic and unspecified astrocytoma (Fig. 1). The incidence of oligodendrogliomas, oligoastrocytomas and ependymomas remained stable at 0.4 (EAPC 0.2%; \( p = 0.713 \)), 0.2 (EAPC 1.5%; \( p = 0.121 \)) and 0.2 (EAPC 1.3%; \( p = 0.120 \)) per 100,000 person-years, respectively.

The incidence rate of low-grade astrocytoma decreased between 1989 and 2010 (0.6–0.5 per 100,000 person-years; EAPC 1.2%, \( p = 0.013 \)), whereas that for low-grade oligoastrocytoma increased (0.1–0.2 per 100,000 person-years; EAPC 2.9%, \( p = 0.014 \)). Incidence rates for other low-grade gliomas remained relatively stable (oligodendroglioma: 0.2 per 100,000 person-years; ependymoma: 0.1 per 100,000 person-years), and no trend was observed for the total group.

### 3.2. Treatment for glioblastoma

Before 2004, roughly half of the glioblastoma patients were treated with surgery plus radiotherapy, while smaller proportions received surgery or radiotherapy alone. Chemotherapy was added to the multi-modal treatment regimen from 2004 onwards (Fig. 2). The proportion of patients receiving chemotherapy increased from 19% in 2004 to 43% in 2005, followed by a steady increase to almost 60% in 2010. Overall, younger patients more often received chemotherapy than elderly patients (\( p < 0.001 \); data not shown). The proportion of patients who did not receive any treatment decreased from 16% in 1989 to 7% in 2010.

### 3.3. Survival

Survival rates were related to tumour grade. Regarding astrocytic tumours, 70% of patients diagnosed with a low-grade astrocytoma were still alive after two years, while this was only 28% for those with an anaplastic tumour, and 9% for glioblastoma patients (\( p < 0.001 \); Fig. 3A). For low-grade and anaplastic oligodendrogliomas and oligoastrocytomas, proportions of surviving patients were 85% versus 52% (\( p < 0.001 \)), and 70%

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**Table 2**

Age-standardised incidence rates for primary gliomas in adult patients according to histological subtype in the Netherlands from 1989 to 2010.

<table>
<thead>
<tr>
<th>Histological group</th>
<th>Men</th>
<th>Rate</th>
<th>Women</th>
<th>Rate</th>
<th>Men and women</th>
<th>Rate</th>
<th>Median age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>12,193</td>
<td>6.8</td>
<td>8,892</td>
<td>4.5</td>
<td>21,085</td>
<td>5.6</td>
<td>59</td>
</tr>
<tr>
<td>Astrocytic tumours</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pleomorphic xanthoastrocytoma</td>
<td>29</td>
<td>0.0</td>
<td>18</td>
<td>0.0</td>
<td>47</td>
<td>0.0</td>
<td>35</td>
</tr>
<tr>
<td>Diffuse astrocytoma</td>
<td>1,043</td>
<td>0.6</td>
<td>748</td>
<td>0.4</td>
<td>1,791</td>
<td>0.5</td>
<td>42</td>
</tr>
<tr>
<td>Anaplastic astrocytoma</td>
<td>1,148</td>
<td>0.7</td>
<td>827</td>
<td>0.5</td>
<td>1,975</td>
<td>0.6</td>
<td>55</td>
</tr>
<tr>
<td>Glioblastoma</td>
<td>5,789</td>
<td>3.2</td>
<td>3,715</td>
<td>1.9</td>
<td>9,504</td>
<td>2.5</td>
<td>61</td>
</tr>
<tr>
<td>Gliomatosis cerebri</td>
<td>21</td>
<td>0.0</td>
<td>13</td>
<td>0.0</td>
<td>34</td>
<td>0.0</td>
<td>51</td>
</tr>
<tr>
<td>Astrocytoma, NOS</td>
<td>279</td>
<td>0.2</td>
<td>199</td>
<td>0.1</td>
<td>478</td>
<td>0.1</td>
<td>53</td>
</tr>
<tr>
<td>Oligodendrogliar tumours</td>
<td>851</td>
<td>0.5</td>
<td>668</td>
<td>0.4</td>
<td>1,519</td>
<td>0.4</td>
<td>47</td>
</tr>
<tr>
<td>Oligodendrogioma</td>
<td>481</td>
<td>0.3</td>
<td>392</td>
<td>0.2</td>
<td>873</td>
<td>0.2</td>
<td>44</td>
</tr>
<tr>
<td>Anaplastic oligodendrogioma</td>
<td>370</td>
<td>0.2</td>
<td>276</td>
<td>0.2</td>
<td>646</td>
<td>0.2</td>
<td>52</td>
</tr>
<tr>
<td>Oligoastrocytic tumours</td>
<td>407</td>
<td>0.2</td>
<td>303</td>
<td>0.2</td>
<td>710</td>
<td>0.2</td>
<td>47</td>
</tr>
<tr>
<td>Oligoastrocytoma</td>
<td>196</td>
<td>0.1</td>
<td>143</td>
<td>0.1</td>
<td>339</td>
<td>0.1</td>
<td>42</td>
</tr>
<tr>
<td>Anaplastic oligoastrocytoma</td>
<td>211</td>
<td>0.1</td>
<td>160</td>
<td>0.1</td>
<td>371</td>
<td>0.1</td>
<td>52</td>
</tr>
<tr>
<td>Ependymal tumours</td>
<td>380</td>
<td>0.2</td>
<td>289</td>
<td>0.2</td>
<td>669</td>
<td>0.2</td>
<td>48</td>
</tr>
<tr>
<td>Ependymoma</td>
<td>330</td>
<td>0.2</td>
<td>244</td>
<td>0.1</td>
<td>574</td>
<td>0.2</td>
<td>48</td>
</tr>
<tr>
<td>Anaplastic ependymoma</td>
<td>50</td>
<td>0.0</td>
<td>45</td>
<td>0.0</td>
<td>95</td>
<td>0.0</td>
<td>50</td>
</tr>
<tr>
<td>Unspecified neoplasms of the brain*</td>
<td>2,246</td>
<td>1.2</td>
<td>2,112</td>
<td>0.9</td>
<td>4,358</td>
<td>1.0</td>
<td>71</td>
</tr>
</tbody>
</table>

* Including glioma malignant, NOS.
versus 41% \((p < 0.001)\), respectively (Fig. 3B). Considering ependymal tumours, 86% of the patients with a low-grade ependymoma survived the first two years, and this was 46% among those diagnosed with an anaplastic ependymoma \((p < 0.001; \text{Fig. 3C})\).

Median survival rates for glioblastoma patients were associated with age \((p < 0.001)\) and improved in all age groups, mainly after 2004 (Fig. 4A). Although median survival for the total population improved from 4.8 months in 1989 to 8.9 months in 2010, this progress was most pronounced among the youngest age group (18–40 years), where median survival increased from 8.4 months to 22.4 months, with two-year crude survival having increased from 13% to 44%. For patients aged 41–55 years, 56–65 years and 66–75-years, median survival improved from 7.1 to 13.1 months, from 6.9 to 9.4 months and from 1.9 to 5.8 months, respectively.

The two-year crude survival increased from 8% to 27% (41–55 years), from 7% to 15% (56–65 years) and from 0% to 6% (66–75-years). Although median survival more than doubled in patients over the age of 75 years (from 1.7 to 3.8 months), two-year survival for these patients was only 3% in 2010.

1018 Glioblastoma patients (11%) deceased within one month after diagnosis. For the remaining patients, the addition of chemotherapy to radiotherapy following surgery (resection or biopsy) was associated with a better survival \((p < 0.001; \text{Fig. 4B})\). Among the patients who received surgery and radiotherapy with concomitant or adjuvant chemotherapy, median survival was 14.2 months, and two-year survival was 26% (not shown).

For patients who had a resection prior to radiotherapy and chemotherapy, two-year survival was 29%, with a median survival of 15.6 months, whereas this was 15% and 10.6 months for those who had a biopsy prior to chemoradiation \((\text{RT} + \text{CT})\). Two-year survival rate for patients who only had radiotherapy following resection was 8% (9.4 months median survival), and this was 4% for those who received radiation following a biopsy (5.3 months).

While the five-year relative survival rates of low-grade astrocytoma and low-grade ependymoma did not change between 1989 and 2010 (with the first showing no improvement from 2000 onwards), an improving trend is observed for low-grade oligodendrogial and mixed tumours, from 61% to 80% and from 48% to 72%, respectively (Table 3). Patients diagnosed with a low-grade ependymoma displayed the highest survival rate (84%), followed by those with an oligodendroglioma (72%). Overall, survival was strongly associated with age, with the youngest age group showing the highest survival rates across all low-grade glioma subtypes, and the oldest groups faring worst. Survival was similar for men and women.

4. Discussion

This study reports the incidence and survival of adults diagnosed with a glioma in the Netherlands from 1989 to 2010. As the data are derived from a near complete cancer registry, our analyses provide reliable estimates of their overall disease burden in the Dutch population. By accounting for unspecified neoplasms retrieved on the basis of patient discharge, we may mitigate artificial trends induced by improved imaging and histopathological examination. We cannot preclude, however, that some of these neoplasms were in fact cranial metastases mistakenly classified as primary tumours. Increased efforts to diagnostically examine asymptomatic tumours could also have influenced observed incidence trends. Although the NCR may miss some clinically diagnosed tumours, in particular histologically unverified low-grade gliomas—for which patients did not receive treatment and for which they were not admitted to hospital—we do not deem this a significant source of bias. In parallel with other population-based studies, it is difficult to distinguish actual shifts in glioma incidence rates from those due to classification changes. The WHO 2000 classification, for instance, induced a shift from anaplastic astrocytoma to glioblastoma, providing less restrictive criteria for diagnosis of the latter (i.e. with necrosis and microvascular proliferation as independently sufficient for distinguishing glioblastoma). A similar trend was expected.
Fig. 3. (A–C) Survival of patients with astrocytic, oligodendrogial, oligoastrocytic and ependymal tumours according to histological subtype.
between anaplastic oligoastrocytoma and glioblastoma following the WHO 2007 edition, which introduced glioblastoma with oligodendroglioma component [28]. The shift from grade III to grade IV tumours appears to be confirmed by our study.

The Dutch incidence rates on brain tumours appear lower than those reported by other countries, for instance the US [2], and Austria [33] and Switzerland [34] in Europe. Contrary to the US report [2], we did observe a slight increase in incidence, with differences in trends across glioma subtypes. Increases were mainly observed in astrocytic and ependymal tumours, which confirms the findings of an earlier Dutch report on gliomas [22]. Considering astrocytic tumours, rising glioblastoma incidence was accompanied by decreases in other subtypes including anaplastic astrocytomas and astrocytomas with unknown malignancy grade. Although we found no significant decrease in incidence of unspecified brain tumours over the total study period, the decreasing trend proved significant from 2005 onwards. It could be speculated that the availability of temozolomide has additionally spurred the identification of glioblastomas that would previously have remained unclassified. However, the decrease was mostly observed in those under the age of 75 years.

In glioblastoma patients, crude two-year survival rates have generally improved in recent years compared to earlier time periods. The introduction of temozolomide...
appears to mark the most significant improvement over the past decades. The advantage of administering temozolomide concurrently with and adjuvant to radiation therapy following surgery as reported in the landmark European Organisation for Research and Treatment of Cancer (EORTC) and National Cancer Institute of Canada Clinical Trials Group (NCIC) trial [5,6] has apparently translated to the general glioblastoma patient population. In our study, median survival and the proportion of patients surviving beyond two years are remarkably similar to those reported by Stupp and colleagues (14.2 months and 26% versus 14.6 months and 27%, respectively). We observed the most favourable results in the group of patients who underwent a surgical resection, either partial or complete, prior to adjuvant treatment, whereas survival was considerably worse for patients whose surgery was restricted to a biopsy. However, bearing in mind the aforementioned shifts from anaplastic gliomas to glioblastoma, part of the survival improvement in both groups should be attributed to a ‘grade migration’ effect. In addition, other developments may also have contributed to better survival, for instance the increased use of modern radiotherapy techniques such as stereotactic radiotherapy during the recent period.

Survival among patients with a low-grade oligodendroglia, oligoastrocytoma and ependymoma showed a continuous improvement over time. For those with low-grade astrocytic tumours, a slight improvement in survival was only observed in the time period 1995–2000, and survival appears to have deteriorated since. This could perhaps be explained by the conduct of trials comparing radiotherapy with and without chemotherapy during this period, after which radiotherapy alone became standard of care. The decreasing trend anyhow warrants further monitoring of low-grade astrocytoma epidemiology.

Further progress may be achieved by more sophisticated patient selection for treatment, specifically on the molecular pathogenesis of gliomas. Methylation of the promoter for the O-6-methylguanine-DNA methyltransferase gene, for instance, proved to be a prognostic marker in glioblastoma [35], indicating a higher chance of benefit from temozolomide [36,37]. In anaplastic oligodendrogliomas and oligoastrocytomas, codeletion of chromosomes 1p and 19q has been demonstrated indicative for particular sensitivity to chemotherapy [38].

Molecular studies such as gene-expression profiling have indeed shown their potential for classifying gliomas into prognostically relevant subtypes alongside histological groups [39–41]. For instance, genetic alterations may aid in distinguishing primary glioblastomas from secondary glial tumours. Next to the differences in localisation and patients’ age distribution and prognosis, tumours that arise de novo display a relatively characteristic spectrum of mutations (e.g. amplification, mutation or overexpression of the gene encoding the epidermal growth factor receptor), while secondary glioblastomas, having progressed from earlier, lower-grade astrocytic tumours, display accumulated alterations (IDH1/2 mutations) that are observed in grade II and grade III astrocytomas [42,43].

Although available data do not yet allow for detailed population-based analyses of the abovementioned developments, cancer registries are invaluable for ascertaining overall trends in incidence, survival and treatment of malignant disease including gliomas. Additional linkages with pathology databanks, clinical registries and pharmaceutical databases should result in a comprehensive source of information for the development of future clinical and aetiologic studies.

5. Conclusions

In summary, the incidence rate for the total group of gliomas including unspecified brain tumours slightly increased, with trends differing between glioma subtypes. Two-year survival rates for glioblastoma have
improved over time, mainly since the introduction of combined chemoradiation. Survival improved for low-grade gliomas except for low-grade astrocytic tumours.

**Conflict of interest statement**

None declared.

**References**


