Economic Evaluations and Health Economic Models of Gliomas: A Systematic Review of the Literature

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INTRODUCTION

- Glioblastoma is regarded as one of the deadliest of all malignant solid tumours and it is the most frequent primary malignant brain cancer.
- The cornerstone of first line glioblastoma management is surgery with maximal safe resection consistent with preservation of neurologic function. Adjuvant radiation therapy is a standard component of therapy and systemic adjuvant chemotherapy has consistently been the third modality.
- ***The severity of the disease and the treatment intensity place a significant economic burden on patients and the health systems*** [1].
- Comprehensive reviews of economic evaluations in various fields of oncology are warranted to understand the trends of health economics evidence generation, identify evidence gaps and supplement the existing analyses.
- In the field of glioblastoma, the latest comprehensive review related to economic evaluations was published in 2014, that reported an overview of 5 cost-effectiveness studies investigating temozolomide [2].

OBJECTIVES

This study aimed to review the literature on economic evaluations and health economic models related to glioblastoma with a special focus on studies from Europe and North America.

METHODS

- ***The systematic literature review protocol was registered in PROSPERO (ID: CRD42023488181) [3]. The protocol originally focused on glioma; however, this poster specifically includes only studies with glioblastoma patients.***
- **Search strategy**
  - Medline (via PubMed), Embase, Scopus, Cochrane Library and PROSPERO databases were searched on 23rd of August 2023.
  - Studies were searched without restrictions on the intervention (i.e. treatment, diagnosis or screening) or on the stage of the disease.
  - Snowball sampling of relevant articles and grey literature search were also conducted.
- **Study selection, data extraction and synthesis**
  - Title and abstract screening, full-text screening, and data extraction were conducted by two researchers independently, using Covidence and Excel.
  - At the full-text screening, we included all health economic evaluations of glioblastoma treatments with a geographical location of Europe and North America.
  - Study characteristics, information on patients and treatment, and the evaluation / modelling method were extracted, then a narrative synthesis was performed.

Table 1: Economic evaluations investigating tumor treating fields in combination with different therapies for newly diagnosed glioblastoma patients

Reference	Study country	Model type	Health states	Investigated vs. comparator therapy	Patient population
Guzauskas, 2019	USA	Partitioned survival model	SD; PD; Death	**Tumor treating fields + maintenance TMZ after surgery and standard concomitant radio-chemotherapy with TMZ** vs. Maintenance TMZ after surgery and standard concomitant radio-chemotherapy with TMZ	Patients with newly diagnosed GB The studies had a patient population with the same characteristics as those in EF-14 trial [a]
Bernard-Arnoux, 2016	France	Markov cohort model	SD; PD; Death		
de Rivera, 2023*	France	Partitioned survival model	Alive not-progressed (SD); Alive progressed (PD); Death		
Connock, 2019	France	Partitioned survival model	Alive not-progressed (SD); Alive progressed (PD); Death		
Connock, 2021	France	Partitioned survival model	Alive not-progressed (SD); Alive progressed (PD); Death		

*Conference poster available only.; [a] adult patients with newly diagnosed grade IV astrocytoma, progression-free after having undergone maximal safe debulking surgery when feasible or biopsy, and had completed standard concomitant chemo-radiotherapy with temozolomide, had a Karnofsky Performance Status score ≥70, with adequate bone marrow, liver, and renal function. [5,6]; PD: Progressed disease; SD: Stable disease; LYG: Life years gained; QALY: Quality-adjusted life years; TTF: Tumor treating fields; TMZ: Temozolomide; GB: glioblastoma

RESULTS

- After deduplication of hits, 4 052 records were screened and 3 842 met at least one exclusion criterion. Therefore, 210 articles were eligible for the full text screening.
- In total 48 studies were found to be relevant, among which 23 specifically included patients with glioblastoma, 24 investigated patients with other types of glioma, while 1 study included 2 analyses; one investigated patients with glioma and the other patients with glioblastoma.
- Out of the 24 studies with glioblastoma patients, 18 studies focused on newly diagnosed glioblastoma patients, 5 studies investigated patients with recurrent glioblastoma, while in 1 study the patient population was not clearly defined.
- From the relevant studies 16 included a health economic model and 8 reported calculations of costs and benefits based on observational studies or clinical trials without economic modelling.
- Details on the economic evaluations with modelling approaches are presented below according to the following categories:
  - Studies investigating tumor treating fields in newly diagnosed glioblastoma patients (**Table 1**).
  - Studies investigating chemotherapy in combination with radiotherapy (and surgery) in newly diagnosed glioblastoma patients (**Table 2**).
  - Studies investigating chemotherapies in recurrent glioblastoma patients (**Table 3**).
  - Studies investigating other types of interventions are presented in the supplementary material.

Table 2: Economic evaluations investigating tumor chemotherapy in combination with radiotherapy (and surgery) for newly diagnosed glioblastoma patients

Reference	Study country	Model type	Health states	Investigated vs. comparator therapy	Patient population
Chen, 2021	USA[a]	Decision tree combined with partitioned survival model	SD; PD; Death	**TMZ + RT** vs. RT	Patients with newly diagnosed GB [WHO grade IV astrocytoma] aged 65 years or older
Connock, 2021	1) USA, 2) Canada	Partitioned survival model	SD; PD; Death	1)**TMZ + RT** vs. RT; 2) **Bevacizumab + TMZ + RT** vs. Placebo + TMZ + RT	Patients with newly diagnosed GB
Fischer, 2016*	Canada	Markov cohort model	PF; PD; Death	**Bevacizumab + TMZ + RT** vs. TMZ + RT + placebo	Patients with newly diagnosed GB[b]
Kovic, 2015	Canada	Markov cohort model	PF; PD; Death	**Bevacizumab + TMZ + RT** vs. TMZ + RT	Patients with newly diagnosed GB[b]
Messali, 2013	USA	Markov cohort model	SD; PD; Death	**TMZ + RT** vs. RT	Patients with newly diagnosed GB[c]
NICE, 2007	UK	Markov cohort model	Surgery; Postoperative recovery; Radiotherapy; SD; PD Progression; Death	**Radiotherapy + TMZ** vs. RT	Patients with newly diagnosed GB[d]
Waschke, 2018	Germany	Markov cohort model	SD; PD; Death	**Open-ended long-term TMZ + RT** vs. 6 cycles of adjuvant of TMZ + RT	Patients with newly diagnosed GB[c]

*Document type: Thesis; [a] The analysis was also performed for China.; [b] The population included adults (≥ 18 years old) of both sexes with newly diagnosed GBM after biopsy or resection, with WHO performance status of 0 to 2; adequate healing of craniotomy or cranial biopsy site; adequate hematologic, hepatic, and renal function; and acceptable blood coagulation levels.; [c] The study had a patient population with the same characteristics as those in the EORTC-NCIC trial: aged 18–70 years with newly diagnosed and histologically proven glioblastoma (WHO grade IV astrocytoma), with a WHO performance status of 0–2 and adequate hematological, renal, and hepatic function. [4]; [d] The patients' characteristics were similar as in the largest RCT of TMZ: patients aged 18–70 years with GBM and a WHO performance status of 0-2.; TMZ: Temozolomide; RT: Radiotherapy; SD: Stable disease; PD: Progressed disease; PF: Progression-free; QALY: quality-adjusted life years; QALY: quality-adjusted life years; GB: glioblastoma

Table 3: Economic evaluations investigating chemotherapy for recurrent glioblastoma patients

Reference	Study country	Model type	Health states	Investigated vs. comparator therapy	Patient population
Garcia Lopez, 2014	Spain	Markov cohort model	Alive without progression; Alive with toxicity; Progression (absorbing state)	**Bevacizumab vs** Carmustine as standard clinical practice (SCP); **Fotemustine** vs SCP; **Extended-dose TMZ** vs SCP	Patients with recurrent GB after standard adjuvant treatment based on Stupp's regimen
Martikainen, 2005	Finland	Markov simulation model	Progression-free; Progressed disease; Death	**TMZ** vs. PCV	Patients with GB that had relapsed after primary treatment with surgery and RT

TMZ: Temozolomide; PCV: Procarbazine + lomustine + vincristine; GB: glioblastoma, RT: radiotherapy

CONCLUSION

- A substantial and increasing amount of data is available on economic evaluations in the field of gliomas, and particularly on patients with glioblastoma.
- Most of the studies specifically focused on patients with newly diagnosed glioblastoma, and there are only a limited number of studies focusing on patients with recurrent glioblastoma.
- Several methodologies were applied for modelling the cost and benefits of technologies, however, in most cases Markov cohort and partitioned survival models were used and a traditional approach for defining the health states was followed (i.e. progression-free, progressed disease, and death).
- An important limitation of our review was the geographical scope, as publications focusing on other parts of the world were excluded. Further reviews focusing on other jurisdictions are warranted.

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Presented at the ISPOR Europe 2024 Conference,
17 – 20 NOVEMBER 2024
BARCELONA, SPAIN

Funded by the European Union

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