European Review for Medical and Pharmacological Sciences 2022; 26: 7566-7571

Burden of brain and central nervous system cancers in China from 1990 to 2019

K. WU[1], L. CHEN[1], Y. CHEN[2], S.-J. TANG[1]

[1]Department of Neurosurgery, Xichang People's Hospital, Liangshan, Sichuan, P.R. China
[2]Department of Anesthesiology, The Third People's Hospital of Chengdu, Chengdu, Sichuan, P.R. China

Abstract. – OBJECTIVE: Primary central nervous system (CNS) cancer is a predominant source of mortality and morbidity globally. This study aims to analyze the burden and variation trends of CNS cancer in China from 1990 to 2019.

MATERIALS AND METHODS: In this cross-sectional study, we analyzed people of all ages with CNS cancer in China from January 1, 1990, to December 31, 2019. We collected the data including incidence, deaths, and disability-adjusted life-years (DALYs) from the Global Burden of Disease (GBD) study 2019. The age-standardized incidence rate (ASIR), age-standardized death rate (ASDR), and DALYs rate were compared by age and sex.

RESULTS: In 2019, there were more than 94 (95% uncertainty intervals [CI]: 73-114) thousand incident cases, 63 (47-76) thousand deaths and 2.0 (1.5-2.5) million DALYs due to CNS cancer in China in 2019. From 1990 to 2019, the absolute number of incident cases, deaths, and DALYs increased by 107.0% (39.0 to 169.0), 67.0% (12.0 to 117.0), and 16.0% (–23.0 to 63.0). The ASIR increased by 28.0% (–16.0 to 64.0). ASDR and age-standardized DALYs rate decreased by –10.0% (–40.0 to 15.0) and –22.0% (–50.0 to 10.0), respectively.

CONCLUSIONS: The overall burden due to CNS cancer in China remains high, as evidenced by the sharp increase in the incident cases, deaths, and DALYs from 1990 to 2019. Elderly patients and neonates show relatively high burden. Sex-specific differences in the incidence of CNS cancer in China are observed.

Key Words:
Burden, Brain, Central nervous system, Cancer, Incidence, Mortality, Trends.

Introduction

Primary brain and central nervous system (CNS) cancers, collectively named CNS cancer, is a predominant source of mortality and morbidity globally, leading to major burdens[1]. In the past few decades, the incident cases of stroke every year continued to increase sharply[2,3]. Results from the Global Burden of Diseases (GBD) study 2016 also suggested that the global incidence rates of CNS cancer increased between 1990 and 2016[4]. China, as the biggest developing countries worldwide, had the most incident cases and deaths of CNS cancer[4]. In this light, comprehensive analysis of the burden of CNS cancer across China will provide evidence to policy makers and healthcare workers on the resource allocation and implement sophisticated diagnostic and therapeutic strategies.

In this work, in order to provide the first comprehensive and systematic analysis of the burden of CNS cancer in China, we acquired the data from the most recent GBD study 2019 including age-standardized incidence rate (ASIR), age-standardized death rate (ASDR), years of life lost (YLLs), years lived with disability (YLDs), and disability-adjusted life-years (DALYs), which were compared across different age groups and sexes.

Materials and Methods

Data including ASIR, ASDR, YLLs, YLDs, and DALYs in 204 countries and regions from 1990 to 2019 were collected through GBD Results Tool (http://ghdx.healthdata.org/gbd-results-tool) on the website of Institute of Health Metrics and Evaluation (IHME). Detailed methods utilized to generate estimates has been described previously[5-8]. Briefly, the GBD study 2019 started on January 1, 1990 and ended on December 31, 2019, and the data analysis completed on October 1, 2020.

In GBD study, the definition of CNS cancer was based on the tenth edition of International Classification of Diseases (ICD) 4. Briefly, CNS cancer included cancers coded as C70 (malignant neoplasm of meninges), C71 (malignant neoplasm of brain), and C72 (malignant neo-

Corresponding Author: Shujun Tang, MD; e-mail: tangsj_xc@126.com

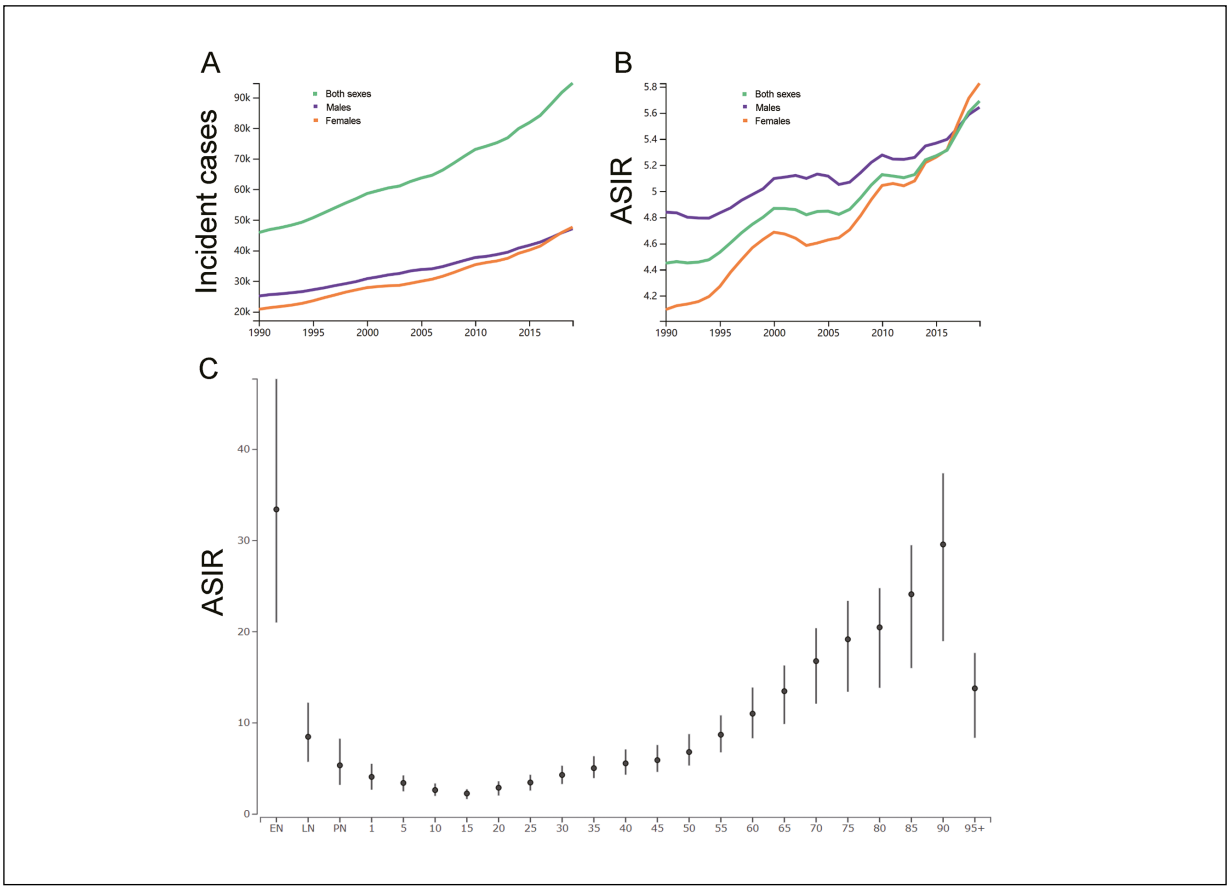

Figure 1. A, The number of incident cases from 1990 to 2019. **B**, The age-standardized incidence rates per 100 000 from 1990 to 2019. **C**, The age-standardized incidence rates per 100 000 of different age groups in 2019. ASIR, age-standardized incidence rate; EN, early neonatal; LN, late neonatal; PN, post neonatal.

plasm of spinal cord, cranial nerves, and other parts of the CNS)[9].

Statistical Analysis

The overall incidence rates and cases were estimated utilizing a Bayesian meta-regression model (DisMod-MR 2.1) and the standard Cause of Death Ensemble modelling (CODEm) methods was utilized to determine the estimates of mortality. Additionally, the statistical methods dealing with incomplete data in low- and middle-income countries has been described previously. Each estimate was calculated from the mean of 1000 draws from the posterior distribution by age, sex, location, and year. 95% uncertainty intervals (UI) were the 25th and 975th values of the ordered draws. All rates in this study were reported per 100 000. Specifically, A 95% UI excluding zero for all estimates was defined as statistical significance. *p*-value (2-side) under 0.05 was considered to have statistical difference.

Results

Incidence

In 1990, the number of incident cases of CNS cancer was 45 k (95% UI 35-61), of whom 25 k (16-37) were males and 20 k (13-28) were females, and was 94 k (73-114) in 2019, of whom 47 k (30-61) were males and 47 k (30-62) were females. The ASIR per 100 000 was 4.45 (3.47-5.94) in 1990 and was 5.69 (4.36-6.78) in 2019. In 1990, the ASIR of males was 4.84 (3.21-7.23) and the ASIR of females was 4.09 (2.75-5.55). In 2019, the ASIR of males was 5.64 (3.61-7.33) and the ASIR of females was 5.83 (4.30-7.77). From 1990 to 2019, as shown in Figure 1A, the number of incident cases of CNS cancer in China has increased by 107.0% (39.0 to 169.0). The number of incident cases increased by 88.0% (6.0 to 177.0) in males and by 129.0% (24.0 to 274.0) in females. As shown in Figure 1B, the ASIR of CNS cancer in China has increased by 28.0% (–16.0 to 64.0) from 1990 to 2019. The ASIR

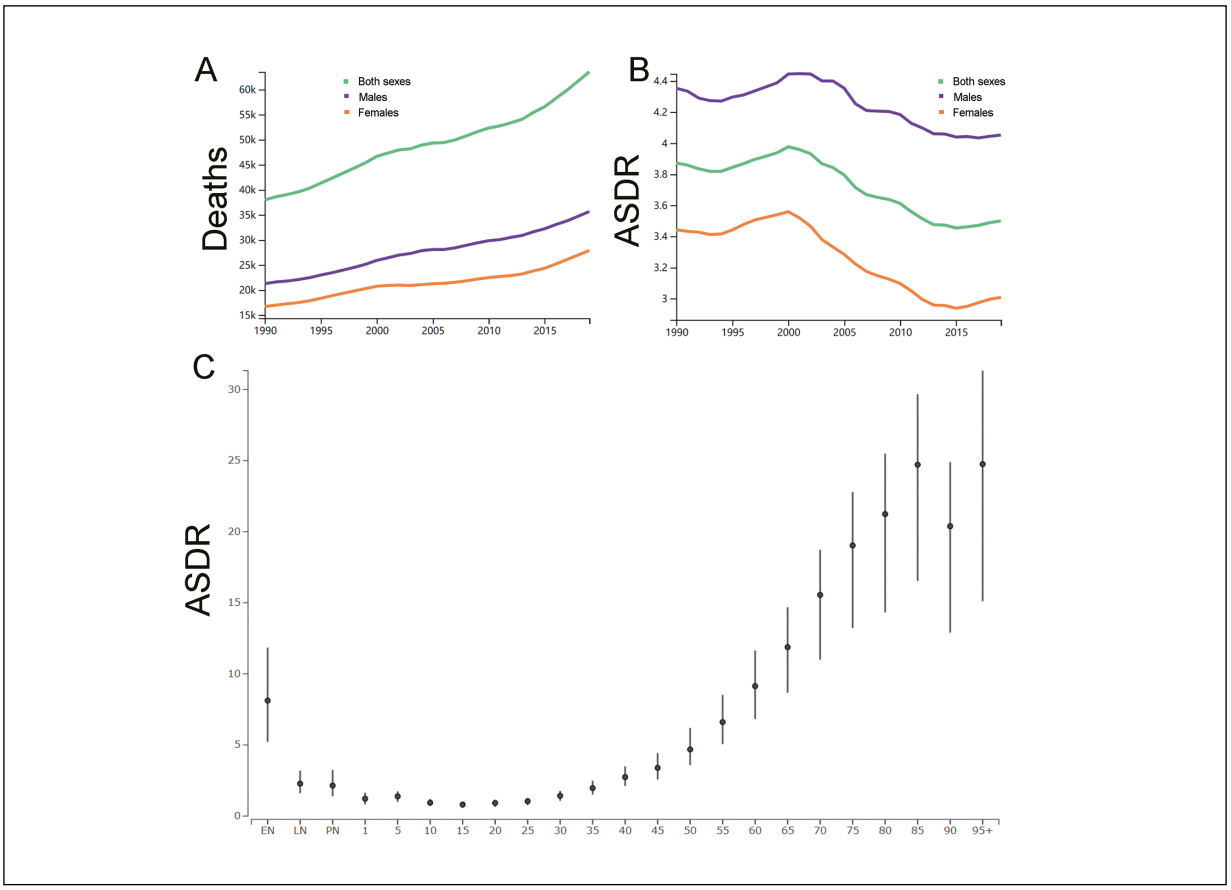

Figure 2. A, The number of deaths from 1990 to 2019. **B**, The age-standardized death rate per 100 000 from 1990 to 2019. **C**, The age-standardized death rates per 100 000 of different age groups in 2019. ASDR, age-standardized death rate; EN, early neonatal; LN, late neonatal; PN, post neonatal.

increased by 17.0% (–34.0 to 68.0) in males and by 42.0% (–24.0 to 133.0) in females.

By age group, in 2019, early neonatal (EN, 0-6 days) group had the highest incidence rate (33.42, 95% UI 21.02-47.72). As shown in Figure 1C, at the ages of 0-19 years, the incidence rate decreased with increasing age. At the ages of 20 years or older, the incidence rate increased with increasing age and peaked at the ages of 90-94 years (29.57, 95% UI 18.97-37.38). The subgroup aged 65 to 69 years (9488, 95% UI 6958-11469) and 60 to 64 years (8652, 95% UI 6539-10901) had the largest number of incident cases.

Mortality

In 1990, the number of deaths of CNS cancer was 37 k (29-50), of whom 21 k (14-31) were males and 16 k (11-22) were females, and was 63 k (47-76) in 2019, of whom 35 k (22-47) were males and 27 k (20-36) were females. The ASDR per 100 000 was 3.87 (3.04-5.10) in 1990 and was 3.50 (2.62-4.21) in 2019. In 1990, the ASDR of males was 4.35 (3.02-6.46) and the ASDR of females was 3.44 (2.44-4.58). In 2019, the ASDR of males was 4.05 (2.53-5.33) and the ASDR of females was 3.01 (2.19-3.88). From 1990 to 2019, as shown in Figure 2A, the number of deaths of CNS cancer in China has increased by 67.0% (12.0 to 117.0). The number of deaths increased by 68.0% (0 to 153.0) in males and by 67.0% (–7.0 to 168.0) in females. As shown in Figure 2B, the ASDR of CNS cancer in China has decreased by –10.0% (–40.0 to 15.0) from 1990 to 2019. The ASDR decreased by –7.0% (–45.0 to 37.0) in males and decreased by –13.0% (–51.0 to 39.0) in females.

By age group, in 2019, 85-89 years (24.71, 95% UI 16.54-29.67) and > 95 years (24.75, 95% UI 15.11-31.33) group had the highest death rate. As shown in Figure 2C, the death rate increased with increasing age except the neonatal groups and >90 years group. The subgroup aged 65 to 69 years had the largest number of deaths (8360, 95% UI 6103-10330).

DALYs

DALYs are the sum of YLLs and YLDs. In 1990, CNS cancer was responsible for 1.7 (1.2-2.4) million DALYs (males: 1.0 million, 95% UI 0.6-1.5; females: 0.7 million, 95% UI 0.4-1.0). In 2019, CNS cancer was responsible for 2.0 (1.5-2.5) million DALYs (males: 1.1 million, 95% UI 0.7-1.5; females: 0.8 million, 95% UI 0.6-1.1). The age standardized DALYs rate per 100 000 was 161.29 (118.00-220.25) in 1990 (males: 178.20, 95% UI 117.52-276.17; females: 144.01, 95% UI 93.80-195.96) and was 126.24 (96.01-154.80) in 2019 (males: 143.02, 95% UI 89.74-189.00; females: 109.48, 95% UI 80.78-144.78). From 1990 to 2019, as shown in Figure 3A, the value of DALYs due to CNS cancer in China has increased by 16.0% (–23.0 to 63.0). The DALYs increased by 17.0% (–32.0 to 88.0) in males and by 15.0% (–40.0 to 106.0) in females. As shown in Figure 3B, the age-standardized DALYs rate in China has decreased by –22.0% (–50.0 to 10.0) from 1990 to 2019. The age-standardized DALYs rate decreased by –20.0% (–54.0 to 28.0) in males and decreased by –24.0% (–61.0 to 38.0) in females.

By age group, in 2019, early neonatal (EN, 0-6 days) group had the highest DALYs rate (737.8.42, 95% UI 474.83-1079.17). As shown in Figure 3C, with increasing age, the DALYs rate decreased at the ages of 0-19 years, increased at the ages of 20-74 years, and then decreased at the ages of 75 years or older. The subgroup aged 50-54 years (220 k, 95% UI 169-291), 55 to 59 years (206 k, 95% UI 158-265), and 60 to 64 years (202 k, 95% UI 152-257) had the most DALYs.

Discussion

The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) updated annually is the unique and systematic assessment of the global burden of 354 diseases and injuries[5]. In this

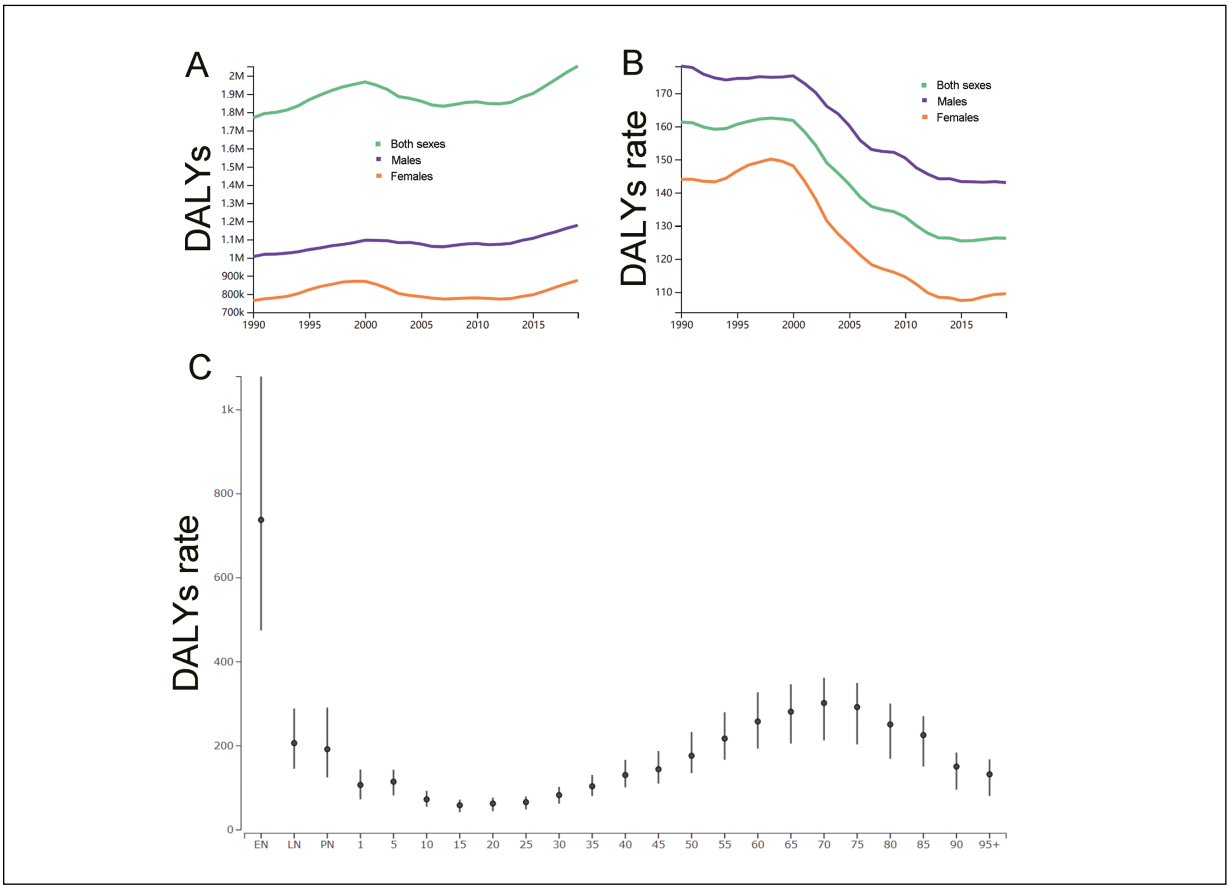

Figure 3. ***A***, The number of DALYs from 1990 to 2019. **B**, The age standardized DALYs rate per 100 000 from 1990 to 2019. **C**, The age standardized DALYs rates per 100 000 of different age groups in 2019. DALYs, disability-adjusted life-years; EN, early neonatal; LN, late neonatal; PN, post neonatal.

work, we systematically analyzed the burden of CNS cancers in China from 1990 to 2019 on the basis of the most recent GBD study 2019. Our results showed the overall burden of CNS cancer in China remained high in the past 3 decades, as evidenced by a sharp increase in the incident cases, deaths and DALYs. Although there was an increase (without statistical significance) in the ASIR, the ASDR and age standardized DALYs rate decreased (without statistical significance) between 1990 and 2019. The improved survival of patients with CNS cancer over time were observed based on our analysis. The results were accordant with the fact that five-year survival probability of CNS cancer almost doubled from 1975 to 2013 according to the National Cancer Institute's Surveillance, Epidemiology, and End Results program (https://seer.cancer.gov). The explanation of the increasing trends in incident cases is poorly understood, to date. The reduction on the ASDR and DALYs rates were possibly ascribed to the sophisticated diagnosis and treatments, particularly the implement of multidisciplinary therapy including neurosurgical care, neurocritical care, radiotherapy, and chemotherapy.

One of the major concerns related to CNS cancer is the need for early and accurate diagnosis. Few patients with CNS cancer require radiological testing in the early stage since they usually present with a spectrum of non-specific symptoms such as headache[10,11]. In these context, early detection and diagnosis through population-based screening test are essential.

The burden of CNS cancer in China is different from other countries in the world. It has long been known that the whites have higher incidence rates of CNS cancer compared with non-whites[12]. Previous GBD study has suggested that the incidence rate, mortality, and DALYs of CNS cancer presented regional variation and were associated with the socioeconomic development, and countries in Europe had relatively high incidence rates and DALYs rate[4]. The latest GBD study showed the incidence rates were higher in the Western and Central Europe than China[9]. As such, the regional variation in the incidence trends of CNS cancer over time has recently been demonstrated by Williams et al[13]. Genetic susceptibilities and environmental exposures are likely contributed to the regional variation in the incidence rates.

As refers to the sex-specific differences, little is known about the sex differences in the incidence and mortality of CNS cancer in China. Reports on the incidence of glioblastoma (GBM), as the most frequent primary malignant tumors of CNS[14], indicated the males had higher incidence rates of GBM than the females while the incidence rates of low-grade glioma were similar[15]. Moreover, female animals and women with CNS cancer appeared to have longer survival and better prognosis in some clinical and animal studies[16,17]. The results were compliant with the work of Araghi et al[18], who indicated that the incidence rates of brain and CNS tumors were higher in men than women in Iran during a 10-year period. In contrast to these findings, our analysis found the incidence rates in women showed more increase than men between 1990 and 2019 in China, and the ASIR was higher in females than males in 2019. Although the mortality was higher in men than women, the DALYs rate was nearly similar. Further studies should elucidate the potential mechanism of sex-specific differences in CNS cancer at the molecular level.

Our study also indicated that the pattens and variation trends of burden due to CNS cancer are diverse across different age groups. Elderly patients and neonates showed relatively high burden due to CNS cancer, as evidenced by the high incidence rates, mortality and DALYs rates. In this light, efforts should be given to the appropriate allocation of health-care resources to allow for highly specialized care for the neonates and elderly patients[13]. The largest limitation of our study is the lack of estimates for CNS cancer subtypes. However, we believe the systematic analysis of the burden of CNS cancer as a group should be the foundation before more detailed data are analyzed.

Conclusions

The overall burden due to CNS cancer in China remains high, as evidenced by the sharp increase in the incident cases, deaths, and DALYs from 1990 to 2019. Elderly patients and neonates show relatively high burden. Sex-specific differences in the incidence of CNS cancer in China are observed.

Conflict of Interest

The authors declare that they have no conflict of interest.

Acknowledgement

We sincerely appreciate all members of the Institute for Health Metrics and Evaluation (IHME), University of Washington, and all collaborators involved in GBD 2019 study.

Institutional Review Board Statement

The Ethical approval is waived for the current study because it used public data available on-line.

Informed Consent Statement

Not appliable.

Data Availability Statement

The datasets presented in this study can be found in online repositories from GBD Results Tool (http://ghdx.healthdata.org/gbd-results-tool) on the website of Institute of Health Metrics and Evaluation (IHME).

References

1) Sampson JH, Gunn MD, Fecci PE, Ashley DM. Brain immunology and immunotherapy in brain tumours. Nat Rev Cancer 2020; 20: 12-25.
2) Mbi Feh MK-N, Lyon KA, Brahmaroutu AV, Tadipatri R, Fonkem E. The need for a central brain tumor registry in Africa: A review of central nervous system tumors in Africa from 1960 to 2017. Neuro-Oncology Practice 2021; 8: 337-344.
3) Kristensen BW, Priesterbach-Ackley LP, Petersen JK, Wesseling P. Molecular pathology of tumors of the central nervous system. Ann Oncol 2019; 30: 1265-1278.
4) GBD 2016 Brain and Other CNS Cancer Collaborators. Global, regional, and national burden of brain and other CNS cancer, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol 2019; 18: 376-393.
5) GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 2020; 396: 1204-1222.
6) GBD 2019 Risk Factors Collaborators. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 2020; 396: 1223-1249.
7) GBD 2019 Demographics Collaborators. Global age-sex-specific fertility, mortality, healthy life expectancy (HALE), and population estimates in 204 countries and territories, 1950-2019: a comprehensive demographic analysis for the Global Burden of Disease Study 2019. Lancet 2020; 396: 1160-1203.
8) GBD 2019 Universal Health Coverage Collaborators. Measuring universal health coverage based on an index of effective coverage of health services in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 2020; 396: 1250-1284.
9) Mohammadi E, Ghasemi E, Azadnajafabad S, Rezaei N, Saeedi Moghaddam S, Ebrahimi Meimand S, Fattahi N, Habibi Z, Karimi Yarandi K, Amirjamshidi A, Nejat F, Kompani F, Mokdad AH, Larijani B, Farzadfar F. A global, regional, and national survey on burden and Quality of Care Index (QCI) of brain and other central nervous system cancers; global burden of disease systematic analysis 1990-2017. PLoS One 2021; 16: e0247120-e0247120.
10) Hoang-Xuan K, Bessell E, Bromberg J, Hottinger AF, Preusser M, Rudà R, Schlegel U, Siegal T, Soussain C, Abacioglu U, Cassoux N, Deckert M, Dirven CM, Ferreri AJ, Graus F, Henriksson R, Herrlinger U, Taphoorn M, Soffietti R, Weller M; European Association for Neuro-Oncology Task Force on Primary CNS Lymphoma. Diagnosis and treatment of primary CNS lymphoma in immunocompetent patients: guidelines from the European Association for Neuro-Oncology. Lancet Oncol 2015; 16: e322-e332.
11) Schmidt-Hansen M, Berendse S, Hamilton W. Symptomatic diagnosis of cancer of the brain and central nervous system in primary care: a systematic review. Fam Pract 2015; 32: 618-623.
12) Chen P, Aldape K, Wiencke JK, Kelsey KT, Miike R, Davis RL, Liu J, Kesler-Diaz A, Takahashi M, Wrensch M. Ethnicity Delineates Different Genetic Pathways in Malignant Glioma. Cancer Res 2001; 61: 3949-3954.
13) Williams LA, Hubbard AK, Scheurer ME, Spector LG, Poynter JN. Trends in paediatric central nervous system tumour incidence by global region from 1988 to 2012. Int J Epidemiol 2021; 50: 116-127.
14) Wesseling P, Capper D. WHO 2016 Classification of gliomas. Neuropathol Appl Neurobiol 2018; 44: 139-150.
15) Carrano A, Juarez JJ, Incontri D, Ibarra A, Cazares HG. Sex-Specific Differences in Glioblastoma. Cells 2021; 10: 1783.
16) Sun T, Plutynski A, Ward S, Rubin JB. An integrative view on sex differences in brain tumors. Cell Mol Life Sci 2015; 72: 3323-3342.
17) Ostrom QT, Rubin JB, Lathia JD, Berens ME, Barnholtz-Sloan JS. Females have the survival advantage in glioblastoma. Neuro-Oncology 2018; 20: 576-577.
18) Araghi M, Roshandel G, Hasanpour-Heidari S, Fazel A, Sedaghat SM, Pourkhani A, Kazeminejhad V, Miranda-Filho A, Bray F, Arnold M. Incidence of Malignant Brain and Central Nervous System Tumors in Golestan, Iran, 2004–2013. Arch Iran Med 2020; 23: 1-6.