HSD15

# The Economic and Humanistic Burden of Glioma in the United States and Canada

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## Background

- Gliomas are the most frequent malignant brain tumor in the United States (US) and in Canada, with six new cases per 100,000 population per year in the US [1]
- Gliomas, particularly glioblastoma are associated with considerable mortality and morbidity, with 5-year overall survival of only 54% in WHO grade 4 *IDH*-wildtype glioblastomas and 56% in H3 K27M-mutat diffuse midline gliomas in the US [14]
- Gliomas are also associated with an economic and humanistic burden, including productivity losses, frequent financial hardship for patients and caregivers, reduced long-term quality of life (QOL), and risks of neurocognitive deficits [2,3], due to often suboptimal treatment patterns [9,17,23]
- Novel treatment options for glioma are rare, however, and immunotherapy and targeted therapy play so far only a minor – marizomib is the latest in a relatively long line of compounds failing their clinical trial program [4]
- These and additional unmet needs in glioma care were reviewed in a recently completed project with a global focus [2], as part of which the economic and humanistic burden in the US and Canada were reviewed specifically to characterize patient experiences and to inform future clinical and economic decision-making in these two countries

## Methods

- The overarching project into research the burden and unmet need associated with glioma was informed by a systematic literature review in April 2023 [2], which was updated using targeted incremental searches in January and April 2024
- Search strategies were developed from published reviews of glioma and search filter fragments for study types of interest and were implemented in PubMed and Embase using the respective native search interfaces
- Screening was performed in Sourcerer (Covalence Research Ltd, Harpenden, UK) by a single researcher

## Results: Humanistic burden

**Table 1** Overview of studies on the humanistic burden associated with glioma

| Study | Source | Outcome | Finding | Conclusion |
|---|---|---|---|---|
| Van Dyk *et al.* [16] | Glioma survivors at a single center, n=23 | Neuropsychological and psychosocial measures in relation to work | • Thirteen participants were working, the remainder were not (of whom seven reported to have stopped work due to glioma)<br>• No neurocognitive differences between those working and those not working were observed, but those not working had higher anxiety levels and worse perceived cognitive impairment, emotional well-being, and symptoms related to brain cancer and a lower sense of self-efficacy | Glioma survivors may see their functioning compromised by cognitive outcomes, including self-reported and psychosocial outcomes, due to glioma |
| Forst *et al.* [22] | Caregivers of patients with malignant glioma, n=21 | Anxiety of caregivers of patients with malignant glioma | • Caregivers, on average, had elevated anxiety<br>• Themes important to caregivers included coping strategies, changes in the relationship with the patient, challenges with social support and in communicating with the healthcare staff, and devaluating self-care for the patient's needs | Authors concluded that distress was common in caregivers of patients with malignant gliomas and that caregivers were interested in receiving an intervention shortly after the patient's diagnosis although they were concerned about their ability to participate in any such intervention due to their time constraints |
| Heffernan *et al.* [23] | Patients from the International Low Grade Glioma Registry resident in select US states and counties, n=320 | Quality of life as measured using the SF-36 | • Frequently reported symptoms included decreased sensation in the face and extremities, difficulties remembering new facts, trouble thinking and difficulties getting words out (all reported by 60% or more of the sample)<br>• Patients with adjuvant treatment did significantly better in social functioning, role-emotional, and mental health but worse in physical functioning | Relative to persons with non-malignant brain tumours and population controls, the – relatively young – patients with LGG reported substantively reduced QoL, leading the authors urge for improved acknowledgement and management of these symptoms |

Literature on the humanistic burden of glioma is sparse of the US and even more so for Canada

- The available evidence, however, clearly demonstrates that patients have a lower quality of life than population controls, including due to cognitive impairments
- Caregivers are similarly affected by the disease, through elevated levels of anxiety and distress

## Abbreviations

| Abbreviation | Term | Abbreviation | Term |
|---|---|---|---|
| CI | Confidence interval | n.r. | Not reported |
| FU | Follow-up | OOP | Out-of-pocket |
| HGG | High-grade glioma | PCV | Procarbazine, Lomustine, Vincristine |
| HR | Hazard ratio | SEER | Surveillance, Epidemiology, and End Results |
| LGG | Low-grade glioma | TMZ | Temozolomide |

## References

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## Results: Economic burden

**Table 2** Overview of cost estimates associated with glioma care in the US

| Glioma | Study | Source | Cost item | Time frame | Cost, $ |
|---|---|---|---|---|---|
| Glioblastoma | Aly et al. [8] | Medicare claims data | Cumulative (cost year n.r.) | 3 months before diagnosis to end of FU | 98,710 (124,138 if progressing beyond 1L therapy) |
| Glioblastoma | Norden et al. [5] | Commercial claims data | Total per patient (2016 $) | 0–6 months after 1L therapy initiation | 117,325 |
| Glioblastoma | Norden et al. [5] | Commercial claims data | Total per patient (2016 $) | 7–12 months after 1L therapy initiation | 45,225 |
| Glioblastoma | Norden et al. [5] | Commercial claims data | Total per patient (2016 $) | 0–6 months after 2L therapy initiation | 126,128 |
| Glioblastoma | Norden et al. [5] | Commercial claims data | Total per patient (2016 $) | 7–12 months after 2L therapy initiation | 117,705 |
| HGG | Jiang et al. [13] | Commercial claims data | Cumulative (2014 $) | 3 months before to 1 year after diagnosis | 201,749 (95% CI: 197,490 to 206,024) |
| HGG | Jiang et al. [13] | Commercial claims data | Cumulative (2014 $) | 3 months before to 5 years after diagnosis | 268,031 (95% CI: 262,877 to 274,416) |
| HGG | Liu et al. [6] | Review of single-center health records | Total per-patient healthcare payments (cost year n.r.) | Diagnosis to death | 184,160 (95% CI: 151,215 to 222,431) |
| LGG | Tuohy et al. [7] | Commercial claims data | Index resection and stereotactic biopsy per patient (cost year n.r.) | Within 90 days of surgery | 39,043–40,661 (of which 1,055–1,077 OOP) |
| LGG | Tuohy et al. [7] | Commercial claims data | Drugs (cost year n.r.) | Within 90 days of surgery | 4,005–2,277 (of which 211–154 OOP) |
| LGG | Tuohy et al. [7] | Commercial claims data | Total (cost year n.r.) | Within 90 days of surgery | 43,219–56,093 (of which 811–1,164 OOP) |

Costs were highly variable but consistently high (Table 2):

- Even for low-grade gliomas, costs reached US$39,043–40,661 for index procedures and US$43,219–56,093 for 90 days after surgery [7].
- Radiotherapy was the main cost driver for 1L glioblastoma therapy by Norden *et al.* [5], while systemic treatment was the main cost in 2L therapy, with more than $85,000 spent on systemic treatment per patient and 6-month treatment period. Liu *et al.* [6] identified outpatient costs as the major cost in HGG and radiology as the largest component of outpatient costs
- In contrast, Aly et al. [8] identified inpatient costs as accounting for >50% of costs in Medicare claims in the peri- and post-diagnosis period. Jiang et al. [13], for commercial claims, found 42% (38%) of peri-/post-diagnosis costs for 1 (5) years to be accounted for by inpatient costs.
- Data for Canada were sparse: Only one recent estimate (in 2017 $) was identified, which put the 2–2.5-year costs associated with glioblastoma at $14,110–38,858 [10].

## Results: Associations of socioeconomic status with glioma care and outcomes

**Table 3** Overview of studies on socioeconomic status associations with glioma outcomes and care

| Study | Source | Outcome | Finding | Conclusion |
|---|---|---|---|---|
| Shin et al. [11] | National Cancer Database, n=4,325 | Overall survival with anaplastic astrocytoma | • Overall 5-year survival was 37.6% but was 46.9% if on private insurance compared with 31.3% if uninsured, 42.9% if Medicaid-insured, and 6.2% if Medicare-insured<br>• In multivariable regression, medical insurance (HR 0.761 [95% CI 0.585 to 0.989]) and higher income (HR 0.894 [95% CI 0.849 to 0.941]) were independent predictors of longer survival | Authors discussed that minority populations, including Black and Hispanic patients, are more likely to be uninsured in the US, thereby putting them at a disproportionate risk of reduced survival also for anaplastic astrocytoma |
| Rong et al. [19] | SEER data, n=13,665 | Overall survival with glioblastoma | • Relative to uninsured patients, those with insurance were more likely to be older, women, and White and to have a smaller tumor size at diagnosis<br>• Being uninsured and Medicaid insurance predicted reduced survival | People without insurance or insured with Medicaid had poorer survival outcomes than those with non-Medicaid insurance |
| Asfaw et al. [20] | Single-center tumor registry, n=276, and health records, public regional data | Length of hospital stay, discharge location associated with glioblastoma | • Being uninsured was associated with a lower chance of home discharge<br>• Private insurance and being in the wealthiest socioeconomic status index quartile were associated with shorter hospital stay | Authors concluded that the social determinants of health, such as insurance and wealth, but not race were associated length of hospital stay and discharge location, with private insurance and more wealth associated with more favorable outcomes |
| Hsu et al. [24] | Single-center data, n=168 | Overall survival, radiotherapy with glioblastoma | Elderly patients and those with Medicare insurance were less likely to receive the same number of radiation fractions (as younger and not-Medicare-insured patients) and to receive TMZ with radiation | |
| Lee et al. [25] | Single-center data on patients aged ≤18y, n=96 | Overall survival, treatment travel associated with diffuse midline and intrinsic pontine glioma | • Patients from higher-income census tracts had more than twice the overall survival than patients living outside these tracts (480 vs. 235 days, p<0.001)<br>• Patients from higher-income census tracts traveled much further for medical care (1,550 vs. 1,114 miles, p=0.048); a similar pattern was observed for patients from the highest (versus the lowest) education quartile | Socioeconomic status is associated with survival and travel distances for medical care in pediatric patients with glioma |

## Discussion

The present review characterized the economic and humanistic burden of glioma in the US and Canada, which was found to be substantial

- In the US, outcomes of glioma as well as access to and quality of glioma care were linked to socioeconomic status (which may also explain at least partly the association between outcomes and race/ethnicity) – patients with higher income and private (relative to no or government) insurance were more likely to have extended survival and receive treatment such as radiotherapy
- **Increased regionalization** of treatment provision may improve outcomes by allowing for better treatment access. This would require a more equitably distributed neurooncological workforce, targeting in particular currently underserved counties and communities in the US [15], which implies considerable investments in care. The benefits of easier access, however, can result quickly in increased treatment rates and reduced patient travel burden as demonstrated in a Canadian study that showed two additional regional cancer centers in Ontario reducing patient travel times while increasing receipt of care, including surgery and chemoradiation, by 11% [18].
- **Active promotion of trial findings** and best practices in order to ensure that patients receive care based on the most recent evidence, e.g. as documented among Canadian neurosurgeons who were reported to have widely integrated RTOG9802 results into their care for patients with LGG (although senior surgeons reported a smaller impact of trial findings than their junior colleagues [22])