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Are reported increases in incidence of primary CNS tumours real? An analysis of longitudinal trends in England, 1979–2003

Ramandeep S. Arora [a,*], *Robert D. Alston* [a], *Tim O.B. Eden* [b], *Edward J. Estlin* [c], *Anthony Moran* [d], *Marco Geraci* [a], *Jillian M. Birch* [a]

[a] *Cancer Research UK Paediatric and Familial Cancer Research Group, Stopford Building, University of Manchester, Oxford Road, Manchester M13 9PL, UK*

[b] *Academic Unit of Paediatric and Adolescent Oncology, University of Manchester, TCT Young Oncology Unit, Christie Hospital NHS Foundation Trust, Withington, Manchester M20 4BX, UK*

[c] *Paediatric Oncology, Royal Manchester Children's Hospital, Oxford Road, Manchester M13 9WL, UK*

[d] *North West Cancer Intelligence Service, Christie Hospital NHS Foundation Trust, Withington, Manchester M20 4BX, UK*

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ABSTRACT

Reported increases in the incidence of CNS tumours in the developed world in the 1970s to 1990s have been a cause for concern and debate. It still remains to be adequately answered whether these increases are true or an artefact of changes in diagnostic and registration practices. Using high-quality national cancer registration data, we have analysed incidence trends for each major histological subgroup of CNS tumour (2000 World Health Organisation (WHO) classification) registered in those aged 0–84 years for the whole of England during the period 1979 through 2003. 134,509 primary CNS tumours of malignant, benign and uncertain behaviour located in the brain, meninges, spinal cord, cranial nerves, other parts of the central nervous system and in the pituitary and pineal glands were registered. In summary, we present the single largest nationwide study on the longitudinal incidence trends of CNS tumours. The increase in incidence observed in the 1970s and 1980s was mainly in the young and the elderly and has now plateaued and may even be decreasing. There is however variation in trends by histology. The incidence of some histological subgroups has continued to increase until the most recent period of analysis. Much of the initial increase can be attributed to the emergence of much more widely available neuroimaging, while the most recent incidence changes for specific sub-groups of CNS tumours appear to be due to greater diagnostic specificity leading to a shift in registered categories. However, the trends for high-grade astrocytomas and other gliomas need further observation and investigation.

1. Introduction

According to global estimates, central nervous system (CNS) tumours account for 1.7% of all new cancers and 2.1% of all cancer deaths worldwide.[1] The highest incidence rates are in the developed world (Australia/New Zealand, Europe and North America) and lowest in Africa which suggests that availability of diagnostic facilities may influence recorded incidence rates in developing countries.[2] There are more than 100 distinct pathological entities reported for the CNS

* *Corresponding author:* Tel.: +44 161 2751446; fax: +44 161 2755348.
E-mail address: reemaraman@doctors.org.uk (R.S. Arora).
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tumours. Around 60% of them are malignant in behaviour[3] although even this proportion depends on registration practices which vary in the extent to which registration of non-malignant tumours occurs in each country.[4,5] Even histologically non-malignant tumours can be life-threatening as a result of their space-occupying effects, degree of local infiltration and, the tendency for some low-grade astrocytomas to undergo malignant transformation, particularly those which have received irradiation.[6]

In late 1980s and early 1990s there were several reports of increasing incidence of CNS tumours, mainly in the elderly, from Europe,[7,8] North America[9,10] and Oceania.[11] By the mid to late 1990s there were similar reports of increasing incidence of CNS tumours in children, initially from Britain[12,13] followed by other parts of Europe[14,15] and North America.[16,17] Recently studies from Asia,[18] Europe[19,20] and North America[21,22] have shown that the increasing incidence of CNS tumours overall (including children and the elderly) may be levelling off and may actually be falling.

It is generally accepted that some of the increase in incidence was not real but a result of advances in neuroimaging[23–26] and better registration of non-malignant CNS tumours.[27,28] However, there is a debate as to whether in all cases, the increases can be attributed to such an artefact of changes in diagnostic and registration practices.[29,30] This is because the incidence increases started prior to the introduction of computerised tomography (CT) scanning.[7] In addition there was not only an increase in the incidence of radiologically diagnosed CNS tumours, but also of those, albeit smaller, diagnosed clinically.[10,31] Alternate explanations proposed for the increases include greater availability of neurologists,[23] attitudinal change in the delivery of healthcare to the elderly[23,25] and increased availability of alternative imaging procedures like arteriography prior to the advent of CT.[11] The case for an artefactual increase seen elsewhere is supported by the observation of no such change in the incidence of CNS tumours in the population of Rochester, Minnesota in United States of America (USA) for the era 1935–1997 although the number of CNS tumours diagnosed over this period was relatively small (373).[32,33] Rochester, which has one of the highest reported incidence rates of CNS tumours in USA, has historically had near-complete case ascertainment, registration of benign tumours, a high autopsy rate to confirm diagnosis, greater than 95% histological confirmation of tumour type, and easy access to neurological and neurosurgical expertise. In such a setting, the effect of any artefact on incidence patterns is likely to be minimal.

Furthermore, no new environmental risk factors have been identified nor has there been an increase in any existing environmental risk factor whose presence could explain the rise in the observed incidence. So far, no consistent evidence linking exposure to mobile phones, extremely low frequency electromagnetic fields, infections and pesticides to CNS tumour development has been identified.[34,35] The heterogeneous pathologies grouped under the term CNS tumours further limit our ability to study the aetiology of individual tumour types. The recent levelling off would suggest that either the exposure to the, as yet unidentified risk factor(s), has reached its peak or that the rise in incidence was indeed artefactual.

Using high quality national cancer registration data, we present here incidence trends of primary CNS tumours in children (0–14 years), adolescents and young adults (15–24 years), older adults (25–64 years) and for the elderly (65–84 years) covering the whole of England during the period 1979 through 2003 with the aim to explore the incidence trend patterns in comparison with those seen elsewhere. Importantly, we analyse the trend for each major histological subgroup of CNS tumours (malignant and non-malignant) using the 2000 WHO classification[6] for each of the four age groups. Much of the published literature lacks such detailed information on specific histologies. The only other study which has applied the detailed 2000 WHO classification in the analysis of trends, looked at 25,258 primary CNS tumours over a shorter time period (1985–1999).[26]

2. Materials and methods

2.1. Source of data

Cancer registration in England is carried out by a network of eight population-based regional registries and the national data are collated by the Office for National Statistics in London.[36] Anonymised individual patient level national cancer registration data were obtained from the Office for National Statistics on all CNS tumours (tumour at any of the following sites: brain, meninges, spinal cord, cranial nerves, other parts of the central nervous system and pituitary and pineal glands) of malignant, benign and uncertain behaviour, newly diagnosed between 1979 and 2003. National population estimates by single year of age, gender and calendar year were supplied by the Population Estimates Unit, Office for National Statistics.

2.2. Classification

The data obtained were classified into diagnostic groups according to the WHO 2000 classification on the basis of ICD-oncology second edition (ICD-O2) morphology codes[37] and International Classification of Diseases 10th revision (ICD-10) topography codes.[38] In addition pituitary tumours and not otherwise specified/unspecified CNS tumours were also included. Metastatic tumours and those where it was uncertain if they were primary or metastatic were excluded. Also excluded were CNS lymphomas, haemopoietic neoplasms, mesenchymal non-meningothelial tumours and olfactory tumours. Details of our classification including morphology and site code allocations have been published elsewhere.[3]

2.3. Statistical methods

Age and sex specific incidence rates were calculated and expressed per 100,000 person years. All rates were adjusted to the world standard population[2] using direct methods except where specifically stated. To assess the variation in the longitudinal trends with age, the total time period was divided into five quinquennia 1979–1983, 1984–1988, 1989–1993, 1994–1998 and 1999–2003. Average annual percentage change (AAPC) along with the 95% confidence intervals (CIs) was calculated

for the entire period from 1979 to 2003 for four different age groups (0–14, 15–24, 25–64 and 65–84 years) and for each of the histological sub-groups. Those above the age of 85 were excluded because of possible under-ascertainment and often lower specificity in diagnosis. *p*-Values for variability in incidence trends by sex within each age group as well as variability among the four age groups were also calculated. SPSS, R[39] and Microsoft Excel were used for analysing the data and producing tables and graphs.

3. Results

During the period 1979 through 2003, 134,509 primary CNS tumours of malignant, benign and uncertain behaviour located in the brain, meninges, spinal cord, cranial nerves, other parts of the central nervous system, and in the pituitary and pineal glands were diagnosed and registered in England in those aged 0–84 years. The population covered, equated to 1.18 billion person years. About 69,408 of the tumours were in males (51.6%) and 65,101 in females. The overall age-standardised incidence rate steadily increased from 7.41 per 100,000 person years in 1979 to 9.73 in 1992 but has not subsequently increased (Fig. 1). Indeed, there seems to be some decrease in overall incidence since 2001. Both benign and malignant tumours show an increase in incidence while those of uncertain/borderline behaviour have decreased (Fig. 2).

Table 1 shows the incidence rates (adjusted to the standard world population) in each quinquennium for all the histological sub-groups in the WHO 2000 classification. Four main patterns have been identified:

(i) No change in incidence throughout the period – specified diffuse astrocytomas (WHO grade II – fibrillary, protoplasmic and gemistocytic), pineal parenchymal tumours, medulloblastomas, hemangioblastomas, craniopharyngiomas and chordomas.
(ii) Increasing incidence throughout each of the quinquennia – anaplastic astrocytomas (WHO grade III), glioblastomas (WHO grade IV), pilocytic astrocytomas (WHO

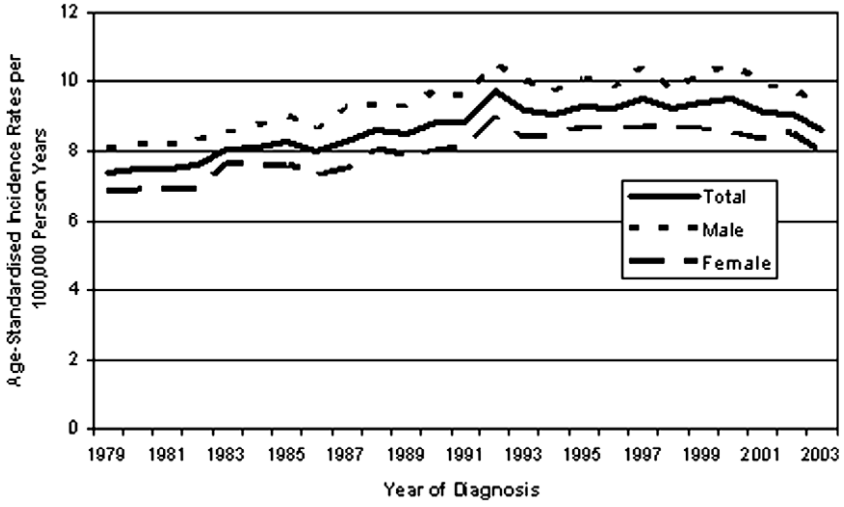

Fig. 1 – Trends in age-standardised incidence rates of primary CNS tumours in England, 1979–2003.

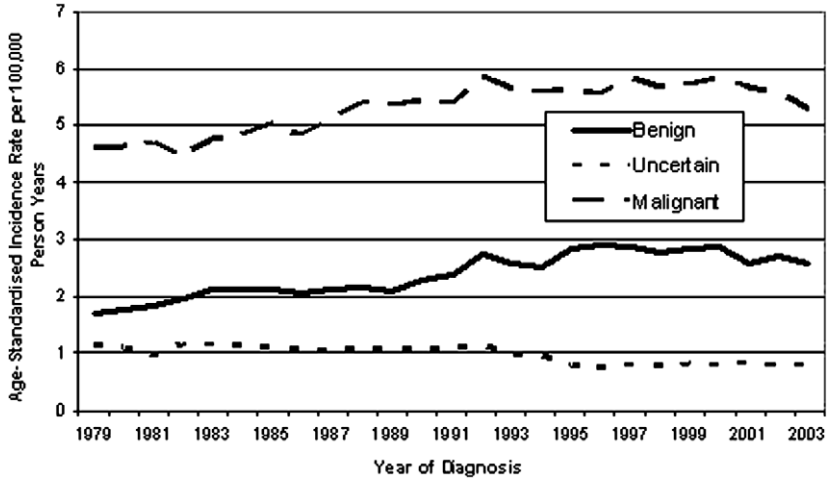

Fig. 2 – Trends in age-standardised incidence rates of primary CNS tumours in England, 1979–2003 by behaviour.

Table 1 – Incidence of primary CNS tumours in those aged 0–84 years in England from for the five quinquennia from 1979 to 2003.

	Number of cases	Age-standardised incidence rates[a] in 100,000 person years					*p*-Value
		1979–1983	1984–1988	1989–1993	1994–1998	1999–2003	
Total CNS tumours	**134,509**	**7.61**	**8.27**	**8.99**	**9.24**	**9.13**	**0.00001**
Tumours of neuroepithelial tissue (total)	**70,048**	**4.16**	**4.55**	**4.68**	**5.26**	**5.22**	**0.00001**
Astrocytic tumours	**40,327**	**2.04**	**2.21**	**2.65**	**3.33**	**3.48**	**0.00001**
Specified diffuse astrocytoma	1036	0.08	0.07	0.09	0.08	0.09	0.3
Anaplastic astrocytoma	1689	0.02	0.07	0.14	0.17	0.19	0.00001
Glioblastoma	18,309	0.47	0.53	0.82	1.60	2.05	0.00001
Pilocytic astrocytoma	1553	0.08	0.12	0.13	0.27	0.33	0.00001
Other specified astrocytoma variants	91	0.00	0.00	0.00	0.01	0.02	0.00001
Astrocytoma NOS	17,649	1.38	1.42	1.48	1.20	0.80	0.00001
Oligodendroglial tumours	**3082**	**0.17**	**0.19**	**0.19**	**0.26**	**0.30**	**0.00001**
Oligodendroglioma	2557	0.16	0.18	0.17	0.21	0.21	0.00001
Anaplastic oligodendroglioma	525	0.01	0.01	0.02	0.05	0.09	0.00001
Glioma NOS	**20,041**	**1.45**	**1.61**	**1.25**	**0.92**	**0.64**	**0.00001**
Mixed gliomas	**765**	**0.03**	**0.04**	**0.05**	**0.06**	**0.10**	**0.00001**
Ependymal tumours	**2380**	**0.17**	**0.19**	**0.20**	**0.23**	**0.25**	**0.00001**
Choroid plexus tumours	**215**	**0.02**	**0.02**	**0.02**	**0.03**	**0.03**	**0.0001**
Glial tumours of uncertain origin	**198**	**0.03**	**0.02**	**0.01**	**0.01**	**0.01**	**0.00001**
Neuronal and mixed neuronal-glial tumours	**475**	**0.01**	**0.01**	**0.02**	**0.08**	**0.09**	**0.00001**
Pineal parenchymal tumours	**543**	**0.05**	**0.04**	**0.04**	**0.06**	**0.04**	**0.67**
Embryonal tumours	**2022**	**0.21**	**0.22**	**0.23**	**0.28**	**0.28**	**0.00001**
Medulloblastoma	1707	0.21	0.21	0.22	0.20	0.20	0.65
Supratentorial primitive neuroectodermal tumour	314	0.00	0.01	0.01	0.08	0.08	0.00001
Tumours of cranial and spinal nerves							
Nerve sheath tumours	8709	0.49	0.55	0.61	0.70	0.63	0.00001
Tumours of the meninges (total)	**21,062**	**1.03**	**1.13**	**1.17**	**1.33**	**1.39**	**0.00001**
Meningioma	19,721	0.94	1.04	1.07	1.24	1.29	0.00001
Primary melanocytic lesions	28	0.001	0.003	0.002	0.004	0.003	0.27
Hemangioblastoma	1313	0.08	0.09	0.09	0.09	0.10	0.15
Germ cell tumours							
Germ cell tumours	488	0.04	0.04	0.06	0.06	0.06	0.00001
Tumours of the sellar region (total)	**13,497**	**0.78**	**0.86**	**1.04**	**1.04**	**0.85**	**0.00001**
Craniopharyngioma	1484	0.13	0.14	0.12	0.14	0.10	0.07
Pituitary tumours	12,013	0.65	0.72	0.91	0.90	0.75	0.00001
Miscellaneous tumours (total)	**485**	**0.05**	**0.04**	**0.03**	**0.02**	**0.02**	**0.00001**
Blood and lymphatic vessel tumours	346	0.04	0.03	0.02	0.01	0.01	0.00001
Chordoma	139	0.01	0.01	0.01	0.01	0.01	0.25
Unspecified tumours							
Unspecified tumours	20,220	1.06	1.09	1.41	0.83	0.95	0.00001

[a] Adjusted to world standard population.

grade I), anaplastic oligodendrogliomas (WHO grade III), mixed gliomas, neuronal and mixed neuronal-glial tumours and meningiomas.

(iii) Initial increase in incidence followed by stabilisation – oligodendrogliomas (WHO grade II), ependymal tumours, choroid plexus tumours, supratentorial primitive neuroectodermal tumours (PNETs), nerve sheath tumours, germ cell tumours and pituitary tumours.

(iv) Initial increase in incidence followed by decrease – astrocytomas not otherwise specified, gliomas not otherwise specified and unspecified tumours.

Age specific incidence rates for ages 0–4 years, and five-year age groups up to 80–84 years for each quinquennium are shown in Fig. 3. The increase in the incidence of primary CNS tumours was seen mainly in the young and the elderly and had been relatively stable for those aged 25–64 years. Within the young, the increase in incidence was the highest in the youngest (38%, 31%, 27%, 26% and 11% for 0–4, 5–9, 10–14, 15–19 and 20–24 year age groups, respectively, between the period 1979–1983 and the period 1999–2003). Among the elderly, the incidence change increased with age (15%, 24%, 54%, 115% and 176% for 60–64, 65–69, 70–74, 75–79 and 80–84 year age groups, respectively). Because of this, the age of peak incidence rate for CNS tumours shifted from 65–69 years in 1979–1983 to 75–79 years in 1999–2003.

Table 2 shows the AAPC for four different age groups (0–14, 15–24, 25–64 and 65–84 years) and for each of the histological sub-groups of the WHO 2000 classification. Overall the incidence significantly increased in all age groups with the highest increases in those aged 0–14 years and 65–84 years. Analysis by histology, however, revealed different patterns. Firstly, for those CNS tumours where incidence had not changed over 25 years (see above), there was also little or no change in each of those four age groups. Secondly, for those CNS tumours where incidence had steadily increased in 25 years or had increased and stabilised, the change was either seen in all age groups (anaplastic astrocytomas, glioblastomas, anaplastic oligodendrogliomas, mixed gliomas, neuronal and mixed neuronal-glial tumours and supratentorial PNETs) or mainly in the elderly (oligodendrogliomas, ependymal tumours, nerve sheath tumours, meningiomas and pituitary tumours) or mainly in the young (pilocytic astrocytomas, other specified astrocytoma variants including pleomorphic xanthoastrocytomas, choroid plexus tumours and germ cell tumours).

4. Discussion

This analysis of 134,509 primary CNS tumours across the whole of England from 1979 through 2003 is the single largest reported study of longitudinal trends in CNS tumour incidence. Availability of such large numbers of cases derived from a high quality national cancer registration system allows us to study in detail the variation in incidence trends by sex, age, tumour behaviour and histology. Overall, the incidence of CNS tumours in England gradually increased from 1979 until 1992 and then levelled-off. Indeed since 2001, there seems to be a slight downturn in incidence and future studies will have to establish whether this decline continues.

This increase in overall incidence was mainly due to increases in the incidence in the young (0–24 years) and the elderly (65–84 years), but in both these age groups the incidence has been stable over the last ten years of the analysis period. Looking beyond the overall trend, there are still some CNS tumours which show an increase in incidence in all age groups (anaplastic astrocytomas, glioblastomas, anaplastic oligodendrogliomas, mixed gliomas and neuronal and mixed neuronal-glial tumours); in those 0–24 years of age (pilocytic astrocytomas); and in those 25–84 years of age (meningiomas) up to and including the most recent time period.

The variation in temporal trends by age and by histology suggests that no single carcinogen (or lack of protective factor) can explain the rise and the subsequent stabilisation in

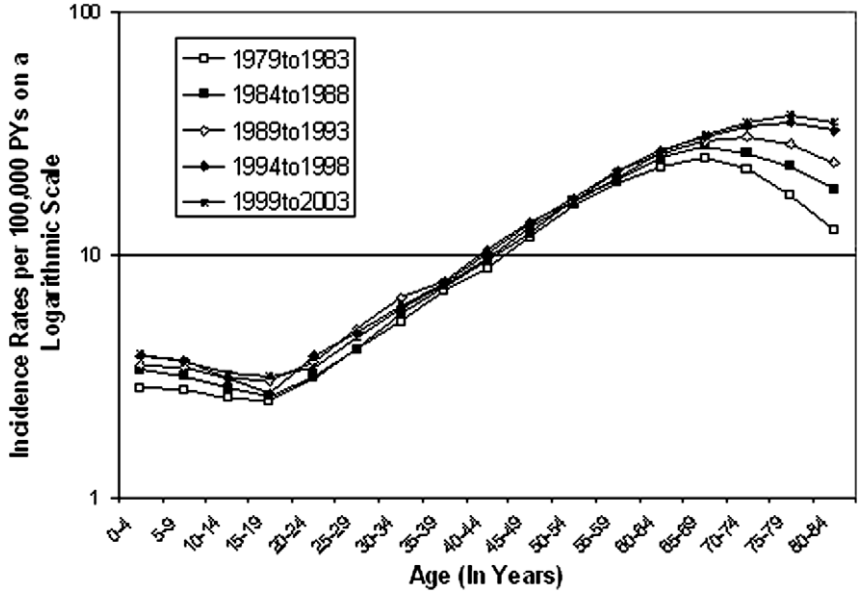

Fig. 3 – Age-specific logarithmic incidence curves of primary CNS tumours in England from 1979 to 2003.

Table 2 – Average annual percentage change (AAPC) of primary CNS tumours in England from 1979 to 2003 across four different age groups.[a, b].

	Number of cases	Average annual percentage change				
		0–14 years	15–24 years	25–64 years	65–84 years	
Total CNS tumours	**134,509**	**1.3 (1.0, 1.6)**	**0.9 (0.6, 1.3)**	**0.4 (0.3, 0.5)**	**2.5 (2.3, 2.6)**	[c]
Tumours of neuroepithelial tissue	70,048	**2.2 (1.8, 2.6)**	**1.6 (1.1, 2.1)**	**0.4 (0.3, 0.5)**	**2.9 (2.7, 3.1)**	[c]
Astrocytic tumours	40,327	**3.0 (2.4, 3.6)**	**2.2 (1.5, 3.0)**	**2.3 (2.1, 2.5)**	**6.2 (5.9, 6.5)**	[c]
Specified diffuse astrocytomas	1036	1.2 (−1.5, 4.1)	**4.3 (1.0, 7.7)**	0.2 (−0.8, 1.2)	−1.0 (−3.6, 1.7)	
Anaplastic astrocytoma	1689	**8.9 (5.3, 12.7)**	**12.2 (8.0, 16.5)**	**7.7 (6.8, 8.7)**	**8.7 (6.9, 10.4)**	
Glioblastoma	18,309	**6.5 (4.2, 8.8)**	**5.6 (3.6, 7.6)**	**7.8 (7.5, 8.1)**	**11.8 (11.4, 12.3)**	[c]
Pilocytic astrocytoma	1553	**8.4 (7.4, 9.5)**	**8.4 (6.4, 10.5)**	**4.5 (2.6, 6.3)**	−0.4 (−4.4, 3.9)	[c]
Other specified astrocytoma variants	91	**19.5 (11.5, 28.0)**	**22.0 (11.3, 33.6)**	2.8 (−2.5, 8.5)	16.7 (−3.7, 41.4)	[c]
Astrocytoma NOS	17,649	**−1.7 (−2.5, −1.0)**	**−1.2 (−2.1, −0.3)**	**−2.7 (−3.0, −2.5)**	**−1.0 (−1.4, −0.6)**	[c]
Oligodendroglial tumours	3082	−1.6 (−4.3, 1.2)	1.6 (−0.6, 3.8)	**3.4 (2.8, 4.0)**	**5.6 (4.0, 7.2)**	[c]
Oligodendroglioma	2557	**−3.5 (−6.5, −0.5)**	0.2 (−2.1, 2.5)	**1.6 (1.0, 2.3)**	**3.3 (1.7, 5.0)**	
Anaplastic oligodendroglioma	525	**10.8 (1.9, 20.5)**	**16.3 (6.8, 26.6)**	**14.8 (12.7, 16.9)**	**18.8 (13.3, 24.5)**	
Glioma NOS	20,041	**1.2 (0.2, 2.2)**	**−4.0 (−5.4, −2.6)**	**−6.1 (−6.4, −5.8)**	**−1.1 (−1.3, −0.8)**	[c]
Mixed gliomas	765	3.4 (−1.2, 8.3)	**8.3 (3.7, 13.1)**	**6.3 (5.0, 7.7)**	**8.3 (4.9, 11.8)**	
Ependymal tumours	2380	0.8 (−0.4, 2.0)	1.56 (−0.2, 3.4)	**2.8 (2.1, 3.6)**	**5.7 (3.8, 7.6)**	[c]
Choroid plexus tumours	215	**6.7 (3.6, 9.8)**	2.5 (−4.2, 9.7)	0.2 (−2.9, 3.3)	−0.3 (−7.7, 7.7)	[c]
Glial tumours of uncertain origin	198	−3.5 (−8.0, 1.1)	**7.2 (0.5, 14.5)**	**−9.5 (−12.2, −6.9)**	−1.1 (−6.7, 4.8)	[c]
Neuronal and mixed neuronal-glial tumours	475	**14.6 (10.8, 18.6)**	**14.2 (10.4, 18.2)**	**11.3 (8.9, 13.8)**	**9.1 (3.3, 15.2)**	
Pineal parenchymal tumours	543	0.1 (−2.4, 2.6)	−2.2 (−5.1, 0.7)	0.0 (−1.7, 1.7)	**4.4 (1.1, 7.8)**	
Embryonal tumours	2022	**1.4 (0.6, 2.1)**	**2.1 (0.4, 3.8)**	**2.8 (1.3, 4.3)**	**8.2 (1.5, 15.3)**	
Medulloblastoma	1707	−0.2 (−1.0, 0.6)	−0.9 (−2.7, 0.9)	0.5 (−1.1, 2.1)	2.5 (−5.4, 11.2)	
Supratentorial primitive neuroectodermal tumour	314	**16.6 (13.1, 20.2)**	**20.4 (14.0, 27.2)**	**13.5 (9.3, 18.0)**	**17.3 (4.3, 32.0)**	
Other embryonal tumours	1					
Tumours of cranial and spinal nerves						
Nerve sheath tumours	8709	**−4.6 (−6.2, −3.0)**	0.4 (−0.9, 1.8)	**2.2 (1.8, 2.6)**	**1.5 (0.9, 2.2)**	[c]
Tumours of the meninges	21,062	1.8 (−0.8, 4.5)	−0.6 (−0.9, 2.1)	**1.2 (1.0, 1.5)**	**2.9 (2.6, 3.3)**	[c]
Meningioma	19,721	1.0 (−1.8, 3.9)	0.9 (−0.9, 2.8)	**1.3 (1.0, 1.5)**	**3.0 (2.7, 3.3)**	[c]
Primary melanocytic lesions	28	8.4 (−2.8, 20.8)		−3.9 (−10.6, 3.3)	**24.3 (−2.1, 57.9)**	
Hemangioblastoma	1313	4.2 (−3.6, 12.6)	−0.3 (−3.0, 2.5)	0.6 (−0.2, 1.5)	0.4 (−1.4, 2.3)	
Germ cell tumours						
Germ cell tumours	488	**3.0 (1.0, 5.1)**	**6.0 (3.5, 8.6)**	0.3 (−2.2, 2.9)	−1.4 (−7.5, 5.1)	[c]
Tumours of the sellar region	13,497	−0.2 (−1.5, 1.2)	−0.2 (−1.2, 0.7)	**0.5 (0.2, 0.8)**	**3.1 (2.6, 3.6)**	[c]
Craniopharyngioma	1484	−0.4 (−1.8, 1.1)	**−2.1 (−4.0, 0.0)**	−0.8 (−1.8, 0.2)	0.9 (−1.0, 2.9)	
Pituitary tumours	12,013	0.7 (−2.6, 4.2)	0.3 (−0.8, 1.4)	**0.6 (0.3, 0.9)**	**3.3 (2.8, 3.8)**	[c]
Miscellaneous tumours	485	**−6.39 (−11.3, −1.2)**	**−10.3 (−14.8, −5.6)**	**−4.3 (−5.8, −2.7)**	−1.9 (−4.6, 0.8)	
Blood and lymphatic vessel tumours	346	**−11.9 (−18.0, −5.4)**	**−12.2 (−17.4, −6.6)**	**−4.8 (−6.6, −3.0)**	−3.3 (−6.8, 0.2)	
Chordoma	139	**14.8 (−0.8, 33.0)**	−5.0 (−13.5, 4.4)	−2.7 (−5.7, 0.3)	0.1 (−4.0, 4.5)	
Unspecified tumours						
Unspecified tumours	20,220	**−2.5 (−3.6, −1.5)**	−0.7 (−2.0, 0.6)	**−1.9 (−2.2, −1.6)**	**1.4 (1.1, 1.6)**[c]	[c]

[a] AAPC was not reported for groups of insufficient size.

[b] Statistically significant AAPC are in bold ($p < 0.05$) and 95% CI are given in parentheses.

[c] The difference in AAPC across the four age groups is statistically significant ($p < 0.05$).

incidence. Prolonged exposure to radiofrequency signals from mobile phones or occupational electric and magnetic fields, which have been under investigation,[34,35] are unlikely to have contributed in a major way specifically to the increase of incidence seen only in the elderly or the young. If the increase in incidence in the young is the result of exposure to a tumourigenic factor in pregnancy or early childhood then the latent period would have to be very short to produce such an effect. Studies which have looked at maternal occupation during pregnancy, paternal occupation during peri-conceptional period, maternal exposure to tobacco smoke, N-nitroso compounds in household water during pregnancy and proximity of home address at birth to high voltage power lines have not found a consistent link or a dose-risk relationship.[40–47] Clearly the aetiology of the majority of CNS tumours is still unknown and these arguments will need to be revisited as our understanding increases.

In the absence of an identifiable causative factor, is there an alternative explanation for the continuing rise of some CNS tumours? Some of the answer probably lies in the observation of a decrease in incidence in the last ten years of CNS tumours characterised by lack of specificity for behaviour (CNS tumours of unknown/borderline behaviour, Fig. 2) or histology (e.g. unspecified CNS tumours, and gliomas not otherwise specified, Table 1). This would suggest that improvements in neurosurgical techniques and developments in neuropathology have enabled more specific diagnosis to be made leading to a shift of tumours previously diagnosed as "not otherwise specified" or "unspecified" to more specific histologies and registered as such. Data on CNS tumours from the European Automated Childhood Cancer Information System show an increasing proportion of microscopically verified CNS tumours over time leading to a decrease in the "not specified" category.[48] Included among tumours that are now being increasingly recognised, are oligodendroglial tumours and mixed gliomas (using 1p/19q chromosomal loss as a diagnostic tool)[49] and neuronal tumours like central neurocytomas where diagnosis is assisted by electron microscopy and immunohistochemistry.[50] However, there is an increase in astrocytic tumours overall and shift alone from astrocytoma not otherwise specified to anaplastic astrocytoma or glioblastoma cannot explain the increase.

There is another interesting facet to the trends of these groups of less specific CNS tumours. As seen in Table 1 their incidence actually increased for the initial period of the analysis (along with most other histological sub-groups of CNS tumours) before declining. This would imply that the initial increase was a result of a factor which affected all groups. It has been proposed elsewhere that a steep increase in the use of CT scan imaging of the head, particularly in the elderly, accounted for a large part of the observed increase in incidence seen in the USA and Nordic countries during the 1970s and 1980s.[23,25,31,51] Our observations support this, as elderly patients with an underlying primary CNS tumour who present with focal neurological symptoms or after accidents are far more likely previously to have been clinically (mis)diagnosed as having cerebrovascular disease or transient ischaemic attack without the benefit of neuroimaging.[52] This argument can be extrapolated to low-grade astroglial and neuronal tumours as well. Smith et al. have attributed the increase in incidence seen in low-grade glial lesions in the brain stem in children to changes in detection and/or reporting of childhood CNS tumours during the mid-1980s in USA.[24] Another consequence of the widespread availability and use of improved neuroimaging has been the diagnosis of slow growing low-grade CNS tumours at an earlier age. In our study the median age at diagnosis for pilocytic astrocytoma decreased from 13 years in the period 1979–1983 to 10 years from 1999 to 2003 (data not shown).

The increase in high-grade astrocytomas (anaplastic astrocytomas and glioblastomas) and high-grade gliomas (anaplastic oligodendrogliomas) is more difficult to interpret. The increase is not restricted to children or the elderly but has happened across all age groups (Table 2) and so cannot be simply attributed to increased availability of neuroimaging or a change in attitude towards the elderly. Due to the aggressive nature and poor outlook of these tumours, they are unlikely to be under diagnosed or picked up coincidentally. As distinct and well-recognised malignant pathological entities, the incidence of this group of CNS tumours is unlikely to be affected by changes in classification or registration practices, although advances in neurosurgery and neuropathology would lead to increased specificity and some shift between tumour categories.

Studies from Europe[19,20] and USA[53] have reported continuing increase of high-grade astrocytomas and gliomas in the 1990s and early part of the 21st century. Lönn et al. reported that the increase in the incidence of glioblastoma from 1993 to 1998 seen in the Nordic countries was confined to those aged 60–79 years with no change in those aged 20–59 years.[19] On the other hand, the increase in incidence of high-grade astrocytomas in Netherlands from 1989 to 2003 was seen in those aged 15–44 years as well as those above 65 years of age with no significant change in adults aged 45–64 years.[20] Finally, McCarthy et al., have recently reported continuing increases in the incidence of anaplastic oligodendroglioma in those aged 20–64 years from USA.[53] Our analysis shows that the increase of high-grade astrocytomas and gliomas in the most recent period is not restricted to those aged 65–84 years (Fig. 4). All these factors make it difficult to dismiss the increase in incidence in high-grade astrocytomas and other gliomas as an artefact. This is a group of tumours for which aetiological studies may yet yield some clues to their changing incidence.

5. Conclusion

In summary, we present the single largest study on the longitudinal trends of CNS tumours derived from data obtained from a high quality national cancer registration system. The overall increase of incidence seen in CNS tumours in England in 1970s and 1980s was mainly in the young and the elderly and has now levelled off and may be decreasing. There is however variation in these trends by histology and the incidence of some histological sub-groups has continued to increase until the most recent period of analysis. Much of the initial increase can be attributed to the emergence of widely available neuroimaging, while more recent changes in trends

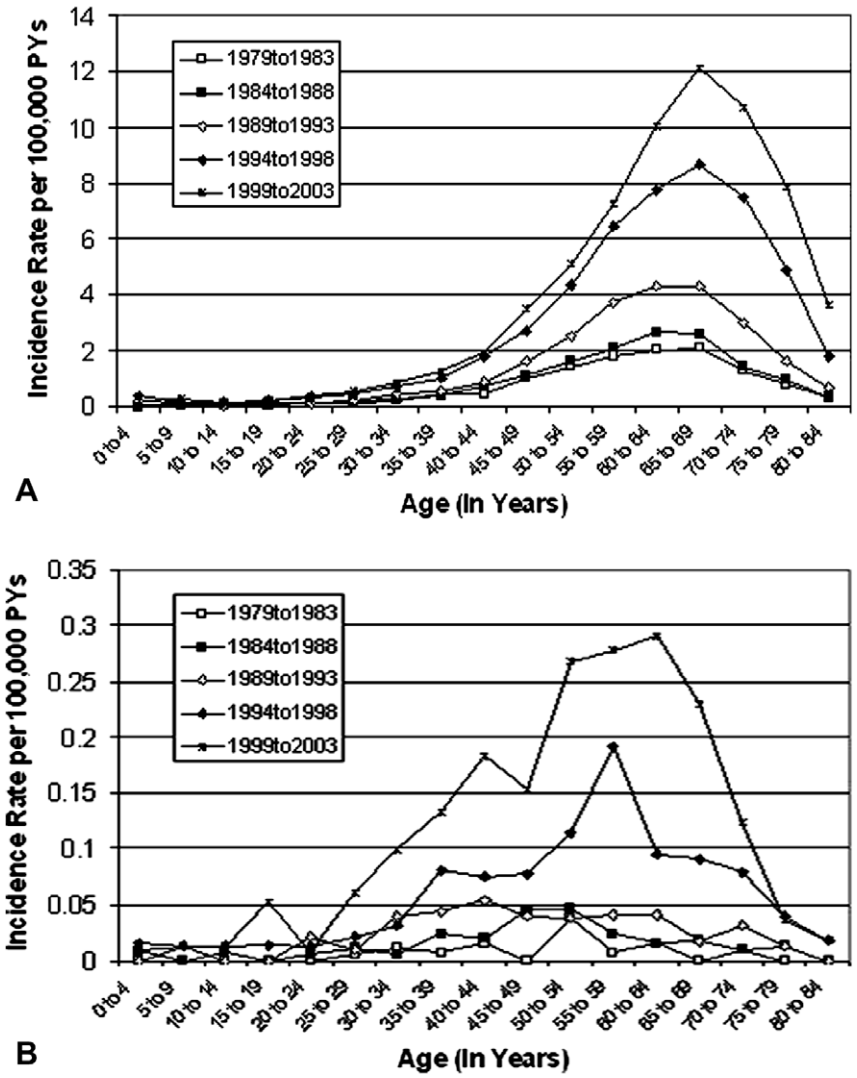

Fig. 4 – Age-specific incidence curves of (A) high-grade astrocytomas, and (B) high-grade oligodendrogliomas in England from 1979 to 2003.

of specific sub-groups of CNS tumours is likely to be as a result of increased specificity of diagnosis leading to a shift in registered categories. However, the trends of high-grade astrocytomas and gliomas as well as pilocytic astrocytomas need further observation and investigation.

Conflict of interest statement

None declared.

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