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The incidence of major subtypes of primary brain tumors in adults in England 1995-2017

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Abstract

Background. Primary brain tumors are a complex heterogenous group of benign and malignant tumors. Reports on their occurrence in the English population by sex, age, and morphological subtype and on their incidence are currently not available. Using data from the National Cancer Registration and Analysis Service (NCRAS), the incidence of adult primary brain tumor by major subtypes in England will be described.

Methods. Data on all adult English patients diagnosed with primary brain tumor between 1995 and 2017, excluding spinal, endocrinal, and other CNS tumors, were extracted from NCRAS. Incidence rates were standardized to the 2013 European Standard Population. Results are presented by sex, age, and morphological subtype.

Results. Between 1995 and 2017, a total of 133 669 cases of adult primary brain tumor were registered in England. Glioblastoma was the most frequent tumor subtype (31.8%), followed by meningioma (27.3%). The age-standardized incidence for glioblastoma increased from 3.27 per 100 000 population per year in 1995 to 7.34 in men in 2013 and from 2.00 to 4.45 in women. Meningioma incidence also increased from 1.89 to 3.41 per 100 000 in men and from 3.40 to 7.46 in women. The incidence of other astrocytic and unclassified brain tumors declined between 1995 and 2007 and remained stable thereafter.

Conclusion. Part of the increase in the incidence of major subtypes of brain tumors in England could be explained by advances in clinical practice including the adoption of new diagnostic tools, classifications and molecular testing, and improved cancer registration practices.

Key Points

1. Between 1995 and 2017, the incidence of glioblastomas and meningiomas increased in England.
2. Primary CNS lymphoma also showed a notable increase.
3. Other astrocytic and unclassified brain tumors declined.

Primary brain tumors are an uncommon and complex group of benign and malignant neoplasms. These tumors are diverse in terms of their morphology, topography, molecular biology, and clinical behavior. The World Health Organisation (WHO, 2016) Classification of Tumours of the Central Nervous System (CNS WHO) grouped these tumors into multiple histologic subtypes.[1] Estimating the burden of brain tumors in the population and evaluating their incidence requires consideration of their heterogeneity according to morphological subtype, sex, and age, as their prognosis varies by these factors.[2]

Brain, spinal, and central nervous system (CNS) tumors are relatively uncommon with 11 444 new cases being recorded in 2016 in the United Kingdom (UK).[3] CNS tumors include those of the brain, spinal cord, meninges, intracranial endocrine glands, and other parts of the CNS. These

Importance of the Study

This is the first study to report the incidence of brain tumor subtypes in England. The information presented will enable us to better understand their burden in the population, and ultimately as registration data become more detailed, to use these data to improve cancer services for these patients.

tumors accounted for 3% of all cancer cases in the UK in 2016[3] and are more frequent in men than women.[4] These UK statistics are provided by Cancer Research UK which gathers data directly from the health systems or governments in England, Scotland, Wales, and Northern Ireland.

Between 1970 and 1990, the incidence has most often been reported overall for CNS tumors combined or for gliomas alone. Results from large-scale cohort and population-based studies in the United States, Japan, and Europe have found variable patterns of incidence trends for brain tumors. Some studies, particularly those in the Far East countries, have shown the incidence of brain tumors is either slightly decreasing or levelling-off,[5–7] while others, mostly in Northern Europe,[8] have found an increasing incidence.

So far, reports on the epidemiology of brain tumors in England are few and lack detail on tumor type, particularly when compared with those from the United States and other European countries. Using the English Cancer Registry and other established databases, this study aims to describe the incidence of primary brain tumors for the main morphological subtypes, including benign and malignant tumors, in adults between 1995 and 2017.

Materials and Methods

Data

In this analysis, primary brain tumors were defined as neoplasms that originate from intracranial tissues and the meninges, varying in their behavior. Data on spinal tumors, endocrinal tumors, tumors of the CNS external to the brain, and metastatic tumors were excluded. Data on meningiomas and primary brain lymphomas were included, as they are considered significant primary brain tumor subtypes.

Data on all adult patients (aged 18 years or over) diagnosed with primary brain tumors in England between January 1, 1995 and December 31, 2017 were extracted from the Cancer Registry—the National Cancer Registration and Analysis Service (NCRAS) within Public Health England (PHE) in England. Patients were identified as diagnosed with primary brain tumors using the International Classification of Diseases [version 10] (ICD-10) tumor sites C70, C71, D32, D33, D42, and D43. For those diagnosed with primary CNS lymphoma, ICD-10 code site was used along with the morphology codes for lymphoma. Other inclusion criteria were patients being resident in England, having a complete tumor registration, and known sex. The brain tumor morphological subtypes considered in this study were based on the 2016 CNS WHO, and by most common types: glioblastoma, other astrocytoma (excluding glioblastoma), meningioma, oligodendroglioma, embryonal tumors, ependymomal tumors, oligoastrocytoma, primary CNS lymphoma, malignant glioma, unclassified malignant, unclassified benign, unclassified uncertain, and other. The subtype "other" includes brain tumor morphologies that could not be assigned to any of the above. These brain tumor subtype groups were based on morphology and not tumor behavior. Categorization of the brain tumor subtypes is shown in Table 1. All tumors extracted from NCRAS were analyzed irrelevant of their pathological confirmation were included. Metastatic tumors were not included in the analysis.

Incidence Rates Analysis

For each brain tumor subtype, the age-standardized incidence rates per 100 000 person-years were calculated to the European Standard Population (ESP 2013). This is a set of population weights that are commonly used to compare incidence rates in European populations. These weights are more similar to the European population than the World Standard Population weights which might be used in studies of other areas of the world. Male to female incidence rate ratios were calculated by year of diagnosis, age, and sex for each of the brain tumor subtypes. Age-specific incidence rates were calculated in 5-year age groups in adults (aged 15 years or over) for males and females. Apart from age-standardization, we did not attempt statistical modeling of trends in incidence, aiming in this first study to describe the actual data over time.

Ethical Approval

NCRAS has approval from the Confidentiality Advisory Group of the National Health Service Health Research Authority to carry out surveillance using the data they collect on all cancer patients under section 251 of the NHS Act 2006. Separate ethical approval for this study was therefore not required.

Results

Patient and Tumor Characteristics

Between 1995 and 2017, a total of 133 669 adult primary brain tumor cases, excluding spinal, endocrinal, and other CNS tumors, were registered in England. There

Table 1 Categorization of Brain Tumor Subtypes Based on Tumor Morphologies

Brain Tumor Subtypes	Morphology Codes
Glioblastoma (GBM)	9440-9442, 9445
Meningioma	9530-9539
Other astrocytic tumors (excluding GBM)	9381, 9384, 9400-9411, 9420-9421, 9424, 9425
Oligodendroglial tumors	9450-9451
Primary CNS lymphoma	9590-9596, 9611-9728, 9735-9766, 9970-9971
Ependymal tumors	9383, 9391-9394
Oligoastrocytoma	9382
Embryonal tumors	9470-9477, 9490, 9500-9501, 9508
Malignant glioma	9380
Unclassified neoplasm, malignant	8000/3[a]
Unclassified neoplasm/tumor cells, benign	8000/0[a], 8001/0[a]
Unclassified neoplasm/tumor cells, uncertain whether benign or malignant	8000/1[a], 8001/1[a]
Other brain tumors	Uncategorized morphologies with recorded site codes C70-71, D32-33, D42-43

[a]Behavior coded by /0 for benign tumors, /1 for unspecified, borderline, or uncertain behavior, and /3 for malignant tumors.

were 65 708 cases in men (49%) and 68 259 in women (51%) (Table 2). The mean age at diagnosis was 62 years. The number of diagnosed brain tumors increased gradually over the 23-year period, from 4471 cases in 1995 to 7580 in 2017.

Around a third of all patients were diagnosed with the most aggressive brain tumor subtype glioblastoma (WHO grade IV) (n = 42 478, 31.8%), followed by the least aggressive subtype meningiomas (27.3%), and other astrocytic tumors (9.4%) (Table 3). The unclassified subtypes, ie, without a known morphology, including malignant glioma, represented 21.0% of all brain tumor diagnoses. Overall, most of the brain tumors were considered malignant (64.2%).

The number of malignant primary brain tumor diagnoses changed over time for specific tumor sites, particularly in the frontal (C70.1) and temporal lobes (C70.2) which increased by a factor of 2.6 and 3.3, respectively. Over the same period, there was a decrease in the numbers recorded for unspecified site (C71.9) (Figure 1). Meningiomas can be malignant or benign, however, in this cohort, it can be seen in Figure 1 that the vast majority were of benign tumor behavior (site code D32—benign neoplasms of cerebral meninges/meninges, unspecified). Also, the number of cases increased over the study period peaking at >2000 cases in 2015. A different picture was seen for the malignant meningiomas (site code C70) where cases remained very low and below 50 cases in 2015.

Incidence Analyses

Over the 23-year period from 1995, the number of primary brain tumor cases recorded in adults increased each year (Table 2). This overall increase in primary brain tumor incidence was examined further by morphological subtype, sex, and age.

Most common brain tumor subtypes.—The most common brain tumor subtypes were glioblastoma, other astrocytoma (excluding glioblastoma), meningioma, and oligodendroglioma. The age-standardized and age-specific incidence rates for these tumors are shown in Figures 2a–d and 3a–d, respectively. The age-standardized incidence for glioblastoma increased from 3.27 per 100 000 population per year to 7.34 in men and from 2.00 to 4.45 in women (Figure 2a). By 2017, the male to female incidence ratio was 1.64:1.00. The age-specific incidence rate for glioblastoma increased continually with age, peaking at 65-74 years, and dropping after 75 years for both men and women (Figure 3a). Overall, the age-specific incidence of glioblastoma did not change over this time except to increase in the 60- to 74-year and over 75-year age groups.

The age-standardized incidence for other astrocytic tumors declined between 1995 and 2007 from 2.50 to 1.25 per 100 000 in males and from 1.65 to 0.79 in females, remaining stable thereafter (Figure 2b). Compared with the age-specific incidence curve for glioblastoma, other astrocytoma subtypes showed a gradual increase with age peaking at 30-39 and 65-74 years and with incidence falling after 75 years (Figure 3b).

Meningioma incidence rates also increased from 1.89 to 3.41 per 100 000 in men and from 3.40 to 7.46 in women (Figure 2c), with a sharper increase noticed in 2011. Rates were low and differed slightly in the age groups 15-29, but increased in each of the older age groups in both males and females, becoming highest in the over 75-year olds (Figure 3c).

Overall, there was a slight increase in the age-standardized incidence over time for oligodendroglioma (Figure 2d). For both sexes, the age-specific incidence curve increased sharply until 35-39 years, flattened out until 65-69 years, and then decreased with advancing age thereafter (Figure 3d). About 47% of the diagnosed adults were aged between 35 and 54 years.

Table 2 Patient Characteristics of 133 669 Patients Diagnosed With Primary Brain Tumor in England, 1995-2017

Variables	Groups	No. of Patients	(%)
Sex	Male	65 559	(49.05)
	Female	68 110	(50.95)
Age at diagnosis	Mean (SD) 62.31 (16.72)		
Age group	18-24	2617	(1.96)
	25-34	7085	(5.30)
	35-44	11 687	(8.74)
	45-54	19 000	(14.21)
	55-64	26 888	(20.12)
	65-74	31 543	(23.60)
	74-84	25 072	(18.76)
	85+	9777	(7.31)
Year of diagnosis	1995	4471	(3.34)
	1996	4502	(3.37)
	1997	4728	(3.54)
	1998	4640	(3.47)
	1999	4845	(3.62)
	2000	5116	(3.83)
	2001	5021	(3.76)
	2002	5079	(3.80)
	2003	4986	(3.73)
	2004	5131	(3.84)
	2005	5294	(3.96)
	2006	5355	(4.01)
	2007	5654	(4.23)
	2008	6114	(4.57)
	2009	6129	(4.59)
	2010	6183	(4.63)
	2011	6325	(4.73)
	2012	6762	(5.06)
	2013	7482	(5.60)
	2014	7221	(5.40)
	2015	7587	(5.68)
	2016	7464	(5.58)
	2017	7580	(5.67)
Quintile of deprivation	1—Least	28 900	(21.62)
	2	29 589	(22.14)
	3	27 728	(20.74)
	4	25 051	(18.74)
	5—Most	22 401	(16.76)
Death certificate	Recorded	4599	(3.44)
	Not recorded	129 070	(96.56)

Less common brain tumor subtypes.—The less common brain tumor subtypes were embryonal tumors, ependymomal tumors, oligoastrocytomas, and primary CNS lymphomas. The age-standardized and age-specific incidence rates for these tumors are shown in Figures 2e–h and 3e–h, respectively. These tumors were slightly more frequent in men than in women. During the period 1995-2017, there was a small decrease in the age-standardized incidence rates for embryonal tumors (Figure 2e) and the opposite trend for ependymomal tumors (Figure 2f). The embryonal tumors were common in young adults as shown in the age-specific

Table 3 General Tumor Characteristics of 133 669 Patients Diagnosed With Primary Brain Tumor in England, 1995-2017

Variables	Groups	No. of Patients	(%)
Brain tumor subtype	Glioblastoma (GBM)	42 478	(31.78)
	Meningioma	36 493	(27.30)
	Other astrocytic tumors (excluding GBM)	12 506	(9.36)
	Oligodendroglial tumors	4368	(3.27)
	Primary CNS lymphoma	2661	(1.99)
	Ependymal tumors	1368	(1.02)
	Oligoastrocytoma	1258	(0.94)
	Embryonal tumors	647	(0.48)
	Malignant glioma	11 458	(8.57)
	Other brain tumors	3873	(2.90)
	Unclassified neoplasm, malignant	8027	(6.01)
	Unclassified neoplasm/tumor cells, benign	1589	(1.19)
	Unclassified neoplasm/tumor cells, uncertain whether benign or malignant	6943	(5.19)
Behavior	Malignant	85 775	(64.17)
	Benign	35 320	(26.42)
	Malignant, uncertain whether primary or metastatic	112	(0.08)
	Uncertain	12 462	(9.32)
Tumor site	C70.0 Cerebral meninges	1078	(0.81)
	C70.9 Meninges, NOS	511	(0.38)
	C71.0 Cerebrum	4838	(3.62)
	C71.1 Frontal lobe	19 274	(14.42)
	C71.2 Temporal lobe	14 201	(10.62)
	C71.3 Parietal lobe	12 110	(9.06)
	C71.4 Occipital lobe	2836	(2.12)
	C71.5 Ventricle, NOS	559	(0.42)
	C71.6 Cerebellum, NOS	1461	(1.09)
	C71.7 Brain stem	1016	(0.76)
	C71.8 Overlapping lesion of brain	4998	(3.74)
	C71.9 Brain, NOS	23 113	(17.29)
	C72.8 Overlapping lesion of brain and other parts of central nervous system	41	(0.03)
	C72.9 Nervous system, NOS	195	(0.15)
	D32.0 Benign neoplasm of cerebral meninges	26 640	(19.93)
	D32.9 Benign neoplasm of meninges, unspecified	7144	(5.34)
	D33.0 Benign neoplasm of brain, supratentorial	639	(0.48)
	D33.1 Benign neoplasm of brain, infratentorial	184	(0.14)
	D33.2 Benign neoplasm of brain, unspecified	768	(0.57)
	D33.9 Benign neoplasm of central nervous system, unspecified	44	(0.03)
	D42.0 Neoplasm of uncertain behavior of cerebral meninges	2162	(1.62)
	D42.9 Neoplasm of uncertain behavior of meninges, unspecified	500	(0.37)
	D43.0 Neoplasm of uncertain behavior of brain, supratentorial	2528	(1.89)
	D43.1 Neoplasm of uncertain behavior of brain, infratentorial	1115	(0.83)
	D43.2 Neoplasm of uncertain behavior of brain, unspecified	5600	(4.19)
	D43.9 Neoplasm of uncertain behavior of central nervous system, unspecified	114	(0.09)
Tumor size	Known	6590	(4.85)
	Unknown	127 079	(95.07)

Table 3 Continued

Variables	Groups	No. of Patients	(%)
Basis of diagnosis	0 Death certificate only	3546	(2.65)
	Non-microscopic	44 849	(33.55)
	1 Clinical—diagnosis made before death	8579	(6.42)
	2 All clinical investigation using diagnostic techniques without tissue diagnosis	32 709	(24.47)
	4 Specific tumor markers	15	(0.01)
	Microscopic	85 359	(63.86)
	5 Cytology	163	(0.12)
	6 Histology of a metastasis	69	(0.05)
	7 Histology of a primary tumor	85 127	(63.68)
	9 Unknown	3461	(2.59)

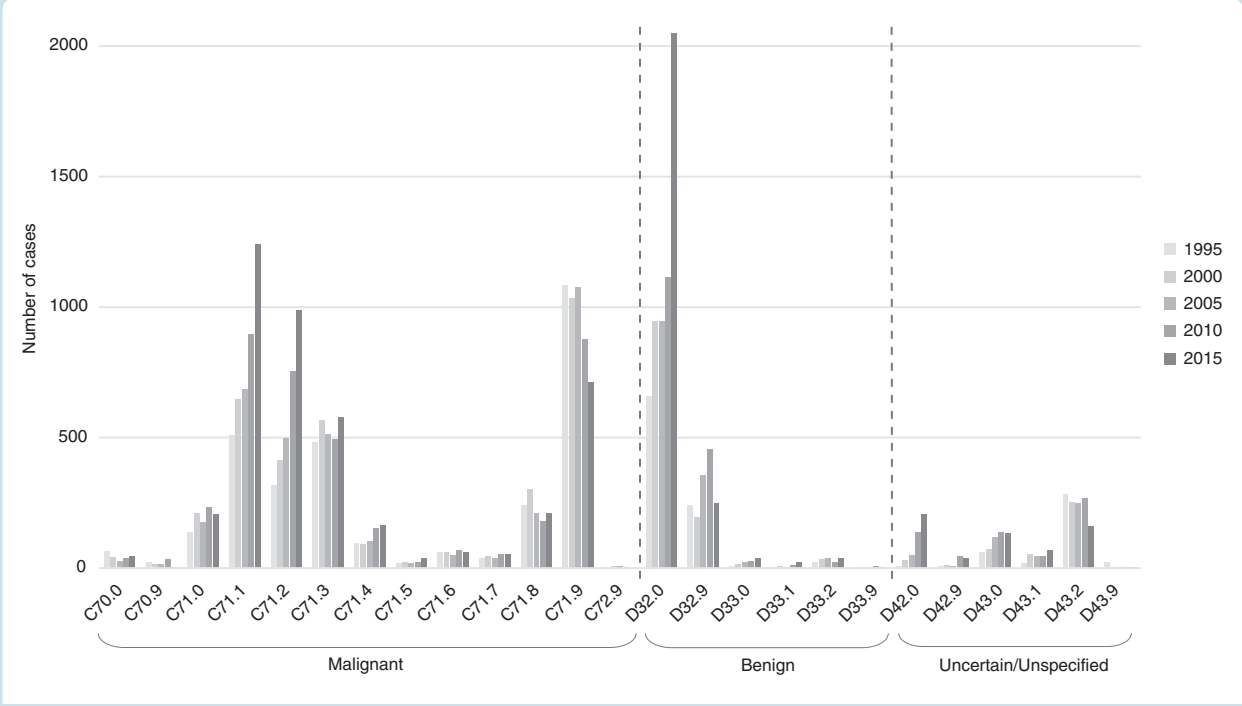

Fig. 1 Distribution of brain tumors based on site of neoplasm in England over time. Cases for year of diagnosis 1995, 2000, 2005, 2010, and 2015, categorized by tumor behavior.

incidence curve where the incidence decreased with age (Figure 3e). The age-standardized incidence rate for oligoastrocytomas increased over the study years peaking at 0.23 per 100 000 population (95% CI: 0.17-0.30) for men, and 0.15 (95% CI: 0.10-0.21) for women in 2010, and the rates significantly dropped to 0.01 per 100 000 population, in 2017 (Figure 2g). Over time, there was a low incidence of primary CNS lymphomas with only a very slight increase from 0.25 per 100 000 population in 1995 to 0.32 in 2011 for men and from 0.13 per 100 000 population in 1995 to 0.29 in 2011 for women. However, from 2012, an increase in the incidence of primary CNS lymphoma was observed reaching 0.70 (95% CI: 0.58-0.81) in men and 0.59 (95% CI: 0.40-0.69) in women (Figure 2h).

Unclassified brain tumor subtypes.—The unclassified brain tumors include malignant glioma, unclassified benign, unclassified malignant, and unclassified with uncertain behavior. The age-standardized and age-specific incidence rates for these tumors are shown in Figures 2i–l and 3i–l, respectively. These subtypes were more common in men than women, except for unclassified benign where

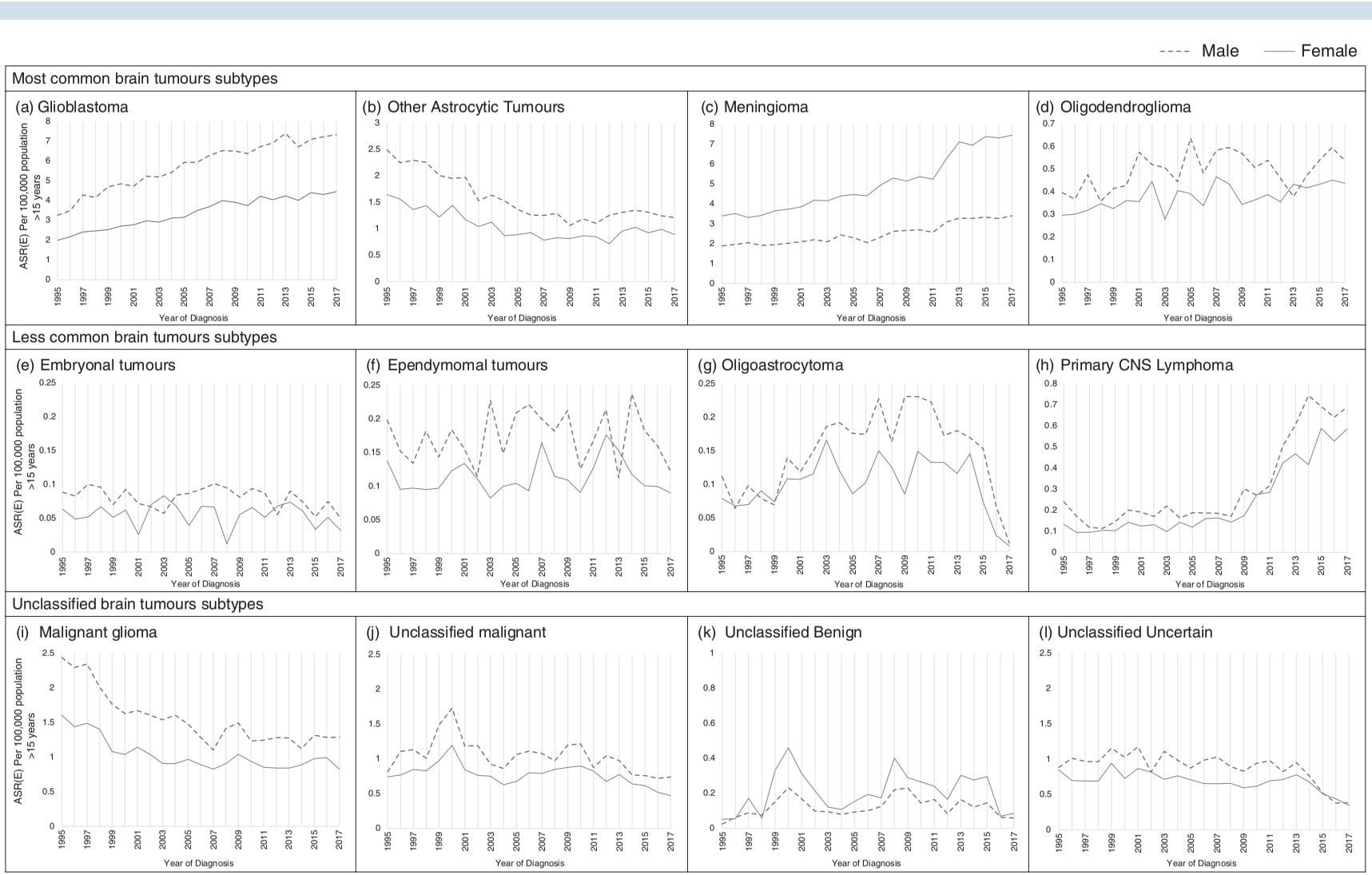

Fig. 2 Age-standardized incidence rates of brain tumor subtypes in England, 1995-2017.

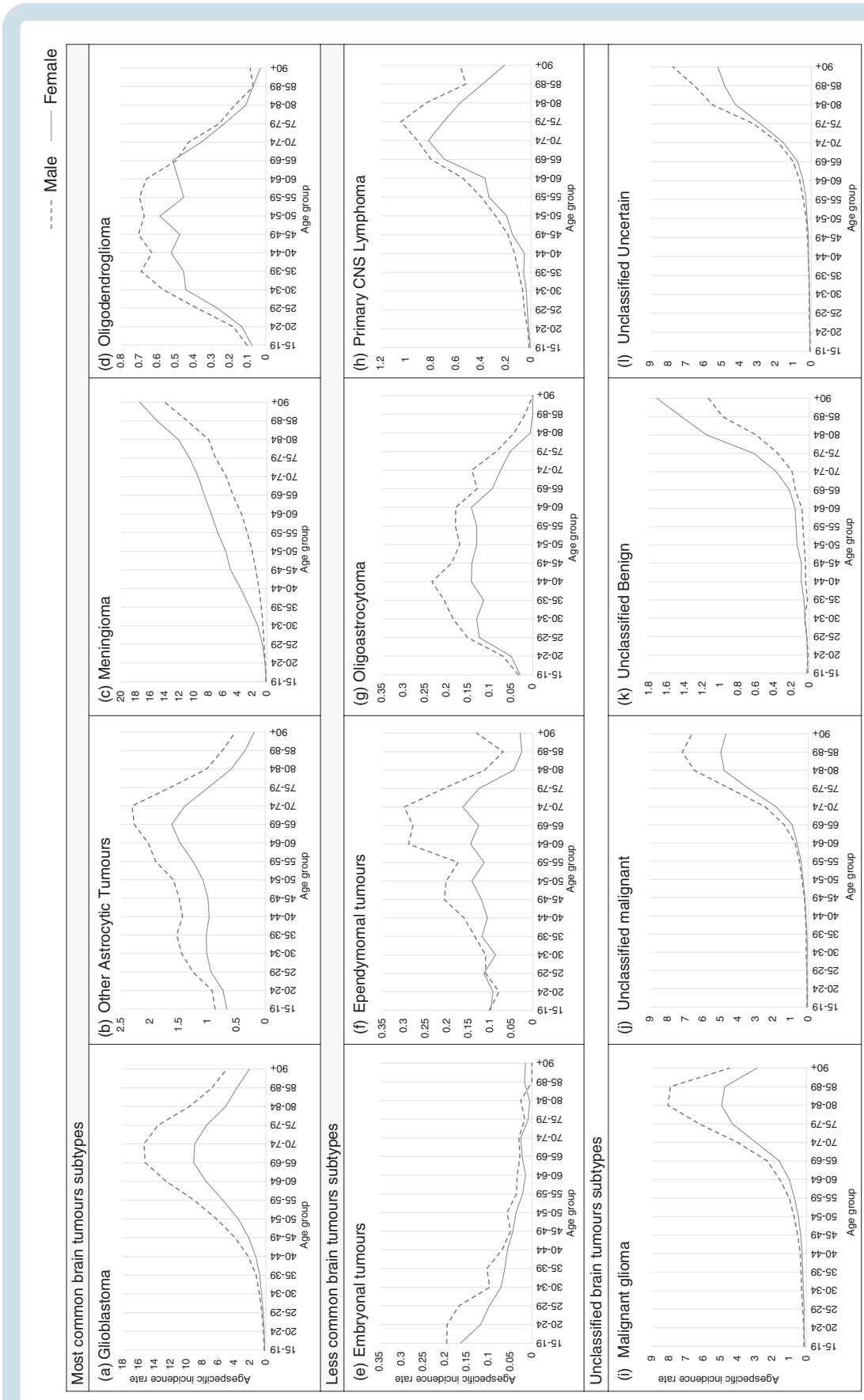

Fig. 3 Age-specific incidence rates of brain tumor subtypes in England, 1995-2017.

the opposite was seen. The age-standardized incidence rate of malignant gliomas showed a decrease over time, similar to that for other astrocytomas (Figure 2i), and remaining stable after 2007. The incidence for unclassified malignant and uncertain behavior brain tumors declined slightly over time, while the unclassified benign incidence remained the same (Figure 2j–l). The age-specific incidence curve for unclassified malignant gliomas, benign, malignant, and uncertain, showed a similar sharp increase in the incidence increased sharply in the elderly (Figure 3i–l).

Discussion

Key Points

This study found an overall rise in the incidence rate of primary brain tumors being diagnosed in England between 1995 and 2017. Glioblastomas were the most frequent tumor subtype, followed by meningiomas. The age-standardized incidence for glioblastomas, meningiomas, and primary CNS lymphomas increased significantly over the study period. The rarer brain tumors did not show much increase during this period. Other astrocytic and unclassified brain tumors declined between 1995 and 2007 and remained stable thereafter.

Comparison With Other Work

Findings from our study can be compared with a recently published paper concerning brain tumor subtypes by Philips and colleagues.[9] These authors analyzed the incidence trends between 1995 and 2015 in England demonstrating an increase in the subtype glioblastoma, which was also shown in our study. However, their study focussed on malignant gliomas in patients of all ages, whereas our study concerned benign, malignant as well as uncertain tumor behaviors in adults only. Since brain tumor subtypes present differently in different age groups, analyzing grouped tumors for all ages combined may be misleading and should preferably be explored independently. Although both studies might be similar due to the overlapping analysis period, our study presents more detailed findings based on grouping of each tumor subtype.

Comparing the incidence of brain tumors found in the present study with those from other Western and European countries appears to show similar increases. A French population-based registry in Gironde showed an increase in primary CNS tumors from 2000 to 2012[10] although this included spinal tumors and excluded pituitary tumors and metastatic tumors. Since the crude incidence of CNS tumors was higher in females than males and in the elderly, the overall rise was explained by the increase in meningioma incidence. For the malignant CNS tumors, which would include glioblastomas, no trend was found.[9] In our study, it seems likely that meningiomas and glioblastomas are the main drivers of the overall increase in the incidence of brain tumors. The Spanish Girona Cancer Registry study[11] also reported similar results with the most frequent brain tumor subtypes being meningiomas (27.6%, incidence rate = 5.11 per 100 000) and glioblastomas (22.2%, incidence rate = 4.15). However, the incidence rates over time were not presented for these subtypes. In Denmark, Finland, Norway, and Sweden, the incidence rate for gliomas also increased in those aged 60-79 from 1974 to 2003, and in the same age group, an increasing incidence was observed for meningiomas in women after the 1990s.[12] Findings from other global studies include incidence data from Australia showing an increase in meningioma during the period 2000-2008, which was more pronounced in men aged 20-64 years (6.3 annual percentage change) than in women (0.6 annual percentage change).[13] Interestingly, by contrast, the age-standardized incidence rates of meningiomas in Osaka, Japan, appeared to have decreased during the period 1995-2004.[7]

According to age distribution, brain tumor diagnoses tend to be aggregated based on biological and epidemiological aspects. Malignant brain tumors are more common in adolescents and young adults (AYA) (aged 15-24 years) than in children. However, the incidence rate in AYA is lower than in older adults. A recent study exploring the incidence trends in AYAs from 12 countries of Southern and Eastern Europe between 1990 and 2014, found a high incidence in most countries except in Croatia which saw an annual decrease of 2.5%.[14]

Data collected for the US Central Brain Tumor Register (CBTRUS), showed an increased incidence for benign CNS tumors, as a consequence of the introduction of the Benign Brain Tumor Cancer Registries Amendment Act (2002)[15] that made collection of benign brain tumors a requirement.[5] The UK Association of Cancer Registries (UKACR, including Scotland, Wales, and Northern Ireland) reported an increase in the incidence of CNS tumors between 1979 and 2006, which was primarily seen in young adults (0-24 years) and the elderly (65-84 years). Different trend patterns were seen for meningiomas where the increase was in those over 25 years old, with pilocytic astrocytomas increasing in the 0-24 age group.[16]

As can be seen from these studies, differing cancer incidence rates are reported in different countries. These could be explained by structural factors such as varying cancer registration systems, the presentation of regional rather than national data, socioeconomic variation between countries, and access to diagnostic and treatment services. Another important issue when making between-country or between-continent comparisons is the age-adjustment procedures. Some studies present their results as crude incidence rates while others as standardized rates based on different standard populations. Finally, how these tumors are recorded in each country play an additional role. For example, the Estonian Cancer Registry only recorded 11% of tumors as benign,[17] compared to other European registries, for example, the Nordic countries, which could be as high as 98%.[12] It was reported that in the earlier years of the Estonian Cancer Registry, benign cases were recorded as malignant.[17]

Limitations

This national study used data from a 23-year period on a very large number of patients diagnosed with primary

brain tumors, excluding spinal, endocrinal, and other CNS tumors. As brain tumors are a heterogenous group of tumors behaving in different ways, it was necessary to investigate differences in incidence for the main morphological subtypes. Those tumors that could not be classified were grouped into "Other" subtypes—a group that represent a vast range of extremely rare morphologies of brain tumors. Due to this, the incidence of this group was not analyzed.

Unfortunately, English cancer registration data do not differentiate between primary and secondary glioblastomas which express different genetic features. Secondary glioblastomas are more common in younger patients where they have transformed from diffuse (WHO grade II) or anaplastic (WHO grade III) astrocytoma. It is difficult to differentiate between primary and secondary glioblastoma histopathologically, but it is recognized that they develop through different genetic pathways.[18] To investigate these tumors more deeply, detailed molecular and pathological data will be required.

To add to the complexity of brain tumor classification, some tumor subtypes that are most common in children are not common in adults, while some subtypes present in childhood, adolescence, and adulthood. This makes analysis of "adult-only" types near impossible. For example, pilocytic astrocytoma, a WHO grade I tumor, is the most common primary brain tumor in children aged 5-14 and the second most common brain tumor in children aged 0-4 and 15-19.[5] However, some adults are diagnosed with this brain tumor, and much of the understanding of it is based on the pediatric literature, as limited papers have been published on adult pilocytic astrocytomas.

Finally, it is necessary to consider the robustness of data within NCRAS. A UKACR agreement to the European Network of Cancer Registries (ENCR) recommendations was implemented in 2000.[19] This recommendation was adopted by the eight former regional registries in England to register all brain and CNS tumors, including nonmalignant tumors. Data collection and completeness have improved over the study years as regional registries have applied further strategies including interrogation of the data by site-specific groups and the merger of the former eight English registries into one in 2013. However, brain tumors are less common compared to other cancers and so collection of data on these complex and morphologically diverse tumors might not be as thorough as for other cancers.

Potential Explanations of Study Findings

This study is the most comprehensive study of the incidence of brain tumors in the English population and reports a general increase in brain tumor cases in adults between 1995 and 2017. It has been recognized that brain tumor incidence has been increasing at least since 1971.[20] Over the last five decades, there have been advances in diagnostic technologies, associated with the introduction of computed tomography (CT) scanning during the 1970s and magnetic resonance imaging (MRI) during the 1980s. Since then, neuroimaging has evolved enabling earlier diagnosis and imaging-guided therapies, thereby improving patient care.[21] It has been hypothesized that ionizing radiation exposure from early CT scans might have contributed to the increased risk of gliomas in the population,[22] although there is no strong evidence for this.

A more plausible reason explaining the increasing incidence of brain tumors is the combination of advances in imaging and surgical procedures, their increasing availability, and clinical guidance recommending that patients with suspicious neurological symptoms should be thoroughly investigated. The National Institute for Health and Clinical Excellence (NICE) guidelines released in 2006 outlined the importance of assessing and coordinating patient care through a multidisciplinary team.[23] This could explain the further increased incidence following 2006 for glioblastomas and meningiomas, and a stable incidence for other astrocytomas and malignant gliomas. In 2015, updated NICE guidance was published aiming to improve investigations in primary care for suspected brain and CNS tumors with progressive, loss of central neurological function.[24] For patients experiencing these symptoms, the referral is considered very urgent and patients are given direct access to MRI or CT scan within 48 hours for children and young adults and within 2 weeks for adults. These advances could have led to more patients are being operated on, and as a result, the number of tumors with histological confirmation increasing.

Historically benign brain tumors have had less priority compared to malignant tumors and so they were not usually included in the national statistics. However, over time, registrations of benign tumor cases have improved. When compared to malignant tumors, histological confirmation has decreased over time with increasing incidence for benign meningiomas in women, particularly from 2011, and this could be explained by a few reasons. With increasing use of MRI and CT scans, more small, slow-growing, and sometimes incidental lesions suggestive of meningioma are being diagnosed. In this scenario, patients are usually followed up rather than being operated on, and hence no histology is obtained. Additionally, the decreasing histology validation for benign tumors and increasing incidence in malignant tumors could possibly be a consequence of the release of a service specification encouraging the delivery of non-surgical therapies such as stereo-radiosurgery and stereo-radiotherapy for meningioma patients in order to improve their life expectancy and quality of life.[25] This was also cited in the latest NICE guidelines in 2018 as Evidence Report for the investigation, management, and follow-up of meningioma.[26] Furthermore, nonmalignant tumor registrations have improved since 2013 when the newly merged national cancer registry (now known as NCRAS) instructed the use of the Cancer Outcomes and Services Dataset (COSD).

During the analysis period, revisions to the WHO classification of CNS tumors[1] have led to changes in diagnostic categories for some brain tumor subtypes. From the WHO classification for CNS tumors 2000 version to 2007, and more recently 2016, it is clear that the incidence of brain tumors is greatly influenced by the diagnostic coding used in any national cancer registry.[1,27,28] The overall decline in the incidence of unclassified brain tumors over the years

could be explained by the advances in neuropathology due to more defined diagnostics criteria for brain tumor morphologies. In the 2016 edition, due to the difficulty in classifying oligoastrocytomas, their use was discouraged in favor of astrocytomas and oligodendrogliomas. The impact of this change was evident in the analysis of this cohort where only 5 cases were recorded in 2017 for oligoastrocytomas (morphology code 9382/3). In addition, the use of this morphology decreased prior to 2016 with increasing use of molecular classification. Other examples of how the 2016 WHO CNS classifications impacted the data include the introduction of diffuse midline glioma giving 7 new cases for 2016 and 2017, and no recorded cases as a result of the deletion of protoplasmic astrocytoma. Going forward, it is expected that more genetic-based classifications will be recorded as practices are developed to converge with the WHO CNS classifications. Furthermore, changes to diagnostic coding within the Registry could be linked to improvements in procedural practices and quality assurance processes as more data are received electronically from NHS hospitals. This was evident in the incidence of primary CNS lymphomas where coding for hematological malignancies was refined from 2012 onwards.

For the most common brain tumors, gliomas, and meningiomas, it is interesting to note that the incidence shows the opposite patterns for each sex. Meningioma is more than twice as common in women compared to men while gliomas are more common in men. In addition to the differences in their incidences, male and female meningiomas differ in their tumor behavior. Meningiomas in females are mostly benign, while those in males are more commonly malignant. For glioblastomas and meningiomas, the largest increase in incidence rates was evident in both sexes for the elderly. This could be explained by the aging of the population together with increasing availability of imaging and less invasive neurosurgical techniques. In other studies, the incidence of primary brain tumors was observed to have tripled in those over the age of 70 years.[29–31] For the younger age groups, incidence remained constant over the study period, with the exception of women diagnosed aged 30-59 years in whom the incidence of meningiomas somewhat increased. The increased risk of meningiomas in women is likely to be due to improved registration of benign brain tumors over the recent years.

Conclusion

This study has described the incidence rates of primary brain tumors, an important measure of the changing burden of cancer in a population over time. It has explored the various brain tumor subtypes based on their morphology, sex, and age. Results show an overall rise in the incidence rate of these tumors being diagnosed in England between 1995 and 2017. While the incidence varied for the different brain tumor subtypes, the most common brain tumors—glioblastoma and meningioma—seem to be driving this overall increase. Explanations for the increase in the number of primary brain tumors are likely to include aging of the population, improvements in access to neurosurgical care and diagnostic tools, and more complete and detailed records, including benign tumors, reaching NCRAS as a result of the regular updates in the coding of the WHO classification for CNS tumors. All these factors are likely to play a role in contributing to the incidence of brain tumors, particularly for glioblastomas and meningiomas.

Keywords

brain tumors | cancer registry | epidemiology | incidence

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