Healthcare Costs for High-grade Glioma

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Abstract. *Background/Aim:* Data on verified healthcare costs for high-grade gliomas (HGGs) are limited. This study aimed to determine the healthcare costs for HGGs. *Materials and Methods:* A total of 88 primary HGGs patients diagnosed and treated at our Institution between 2011 and 2017 who had insurance plans administered with Excellus BCBS were retrospectively identified. Patient clinical information was linked with all verified insurance payment data. *Results:* Median insurance payments for clinical management of HGGs were \$184,159.83. The leading cost was therapeutic radiation oncology. Patients under commercial insurance had a longer survival time, and higher healthcare expenditures in total and in each phase of clinical care. Healthcare costs were higher during therapy initiation and at disease recurrence and lower during the interim. A generalized linear model showed that patients with commercial insurance, better Karnofsky Performance Status, and longer survival time had higher healthcare expenditures. *Conclusion:* Healthcare payments for HGGs patients were substantial and such high healthcare expenditures were positively associated with patient survival and commercial insurance.

Malignant gliomas account for 70% of malignant primary brain tumors diagnosed in the US every year and they continue to present a difficult therapeutic challenge (1-5). In addition to challenging clinical management, malignant brain tumor patients incur higher healthcare costs when compared both to healthy individuals, as well as patients with other

forms of cancer (6-8). Total monthly costs for glioma patients can be 20 times more than for healthy controls (6, 9). Previous studies to estimate the cost of glioma care have been based on commercial claims databases, however, such databases suffer several limitations including lack of detailed and verified clinical information (6, 10, 11). Ray *et al.*, estimated that healthcare costs for these patients were \$106,896 in the 6 months postindex surgery and \$131,815 in the 12 months postindex surgery (10). Similarly, Jiang *et al.* reported that total medical costs for 6 months and 12 months post GBM diagnosis were \$160,974 and \$201,749, respectively (11). Both of these studies suffer from the advantage and disadvantage of using a large commercial database. The large number of patients strengthens some estimates but it also prevents more granular examination and verification of individual patient data.

In addition, as US cancer care costs continue to increase (12-14), there is a movement toward bundled care and simplified payment schemes (15, 16). Data regarding the actual payments and costs associated with glioma care are critical to make informed decisions regarding healthcare management. Many previous studies of healthcare costs on high-grade gliomas (HGGs) were performed either before 2000 or used estimated data from Surveillance, Epidemiology and End Results (SEER) - Medicare or commercial claims database (9-11, 17, 18). It is known that the treatment paradigm for patients with HGGs changed significantly since the introduction of Stupp regimen in 2005 (5) and data from SEER-Medicare or commercial claims database suffer the aforementioned limitations.

In this study, patients with primary HGGs diagnosed and treated at our Institution were retrospectively included and patient clinical information from electronic health record (EHR) was linked with relevant healthcare costs from the time of diagnosis to the time patients died or end of study from a single health insurance company, Excellus BlueCross BlueShield (BCBS) of Rochester, New York which managed both commercial and non-commercial (Medicare HMO, Medicaid HMO, *etc.*) products. We sought to investigate total healthcare costs for these patients, how these costs are

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distributed and any potential factors associated with these costs. The patient cohort involved 88 patients with over 44,000 separate insurance claims. This dataset represented a happy medium that is large enough to provide a good estimate of overall patient costs, but small enough to individually verify each patient diagnosis and treatment rather than relying on administratively coded national datasets.

Materials and Methods

Data source. This retrospective study was approved (protocol 00071072) by the University of Rochester Research Subjects Review Board with a waiver of informed consent. Adult patients (aged ≥ 18 years) with initial diagnosis of HGGs (ICD-9: 191.XX and ICD-10: C71.XX) who were treated at our institution between January 1, 2011 and February 28, 2017 and who were under Excellus BCBS coverage during the entire study period were included. Clinical information for these patients were collected from EHR at our institution and matched to all payment data provided by Excellus BCBS. Overall survival time from the date of diagnosis to the date of death for any reason, or the date the patient was last known to be alive and relevant costs during the course of treatment were calculated. Healthcare costs were divided into three clinically relevant phases: 1), initiation care when surgery, radiation therapy and chemotherapy were implemented; 2), maintenance care when temozolomide or no chemotherapy was used and 3), recurrence care when new chemotherapy or radiation therapy was implemented.

Statistical analyses. Descriptive statistics were used to describe the demographic and clinical characteristics of the study cohort. Generalized linear model (GLM) with gamma distribution and log link function was conducted to examine potential factors associated with healthcare costs. Total healthcare costs were used as dependent variable and age, gender, Karnofsky Performance Status (KPS) score, married status, insurance type and survival as predictors. Wald chi-square was used for the model. All analyses were conducted using IBM SPSS Statistics (version 24).

Additionally, we ran two sensitivity analyses (SA) to ensure the results were not affected by analytical decisions. In SA1, tumor grade and the aforementioned predictors were included. In SA2, in addition to those predictors mentioned above, vital status was included.

Results

In the present study, 88 eligible patients with primary HGGs diagnosed and treated at our institution between January 1, 2011 and February 28, 2017 were identified and all claims data available for the study period were collected. Table I shows the demographic and clinical characteristics for these patients. Among them, 53.4% (47/88) were males while 46.6% (41/88) were females. The median age at diagnosis was 59 years (min. 30 years and max. 89 years). The majority of the patients were white (94.3%, 83/88) with GBM (80.7%, 71/88). Most of the patients (72.7%, 64/88) had died (all causes) during the follow-up interval. The median survival time of these patients was 402 days (min. 37 days, max. 2059 days).

Table I. Demographic and clinical characteristics of the study cohort (n=88).

Gender	
Male	47 (53.4%)
Female	41 (46.6%)
Age (year)	
Median (min, max)	59 (30, 89)
Race	
White	83 (94.3%)
Non-white	4 (4.6%)
Unknown	1 (1.1%)
Pathology	
Glioblastoma	71 (80.7%)
Anaplastic astrocytoma	12 (13.6%)
Anaplastic oligoastrocytoma	2 (2.3%)
Anaplastic ependymoma	1 (1.1%)
Gliosarcoma	1 (1.1%)
Malignant glioma	1 (1.1%)
KPS	
Median (min, max)	90 (50, 100)
Vital status	
Dead	64 (72.7%)
Alive	26 (27.3%)
Overall survival (days)	
Median (min, max)	402 (37, 2059)
Insurance type	
Commercial	55 (62.5%)
Non-commercial*	33 (37.5%)

*Medicare (25), Medicaid (6), Healthy New York (2).

Overall, our patient cohort generated approximately 44,000 insurance claims from the date of diagnosis to the date of death for any reason, or the date the patient was last known to be alive, incurring total healthcare payments (median) of \$184,159.83 (95%CI=\$151,214.98-\$222,431.36) (Table II). Among these payments, spending was highest for outpatient facilities (\$64,628.88, 95%CI=\$56,108.61-\$78,285.72), followed by inpatient costs (\$46,210.03, 95%CI=\$40,813.55-\$53,710.87), while costs for professional and prescription drugs were lower and nearly the same (\$22,069.09 and \$22,119.39, respectively) (Table II). When payments were further examined by service type, the highest costs (median) were found to be those of outpatient radiology (\$46,294.91), followed by inpatient surgery (\$30,786.47), prescription drugs (\$22,102.29), inpatient medical care (\$20,402.38) and pharmacy (\$20,137.72) (Table II). As expected, the majority of outpatient radiology costs were for therapeutics (radiation oncology) (\$40,938.71) while radiology costs for non-therapeutics (diagnosis) were \$3,825.69 (Table II).

Next, healthcare payments in each phase of care for these patients were studied. Unlike previous studies that used calendar months after diagnosis (7, 10, 11, 13, 14), total costs were divided into three clinically relevant phases, *i.e.*,

Table II. Healthcare costs (median with 95%CI) (\$) for HGGs by setting* and service type (number of patients).

	Median	Lower	Upper		Median	Lower	Upper
Inpatient	46,210.03	40,813.55	53,710.87	Professional	22,069.09	18,269.47	24,734.59
Surgical (70)	30,786.47	28,487.20	33,686.99	Radiology (88)	6,975.37	5,959.88	8,056.14
Medical (71)	20,402.38	15,495.69	26,558.72	Diagnosis (87)	4,001.36	3,000.51	4,219.61
SNF (13)	8,100.00	2,750.00	14,143.08	Therapeutics (81)	3,034.39	2,476.05	3,415.79
Maternity - Mother (1)	6,058.19	NA	NA	Inpatient Surgery (85)	4,108.15	3,434.57	6,229.60
Outpatient	64,628.88	56,108.61	78,285.72	Office/Home Visits (88)	3,586.57	2,925.25	4,085.58
Radiology (88)	46,294.91	40,725.44	52,195.06	Allergy Immunotherapy (1)	2,397.68	NA	NA
Therapeutics (85)	40,938.71	35,756.13	48,566.49	Inpatient Anesthesia (85)	1,797.12	1,530.00	1,979.60
Diagnosis (79)	3,825.69	2,275.18	5,139.95	Hospital Visits (78)	1,188.79	977.17	2,219.88
Pharmacy (76)	20,137.72	7,189.46	38,914.38	Maternity - Non-Del. Services (1)	934.88	NA	NA
Non-chemotherapy (76)	19,091.57	7,033.47	37,618.78	Maternity - Cesarean Deliveries (1)	772.68	NA	NA
Chemotherapy (52)	2,605.52	1,899.91	3,477.01	Outpatient Surgery (44)	748.07	480.60	1,023.22
Outpatient observation (8)	2,362.66	623.76	5,419.39	Emergency Room Visits (81)	583.23	422.79	672.40
Outpatient alcohol/drug (1)	1,982.77	NA	NA	Physical Therapy (19)	504.00	251.29	1,120.34
Outpatient surgery (34)	1,757.34	1,258.59	2,737.98	Outpatient Psychiatric (17)	474.20	261.47	1,155.62
Emergency room (58)	1,732.95	1,303.82	3,153.16	Allergy Testing (2)	408.12	NA	NA
Pathology (86)	1,567.36	1,070.33	2,001.14	Outpatient Anesthesia (21)	390.00	271.44	494.90
Other outpatient facility (85)	980.09	762.37	1,197.97	Miscellaneous Medical (77)	358.67	241.22	396.73
PT/OT/ST (30)	934.49	530.61	1,362.79	Office Surgery (59)	338.56	212.65	657.60
Cardiovascular (41)	79.47	72.49	85.96	Maternity - Anesthesia (1)	328.80	NA	NA
Prescription drugs	22,119.39	18,494.81	27,059.70	Chiropractor (17)	295.69	174.23	987.00
Prescription drugs (83)	22,102.29	18,095.19	27,755.19	Vision Exams (58)	265.36	147.29	360.62
Other	5,364.84	3,900.84	8,200.91	Physical Exams (49)	249.16	141.86	350.12
Home health care (60)	4,716.16	3,164.89	6,612.52	Pathology (67)	155.40	104.22	321.56
Ambulance (56)	1,635.00	1,090.40	2,424.60	Urgent Care Visits (27)	140.00	119.63	190.12
Unknown (9)	434.00	153.36	1,106.00	Office Administered Drugs (77)	136.12	89.75	182.98
Durable medical equipment (44)	226.06	136.69	459.53	Immunizations (57)	99.74	72.51	147.10
Glasses/Contacts (34)	115.00	60.00	120.00	Hearing/Speech Exams (5)	67.02	36.00	193.51
				Cardiovascular (81)	56.93	38.22	113.39
Grand total	184,159.83	151,214.98	222,431.36				

*Milliman Health Cost Guidelines. SNF: Skilled nursing facility; PT: physical therapy; OT: occupational therapy; ST: speech therapy; NA: not available.

initiation, maintenance and recurrence care. The leading cost was incurred in the initial treatment period (\$66,673.80). After relatively low costs for maintenance care (\$14,490.53), healthcare costs increased to \$52,125.77 for recurrence care (Figure 1). This is consistent with the intensity of treatment, *i.e.*, intensive care is required for initiation and recurrence treatment for patients with HGGs.

In our patient cohort, most (62.5%, 55/88) patients were under commercial insurance while the rest of the patients (37.5%, 33/88) were under non-commercial insurance including Medicare, Medicaid and Healthy New York (Table I). Furthermore, patients with commercial insurance appeared to have longer survival time (411 days, 95%CI=366.0-460.0 days) compared with patients with non-commercial insurance (358 days, 95%CI=220.0-658.4 days) ($p=0.563$) (Table III). The benefit of survival time for patients with commercial insurance was associated with

higher number of medical claims (Table III), and higher healthcare costs (\$235,732.85, 95%CI=\$218,933.12-\$278,243.92) than those patients with non-commercial insurance (\$142,134.07, 95%CI=\$98,623.82-\$148,634.70) ($p<0.001$) (Table III). Additionally, higher healthcare costs in each setting and each phase of care were observed for patients under commercial insurance compared to those under non-commercial insurance including Medicare, Medicaid and Happy New York (Table III).

In order to investigate potential factors associated with healthcare costs for these patients, a GLM was run using total healthcare costs as dependent variable and age, gender, KPS, married status, insurance type and survival as predictors. Patients with commercial insurance and longer survival had significantly higher healthcare costs, and better KPS score was marginally correlated with higher healthcare costs. Age, gender and married status were not significantly

associated with healthcare costs (Table IV). To further examine the robustness of our model, we ran sensitivity analyses including tumor grade and vital status, respectively. In both cases, similar findings were obtained, *i.e.*, survival and commercial insurance were significantly associated with healthcare costs (data not shown).

Discussion

Despite the relatively small number of patients with HGGs, these patients have shorter survival time and incur higher healthcare costs compared to other types of cancers (6, 9). However, the majority of these studies were performed a decade ago. Two recent cost studies on HGGs, although with large number of patients from two commercially insured populations, didn't have detailed stage information and they used proxy criteria to identify GBM patients (presumed GBM), and many of their patients might have had low-grade histology (10, 11). Additionally, these studies, like many previous reports, did not have patient survival and performance (KPS) information. All this information is of utmost importance clinically as it impacts treatment regimen, and likely affects costs. In the present study, we identified patients with HGGs diagnosed and treated at our institution between January 1, 2011 and February 28, 2017, and linked patient clinical information from EHR with corresponding health insurance claims and payment data from Excellus BCBS. In this manner, we were able to individually review diagnosis, treatment, and payment data for each patient rather than relying on national databases with their inherent limitations. Total healthcare costs for HGGs were calculated from diagnosis to the date of death or the date the patient was last known to be alive. The median total healthcare payments for these patients were \$184,159.83 (95%CI=\$151,214.98-\$222,431.36). The largest component of healthcare costs was outpatient services (\$64,628.88 with 95%CI=\$56,108.61-\$78,285.72), followed by inpatient services (\$46,210.03 with 95%CI=\$40,813.55-\$53,710.87) (Table II). Furthermore, the highest cost was for outpatient radiology therapeutics (\$40,938.71) (Table II), consistent with a recent study showing that radiation therapy is the strongest contributor to costs for HGGs patients (11).

Furthermore, the healthcare costs were studied in different phases of care, *i.e.*, initiation, maintenance and recurrence care. This way may be more clinically relevant, unlike previous studies which used calendar months after diagnosis (7, 10, 11, 13, 14). Consistent with the intensity of clinical care in different phases, initial care of these patients incurred \$66,673.80, leading the total healthcare costs (Figure 1). This trend is in line with recent reports that the majority of healthcare costs for one-year postindex surgery for patients with malignant gliomas were incurred in the 6 months postindex surgery although total healthcare costs were not

Figure 1. Healthcare costs by phase of care for the study cohort (n=88). Data are shown as median $\pm$ 95%CI.

available in those studies (10, 11). Furthermore, the second peak of healthcare costs for these patients was during recurrence care (\$52,125.77). Costs for maintenance care were relatively low (\$14,490.53) (Figure 1). Such pattern has been reported in many types of cancers including brain cancer (7, 13, 14).

It has been well documented that cancer patients with Medicaid or no insurance had a decreased likelihood of receiving advanced treatment, had greater burden of diseases and worse survival compared with those with private insurance (19-21). The impact of insurance status on malignant gliomas has been recently reported with mixed results. For example, Medicaid insurance and uninsured status were associated with shorter survival compared with non-Medicaid insurance for patients with GBM (22, 23) and higher inpatient mortality after brain tumor resection (24). Similarly, Hooten *et al.* reported a higher patient safety indicators and hospital-acquired conditions for brain tumor patients with Medicare/self-pay compared with private insurance patients (25). In contrast, Kasl *et al.* observed that longer overall survival time for patients with GBM was associated with Veterans Affairs/Tricare/Medicaid insurance (26). In our study, approximately two-third of patients were under commercial insurance, this proportion is very close to state-wide and nation-wide brain tumor patients (11, 27). Furthermore, patients with commercial insurance appeared to have longer survival time compared to those with non-commercial insurance (411 days *vs.* 358 days, $p=0.563$) (Table III), in line with a recent SEER study (22). In addition, patients with commercial insurance coverage had higher healthcare costs (\$235,732.85 *vs.* \$142,134.07, $p<0.0001$) (Table III). This finding is supported by Chang's study that cancer patients (including brain cancer) with Medicare coverage had costs half that of commercial patients although no detailed clinical outcomes were available in their report (6). Similarly, Jiang *et*

Table III. Comparisons between commercial and non-commercial segment cohort.

	Commercial (55)	Non-commercial (33)*
Gender		
Male	28 (50.9%)	19 (57.6%)
Female	27 (49.1%)	14 (42.4%)
Age (year)		
Median (min, max)	55 (33, 82)	70 (30, 89)
KPS		
Median (min, max)	90 (50, 100)	90 (60, 100)
Healthcare costs (median with 95%CI) (\$)		
Inpatient	54,675.52 (46,157.01-72,413.63)	29,727.76 (21,416.41-42,188.36)
Outpatient	87,841.00 (66,439.04-114,240.96)	46,079.81 (24,674.15-51,398.57)
Professional	27,121.10 (24,144.93-33,310.11)	13,420.47 (10,975.67-15,761.69)
Prescription drugs	25,710.30 (22,102.29-30,633.15)	11,793.07 (8,185.12-19,524.73)
Other	7,562.82 (4,122.69-10,807.53)	3,748.76 (1,661.87-7,965.82)
Grand total	235,732.85 (218,933.12-278,243.92)	142,134.07 (98,623.82-148,634.70)
Number of claims per patient	514	460
Healthcare costs by phase of care (median with 95%CI) (\$)		
Initiation	81,159.92 (72,505.13-89,294.47)	53,426.03 (39,751.45-61,898.82)
Maintenance	23,978.38 (6,281.83-29,895.79)	7,006.10 (0.00-17,349.46)
Recurrence	76,349.05 (57,475.75-102,654.19)	21,564.76 (7,189.81-38,131.13)
Survival (median with 95%CI) (days)	411.0 (366.0-460.0)	358.0 (220.0-658.4)

*Non-commercial: Medicare (25), Medicaid (6), Healthy New York (2).

al. recently found that for GBM patients, commercial payer coverage was associated with more costs compared to non-commercial payer coverage (11).

In order to further identify drivers of healthcare costs for HGGs, a generalized linear model was run using healthcare costs as dependent variable and potential factors associated with healthcare costs as predictors. In line with a recent study (22), patients with commercial insurance had higher healthcare costs. In addition, patients with better KPS tended to have higher healthcare costs (marginally significant, Table IV). This is because patients with good KPS most likely receive aggressive treatments and thus, incur higher healthcare costs. More interestingly, it was also observed that patients with longer survival had higher healthcare costs. We further conducted two sensitivity analyses to examine the robustness of our model adding tumor grade and vital status, respectively, and obtained similar results. Higher healthcare costs didn't necessarily lead to better survival time for many types of cancer (28, 29) and correlation between healthcare costs and HGGs patient survival remains elusive. Our findings suggest HGGs patients at our institution received high-value care although relative low healthcare costs in our region compared to other areas of the nation (30).

Our study has several limitations. First, our study cohort was limited to our single institution and a single financial payer. However, our patient demographics and insurance coverage (Table I) is similar to regional and national data (11, 27), and thus our study may be representative of

Table IV. Results of GLM for healthcare costs for HGGs.

Variables	Beta	SE	Sig.
Intercept	11.773	0.5583	0.000
Age	-0.007	0.0045	0.106
Gender			
Male (Ref.)			
Female	-0.106	0.1008	0.294
Married status			
Married (Ref.)			
Others	0.033	0.1107	0.766
Insurance type			
Commercial (Ref.)			
Non-commercial	-0.595	0.1154	0.000
KPS	0.010	0.0052	0.057
Survival	0.001	0.0002	0.005

Ref.: Reference; Sig.: significance.

national trends. Second, healthcare costs in the present study were all paid by Excellus BCBS (based on the contractual rate). As such, our payments may be less than the total medical charge. Third, there is significant variation in healthcare costs in the US (27, 31, 32) and healthcare costs in Rochester, NY are low compared to national benchmarks (30). Therefore, healthcare costs for HGGs in other regions of the nation are most likely higher than our data.

The strengths of our study include detailed clinical information *i.e.* individual review of diagnosis, treatment,

performance status, and payment data for each patient, excluding those inherent limitations in national databases. Furthermore, the healthcare costs were divided based on clinical care for each individual patient, which we believe are more clinically relevant, unlike calendar months after diagnosis in the literature (7, 13, 14). Additionally, rigorous methodology was used, not considered in previous studies (6, 7, 9, 10). The healthcare costs for these patients are substantial and high in the phases of initiation and recurrence care and relatively low between these two phases, suggesting that attempts to reduce costs are probably best focused on the period of disease recurrence where expenditures are high, but effectiveness seems low. Additionally, the significant administrative costs and patient burden of processing over 44,000 claims for 88 patients (500 claims/patient) represent an attractive target for improvement and a strong argument for payment bundling for disease management. Therefore, our findings are particularly useful for physicians, payers (public and private sectors) and policy makers to understand allocation of healthcare costs and provide high-value healthcare for these patients.

Conflicts of Interest

The Authors declare that they have no conflict of interest.

Authors' Contributions

YL: Study design, data collection and analyses, manuscript writing; ET: data collection and critical reading; ML: data collection and critical reading; DK: data collection and critical reading; KW: study design and manuscript writing.

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