

in this Article support the need for intervention, and the prevalence-based assessment used by the GBD Collaborators will provide a timely and useful metric to evaluate change.

W Allen Hauser

Sergievsky Center, Columbia University, New York, NY 10032, USA
wahauser@optonline.net

I declare no competing interests.

Copyright © 2019 The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY-NC-ND 4.0 license.

1 GBD 2016 Epilepsy Collaborators. Global, regional, and national burden of epilepsy, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2019; **18**: 357–75.

- 2 Cardenas VM, Roman GC, Perez A, Hauser WA. Why U.S. epilepsy hospital stays rose in 2006. *Epilepsia* 2014; **55**: 1347–54.
- 3 Ding D, Hong Z, Wang WZ, et al. Assessing the disease burden due to epilepsy by disability adjusted life year in rural China. *Epilepsia* 2006; **47**: 2032–37.
- 4 Nord E. Uncertainties about disability weights for the Global Burden of Disease study. *Lancet Glob Health* 2015; **3**: e661–62.
- 5 Scheffer IE, Berkovic S, Capovilla G, et al. ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. *Epilepsia* 2017; **58**: 512–21.
- 6 No authors listed. Proposal for revised classification of epilepsies and epileptic syndromes. Commission on Classification and Terminology of the International League Against Epilepsy. *Epilepsia* 1989; **30**: 389–99.
- 7 Kwan P, Wang W, Wu J, et al. Long-term outcome of phenobarbital treatment for epilepsy in rural China: a prospective cohort study. *Epilepsia* 2013; **54**: 537–42.
- 8 Wang W, Wu J, Dai X, et al. Global campaign against epilepsy: assessment of a demonstration project in rural China. *Bull World Health Organ* 2008; **86**: 964–69.



Global consequences of malignant CNS tumours: a call to action

Published Online
February 20, 2019
[http://dx.doi.org/10.1016/S1474-4422\(19\)30083-3](http://dx.doi.org/10.1016/S1474-4422(19)30083-3)
See [Articles](#) page 376

Tumours of the CNS are among the most feared cancers because they affect the very organ that defines personality and assures physical and cognitive independence. CNS tumours can cause severe disability, including seizures, poor memory or speech problems, and physical dysfunction. These effects can make caring for someone diagnosed with a CNS tumour challenging and often necessitate full-time assistance once the disease has progressed into its later stages.¹ CNS tumours can affect the brain or spinal cord and occasionally can disseminate within the CSF. They might occur in individuals at any age and from any background. No environmental exposure, other than previous ionising radiation, or behavioural or lifestyle choices are known to increase the risk of developing these tumours.² Atopic conditions might protect against the development of a malignant brain tumour, but the biological basis for this association is unknown.³

In *The Lancet Neurology*, the Global Burden of Diseases, Injuries, and Risk Factors (GBD) Study 2016⁴ reports a 4.63 per 100 000 person-years global incidence of malignant CNS tumours, which represents a 17.3% increase from 1990 to 2016. Despite this increase over time, the GBD incidence is lower than the 5.57 per 100 000 person-years incidence reported⁵ for 2003–07, which uses data from international cancer registries. The difference is likely due to variations in recording information in different cancer registries, but the relative

distribution of cases throughout the world was similar to the GBD report. Additionally, the GBD study⁴ notes an accompanying stable mortality rate, suggesting improvements in treatments over time.

The global incidence encompasses wide variation in estimates around the world, possibly attributed to different environmental exposures or variable genetic influences within a population. Incidence is also dependent upon ascertainment, and accurate diagnosis of a CNS tumour requires access to modern neuroimaging and neurosurgery. Thus, it is unsurprising that incidence is lowest in resource-limited environments, such as sub-Saharan Africa and Central America, and the highest incidence is observed in the highest quintile of the Socio-demographic Index (SDI). However, these differences cannot be attributed to health-care access alone, and there might well be important causal indicators within this regional and racial or ethnic variability. For example, the highest incidences are seen in the Nordic countries, with a substantially lower incidence evident in their surrounding countries. In the USA, the incidence of most malignant CNS tumours among the African American population is much lower than in the white population, which reflects what is seen globally.⁶ Genetic susceptibility loci have been identified for gliomas, but they have been examined only in populations of European ancestry;⁷ studies of populations from different genetic backgrounds might provide

important insights into cause or protection against CNS tumours.

The high mortality of CNS tumours is reflected in the much larger rates of years of life lost (YLLs) than of years lived with disability (YLDs); even though disability can be severe from these diseases, early mortality overwhelms the effect of short-term disability. The overall assessment of the effect of these metrics is captured in disability-adjusted life-years (DALYs), which comprises YLLs plus YLDs. The GBD 2016 Brain and Other CNS Cancer Collaborators⁴ show the effect of SDI on DALYs; increasing SDI until an inflection point around 0.80 is associated with increasing DALYs regardless of incidence.

The GBD report⁴ provides data on the incidence and consequences of malignant CNS tumours on the world's population. However, low grade and benign tumours can cause severe disability and early death as well. Unlike benign tumours in other areas of the body, benign CNS tumours can cause the same disabling symptoms as seen with malignant tumours. However, their slower growth often means that the patient has these disabilities for many years, if not decades. These tumours often cause early death because they can transform into a malignancy or cause such disability that the patient succumbs to a benign CNS tumour. The GBD report does not clarify which of the malignant tumours included in this study might have started as a lower grade tumour, and it might never capture the transformation if a repeat histology is not obtained. More importantly, it does not measure the considerable burden of these lower grade lesions, which tend to occur in young adults. These patients, even if they remain independent in their own activities of daily living, are often unable to work or be employed in accordance with their level of education, causing substantial financial hardship for a family. Such patients might be erroneously classified as cured according to the definition of 10-year survival of the GBD study even though they usually succumb to

their CNS tumour. Those patients who present with a seizure, but are otherwise well, might have a delayed diagnosis in resource-poor regions of the world, leading to underestimation of YLDs.

Therefore, the GBD Study gives us the most up-to-date assessment of the minimum burden of malignant CNS tumours over time. Ascertainment bias, poor consensus on histological diagnoses, and access to therapy all affect the incidence and DALYs chronicled here. Furthermore, understanding the effect of lower grade and benign CNS tumours remains a challenge that can no longer be ignored while understanding is sought of the cause of these illnesses and their full effect on the global population.

Lisa M DeAngelis

Memorial Sloan Kettering Cancer Center, New York, NY 10065, USA
deangell@mskcc.org

LMD reports personal fees from BTG International, Juno Therapeutics (now Celgene), Sapience Therapeutics, Roche (formerly Genentech), and Tocagen, Inc, outside of the submitted work.

Copyright © 2019 The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY-NC-ND 4.0 license.

- Schubart JR, Kinzie MB, Farace E. Caring for the brain tumor patient: family caregiver burden and unmet needs. *Neuro Oncol* 2008; **10**: 61–72.
- Braganza MZ, Kitahara CM, Berrington de Gonzalez A, Inskip PD, Johnson KJ, Rajaraman P. Ionizing radiation and the risk of brain and central nervous system tumors: a systematic review. *Neuro Oncol* 2012; **14**: 1316–24.
- Amirian ES, Zhou R, Wrensch MR, et al. Approaching a scientific consensus on the association between allergies and glioma risk: a report from the glioma international case-control study. *Cancer Epidemiol Biomarkers Prev* 2016; **25**: 282–90.
- 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**: 376–93.
- Leece R, Xu J, Ostrom QT, Chen Y, Kruchko C, Barnholtz-Sloan JS. Global incidence of malignant and other central nervous system tumors by histology, 2003–2007. *Neuro Oncol* 2017; **19**: 1553–64.
- Ostrom QT, Gittleman H, Truitt G, Boscia A, Krunchko C, Barnholtz-Sloan JS. CBTRUS statistical report: primary brain and other nervous system tumors diagnosed in the United States in 2011–2015. *Neuro Oncol* 2018; **20** (suppl 4): iv1–86.
- Melin BS, Barnholtz-Sloan JS, Wrensch MR, et al. Genome-wide association study of glioma subtypes identifies specific differences in genetic susceptibility to glioblastoma and non-glioblastoma tumors. *Nat Genet* 2017; **49**: 789–94.

Stroke epidemiology in China: which are the next steps?

In China, stroke epidemiology is not terra incognita; several epidemiological trends are known. Among them are the north–south disparity, with differences in the epidemiology of risk factors, and higher prevalence and incidence of stroke in the north; and rural–urban

differences, to the disadvantage of rural regions.¹ Nevertheless, a lot of variation is to be expected because of the vastness of the country, harbouring so many people with differing genetic backgrounds, risk behaviours, and access to health services. Whether one epidemiological



See Series page 394