



The role of neurosurgery in advancing pediatric CNS tumor care worldwide



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ABSTRACT

Introduction: There is substantial inequity in survival outcomes for pediatric brain tumor patients residing in high-income countries (HICs) compared to low- and middle-income countries (LMICs). To address disparities in pediatric cancer survival, the World Health Organization (WHO) established the Global Initiative for Childhood Cancer (GICC) to expand quality care for children with cancer.

Research question: To provide an overview of pediatric neurosurgical capacity and detail the burden of neurosurgical diseases impacting children.

Material and methods: A narrative review of the current context of global pediatric neurosurgical capacity as it relates to neurooncology and other diseases relevant to children.

Results: In this article, we provide an overview of pediatric neurosurgical capacity and detail the burden of neurosurgical diseases impacting children. We highlight concerted advocacy and legislative efforts aimed at addressing unmet neurosurgical needs in children. Finally, we discuss the potential implications of advocacy efforts on treating pediatric CNS tumors and outline strategies to improve global outcomes for children with brain tumors worldwide in the context of the WHO GICC.

Discussion and conclusion: With both global pediatric oncology and neurosurgical initiatives converging on the treatment of pediatric brain tumors, significant strides toward decreasing the burden of pediatric neurosurgical diseases will hopefully be made.

1. Introduction

Addressing inequitable outcomes for children with cancer are increasingly recognized as a health priority. In high-income countries (HICs), 80% of children diagnosed with cancer will survive (Rodriguez-Galindo et al., 2015). On the contrary, 80% of children in low- and middle-income countries (LMICs), where 90% reside, will succumb to their disease (Ward et al., 2019a, 2019b). Insufficient resources impacting prompt referral mechanisms and timely access to comprehensive multidisciplinary care further exacerbate existing treatment

challenges (Rodriguez-Galindo et al., 2013). To address these disparities, the World Health Organization (WHO) established the Global Initiative for Childhood Cancer (GICC) (World Health Organization, 2021). This initiative seeks to reach a 60% survival rate for pediatric cancers globally by 2030.

Within the WHO GICC, low-grade glioma (LGG) is one of six designated index cancers and serves as a tracer for the complex care needed for children with CNS tumors. For children with LGG, the extent of resection is a strong predictor of long-term outcome; hence, timely access to quality neurosurgical care is essential (Upadhyaya et al., 2018; Wisoff

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et al., 2011). For children with central nervous system (CNS) tumors in LMICs, underdiagnosis, delayed presentation, and treatment abandonment are significant barriers to care (Moreira et al., 2020a). As neurosurgery assumes a critical role towards reaching the goals of the WHO GICC, the neurosurgical community will be tasked with helping to improve access to quality care for pediatric CNS tumor patients.

In this article, we provide an overview of the burden of pediatric CNS tumors and pediatric neurosurgical capacity as it relates to the burden of neurooncologic diseases impacting children worldwide. We highlight concerted advocacy and legislative efforts aimed at addressing unmet care needs. Finally, we discuss the potential implications of advocacy efforts on the treatment of children with CNS tumors.

2. The global burden of pediatric CNS tumors

CNS tumors comprise approximately 20% of pediatric cancer cases (Steliarova-Foucher et al., 2017; Ward et al., 2014). However, a paucity of population-based cancer registries in much of the world has contributed to a lack of comprehensive analyses for pediatric CNS tumors at the global level. Importantly, quality population-based cancer registries cover less than 15% of pediatric patients globally (Steliarova-Foucher et al., 2017). Furthermore, the largest population-based reports on incidence and survival have less information on CNS tumors than other pediatric cancers (Steliarova-Foucher et al., 2017; Allemanni et al., 2018). Beyond population-based cancer registries, sparse peer-reviewed reports have been published on the outcomes of pediatric CNS tumors LMICs (Ward et al., 2022).

To provide a global description of the burden of pediatric CNS tumors, GLOBOCAN can be used as it estimates national level data on incidence and mortality for 36 of the most common malignancy types across 185 countries, extrapolating data to provide a comprehensive evaluation of cancer statistics (Sung et al., 2021). GLOBOCAN is created and maintained by the International Agency for Research on Cancer (IARC) and has a public data platform. (Global Cancer Observatory).

Based on GLOBOCAN, in 2020 an estimated 30,766 children and adolescents (ages 0–19 years) were diagnosed with CNS tumors and 15,337 died from these tumors. Globally, the age-standardized incidence of CNS tumors was 1.2 per 100,000. When evaluated by region, Asia has the highest number of pediatric CNS tumor incident cases (16,572), while Oceania reported the least (189) (Table 1). The age-standardized incidence rate was lowest in Africa (0.62) and highest in Northern America (3.3). Similarly, Africa had the lowest age-standardized mortality rate per 100,000 children at 0.37, while the highest rates were observed in Europe (0.76) and Northern America (0.77). Based on World

Table 1
Incidence and mortality for geographic regions and World Bank country income groups.

	Incident cases	Age-standardized incidence rate ^a	Deaths	Age-standardized mortality rate ^a
Regions				
Asia	16572	1.2	9332	0.65
Europe	3645	2.4	1184	0.76
North America	2922	3.3	1593	0.77
Latin America and the Caribbean	3200	1.6	616	0.69
Africa	4238	0.62	2550	0.37
Oceania	189	1.5	62	0.47
World Bank Income Groups				
High-	6662	2.5	1854	0.69
Upper-middle-	11745	1.5	6138	0.78
Lower-middle-	10624	0.88	6191	0.51
Low-	1734	0.56	1154	0.37
World	30766	1.2	15337	0.59

MIRR: Mortality:Incidence Rate Ratio.

^a Per 100,000 children at risk.

Bank group, 24,104 incident cases, representing 78% of the total cases, and 13,483 deaths, representing 88% of worldwide deaths, occurred in LMICs. The age-standardized incidence rate was the lowest in low-income countries (0.56) and highest in high-income countries (2.5), an almost 5-fold difference.

These data describe critical disparities for this patient population with marked variation of incidence and mortality rates across countries and regions, especially in limited resource settings. These inequalities could be influenced by not only the strength of cancer registries, but also the national diagnostic capacity and treatment infrastructure. Understanding the global burden pediatric CNS tumors is essential for quantifying the disparities in burden between LMICs and high-income countries, recognizing areas of deficiencies, and prioritizing interventions. Furthermore, considering that almost all of these patients will require neurosurgical care and interventions, understanding the neurosurgical capacity around the globe will be key to inform cancer control strategies.

3. Pediatric neurosurgical capacity around the globe

The global neurosurgical workforce comprises nearly 50,000 physicians, with less than 3000 sub-specializing in the care of children (Dewan et al., 2018a, 2018b). Disparities in the distribution of the neurosurgical workforce are especially pronounced in pediatric neurosurgery, as nearly 86% of subspecialists practice in HICs. While detailed information on the status of pediatric neurosurgery in LMICs is sparse, nine out of ten LMICs evaluated in a 2007 survey did not meet the optimal ratio of pediatric neurosurgeons to population (Choi, 2007). Current estimates report that only about 330 pediatric neurosurgeons are available for the care of more than 1.2 billion children in LMICs (Dewan et al., 2018b). With prevention and treatment of communicable diseases leading to a substantial decrease in childhood mortality in many regions of the world, an epidemiological shift has placed a significant focus on caring for children with non-communicable illnesses, including cancer (Perin et al., 2022).

Pediatric patients with CNS tumors require complex medical care delivered by a multidisciplinary team of specialists with access to advanced technologies. Specifically, providing essential neurosurgical care requires access to specialized surgical equipment, ancillary clinical support, and a dedicated neuro-intensive care unit staffed by a multidisciplinary team. In a recent global survey of neurosurgeons in 61 countries, the evaluation of services and infrastructure showed disparities in pediatric neurosurgical capacity to care for children with CNS tumors based on the country income level (Roach et al., 2023). Nonetheless, the essential infrastructure to provide care does exist in most LMICs, although strategies to strengthen multidisciplinary CNS tumor programs will be key to optimize available resources.

Given the complexity of factors needed to deliver comprehensive pediatric neurosurgical care, patients frequently require transfer to referral centers, often located in urban locations (Dewan et al., 2018a). Geographic distance, financial constraints, suboptimal referral systems, and complex socio-cultural structures further exacerbate disparities in equitable care. Failing to recognize these barriers to care and to integrate a socio-cultural approach in disease management and public health policy undoubtedly contributes to reduced reliance on conventional care systems and treatment abandonment in marginalized populations.

Additionally, many treatment approaches for pediatric CNS tumors rely on novel molecular tests which makes navigating the complex treatment process challenging for clinicians. However, with increased collaboration and the development of resource-adapted treatment guidelines in parallel with cutting edge technological advancements, international collaboration can assist in improving neuro-oncology care for children in resource-limited settings (Chan et al., 2015).

Owing to the current shortage and distribution of pediatric neurosurgery specialists around the globe, most pediatric neurosurgical care outside of HICs is administered by general neurosurgeons. For example, only two-thirds of pediatric CNS tumor patients in Asia and Australasia

were reported to be managed by pediatric neurosurgeons (Dewan et al., 2018a, 2018b; Baticulon et al., 2020; Park et al., 2016). In the context of childhood CNS tumors, pediatric neurosurgeons were more likely to remove greater than 90% of the tumor and leave less than 1.5 cc of residual tumor compared to general adult neurosurgeons (Albright et al., 2000). While sub-specialization translates to better CNS tumor care, specialized pediatric neurosurgery remains inaccessible or unaffordable to much of the world. Moreover, population growth and unmet neurosurgical disease burden are additional challenges that impact the availability and timely access to care for children with CNS tumors in resource-limited settings.

4. Neurosurgical disease burden impacting pediatric CNS tumor care

As our world population has recently surpassed 8 billion people, the burden of unmet neurosurgical disease is best depicted by the more than 5 million individuals around the globe who are unable to receive care for a treatable neurosurgical condition each year (Dewan et al., 2018a). In pediatric neurosurgery, a substantial number of cases attributed to traumatic brain injury, hydrocephalus, and neural tube defects, continues to place enormous pressure on the global neurosurgical workforce. According to a recent report from members of the International Society for Pediatric Neurosurgery (ISPN), hydrocephalus is the most commonly treated disease by pediatric neurosurgeons, with an estimated 400,000 cases occurring worldwide each year (Dewan et al., 2018c; Boop, 2022). For neurosurgeons in African, Latin American, and Southeast Asian countries, the compounding effects of high birth rates, infectious disease, and neural tube defects have led to a significant pediatric hydrocephalus case volume.

While cases of anencephaly are uniformly fatal, neural tube defects such as spina bifida more commonly mirror a chronic disease. For patients with myelomeningocele, managing complex comorbidities often requires further treatment following surgical repair. (Mitchell et al., 2004).. In countries lacking mandatory folic acid fortification of staple foods for the prevention of spina bifida and anencephaly, the prevalence of neural tube defects is disproportionately high (Kancherla et al., 2021). This is especially burdensome for neurosurgeons in regions without adequate resources to care for all children requiring neurosurgical intervention, especially those with complex CNS tumors.

In addition to hydrocephalus and neural tube defects, traumatic head injury requiring neurosurgical intervention is a global health concern. Head injuries are the number one cause of traumatic death in children (Dewan et al., 2018a). This has prompted the World Health Organization to adopt a resolution on emergency and trauma care with the goal of achieving a 50% global decrease in death from trauma over the next decade. (World Health Organization, 2019).. Sadly, the current epidemic of gun violence in the United States has allowed gunshot wounds to surpass head injury as the leading cause of traumatic death in children, which has prompted new advocacy efforts (Goldstick et al., 2022).

With hydrocephalus, neural tube defects, and traumatic injuries inundating pediatric neurosurgeons across the globe, there continues to be limited capacity to care for children with complex CNS tumors. Although competing priorities are one element of limitations in access to specialized neurosurgical care, in a field of increasing complexity, neurosurgical teams who understand the nuances of the evolving care of children with CNS tumors are needed. Innovative policy efforts and advocacy are necessary to address the burden of neurosurgical diseases and achieve expanded care for children with CNS tumors.

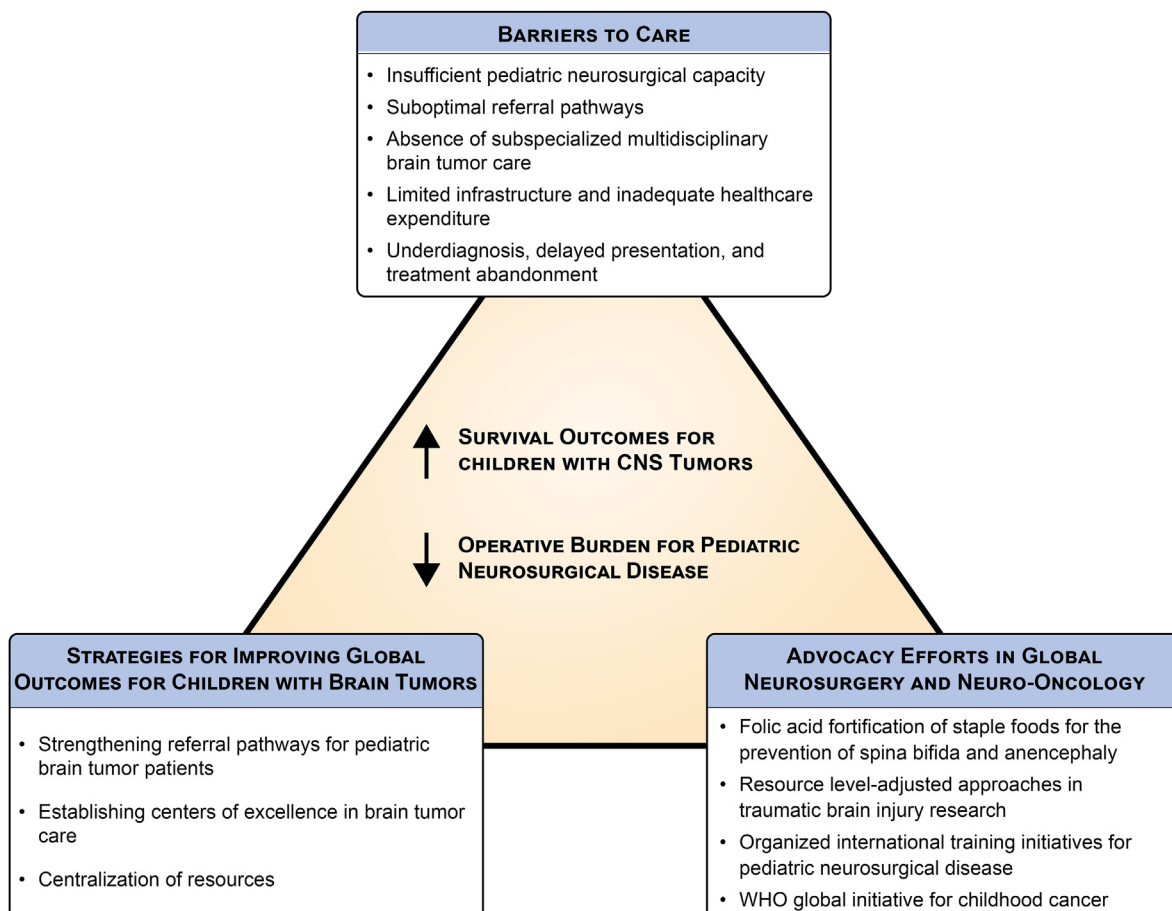


Figure 1. Context of pediatric CNS tumor care globally.

5. Neurosurgeons as advocates to address global healthcare challenges

Advocacy efforts influencing public health policy are essential to achieving equitable access to neurosurgical care. The neurosurgical community has already been involved by leading initiatives that seek to expand services globally. In this section, we will provide examples of initiatives where the neurosurgical community is driving efforts at the intersection of neurosurgery and public health.

With hydrocephalus representing the most common neurosurgical condition in children, there is significant urgency to address the unique challenges associated with providing safe, cost-effective, and sustainable treatment for pediatric hydrocephalus in limited resource settings. By developing training initiatives, organizing surgical outreach efforts, and providing high-quality educational tools at no cost, the International Society for Pediatric Neurosurgery (ISPN), the International Federation of Neuroendoscopy (IFNE), the Foundation for International Education in Neurological Surgery (FIENS), and the World Federation of Neurosurgical Societies (WFNS) have substantially impacted global neurosurgical care (Mosberg et al., 1970; Blankstein et al., 2011; Teton et al., 2020). In countries with a limited number of pediatric neurosurgeons, educational courses such as the Asian Australasian Advanced Course in Pediatric Neurosurgery (AAACPN) and others on all continents serve as transitional measures to educate general neurosurgeons on the standards of neurosurgical care for children.

Preventing permanent disability from myelomeningocele and death from anencephaly through folic acid fortification of staple foods is at the forefront of global policy efforts. At the 75th World Health Assembly Meeting in Geneva, Switzerland, the Global Alliance for the Prevention of Spina Bifida-F (GAPSBiF), a multidisciplinary coalition of neurosurgeons, pediatricians, geneticists, epidemiologists, food scientists, and policy experts, convened alongside members of the ISPN, WFNS, and the G4 Alliance to advocate for a resolution mandating the fortification of staple foods with folic acid for the prevention of neural tube defects worldwide. (Resolution) This effort has engaged key global health organizations, enabling changes at the level of health systems and ministries of health.

To complement policy development, research efforts incorporating resource-level adjusted approaches are desperately needed to improve outcomes for children across diverse economic settings. In 2017, £162 million was allocated by the UK Department of Health to advance research efforts benefitting patients in LMICs (Kolias et al., 2019). In the context of neurosurgical disease, £1.8 million was awarded to establish the NIHR Global Health Research Group on Neurotrauma. By assembling a diverse coalition of researchers and clinicians from LMICs and HICs, the neurotrauma research team is poised to evaluate resource-level adjusted interventions capable of effectively reducing the impact of traumatic brain injury in limited-resource settings (Kolias et al., 2019). As traumatic head injury is the number one cause of death in children, these efforts will undoubtedly play a leading role in improving neurosurgical capacity by reducing the operative burden and decreasing child mortality in LMICs (Goldstick et al., 2022).

These initiatives highlight areas where advancements have been made to decrease the burden of neurosurgical disease, led by the neurosurgical community. These public health measures are vital to expanding neurosurgical capacity for the diagnosis and treatment of CNS tumors in children by decreasing the overall operative burden in LMICs.

6. Strategies for improving global outcomes for children with CNS tumors

To improve global outcomes for children with CNS tumors, pediatric neurosurgical capacity and neurosurgical disease burden must be embraced at the national policy level. As pediatric neurosurgeons in LMICs continue to provide care for an overwhelming number of children with hydrocephalus, myelomeningocele, and traumatic brain injury, it is imperative to support advocacy efforts aimed at decreasing the burden

for preventable conditions. Given the vital role that general neurosurgeons play in providing care for children in LMICs, expanding workforce capacity through training opportunities may help reduce the number of cases referred to regional children's hospitals. Together, these strategies may allow pediatric neurosurgeons at specialized children's hospitals to dedicate more time and resources to providing multidisciplinary care for children with CNS tumors.

In addition to neurosurgical care, improving early disease detection and reducing treatment abandonment are critical in the setting of pediatric neuro-oncology. While the ratio of neurosurgeons per 100,000 people strongly correlates with the diagnosis of a CNS tumor, access to diagnostic imaging and health expenditure per capita are other associated factors (Moreira et al., 2020b). Underdiagnosis and the lack of national cancer registries in many LMICs make quantifying the true burden of pediatric CNS tumors challenging. These factors contribute further to healthcare disparities, as many governments allocate financial resources based on disease incidence and anticipated volume of cases. By establishing high quality cancer registries, policymakers can be apprised of the true magnitude of pediatric CNS cancer and contribute additional resources where needed.

Adequate health financing and access to expert-guided treatment recommendations are further measures to improve outcomes for children with CNS tumors. Similar to countries without universal healthcare coverage, families in LMICs seeking costly medical care such as neurosurgery face the possibility of substantial financial toxicity. To protect families from impoverishment and catastrophic health expenditure following a CNS tumor diagnosis, neurosurgeons must aid in lobbying for special funding packages for families in need. In the absence of a national healthcare plan, one approach is to engage non-governmental organizations invested in the care and support of children with cancer.

To ensure long-term improvement in the diagnosis, treatment, and survival of pediatric CNS tumor patients, establishing multidisciplinary centers for CNS tumor care and strengthening referral systems is essential. By centralizing CNS tumor patient referrals to a dedicated pediatric treatment center, these centers optimize resources and improve outcomes for children (Chan et al., 2015; Qaddoumi, 2016). From a neurosurgical perspective, such centralization is associated with higher tumor resection rates, lower complication rates, and lower mortality (Albright et al., 2000; Smith et al., 2004). Furthermore, the development of protocols for pediatric CNS tumors tailored to the availability of resources will contribute to improved survival outcomes, increased patient acceptance, and reduced rates of treatment abandonment. Such measures will also reduce discrepancies in disease classification and improve the administration of quality care (Joannon et al., 2016; Elzomor et al., 2017). Importantly, understanding the unique aspects of pediatric CNS tumor care can substantially improve the number of functional survivors within this patient population (Fischer et al., 2016; Howe et al., 2023).

7. Conclusion

To achieve meaningful progress in advancing pediatric CNS tumor care for children worldwide, collective efforts from the neurosurgical community are paramount. These efforts extend beyond the operating theatre to address neurosurgical capacity-building efforts, resource-level adjusted research, and advocacy for patient-centered global initiatives. Due to the multifaceted care required to diagnose and successfully treat CNS tumors, investing in cancer care to improve outcomes for children with CNS tumors will undoubtedly enhance the coordination and integration of health systems, thereby benefitting the greater pediatric cancer population. Through globally focused interventions, equitable survival outcomes for children with CNS tumors can be achieved.

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Contributors

FAB and DCM developed the idea. JTR drafted the manuscript. All authors contributed to the critical review and editing of this article. All authors approved the final submitted version.

Declaration of competing interest

The authors declare no competing interests.

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