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Treatment strategies for non-recurrent glioblastoma in Latin America and the Caribbean: a scoping review of the regional evidence

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Abstract

Glioblastoma (GBM) is the most common and aggressive malignant brain tumour in adults, characterised by rapid growth, infiltration and a high rate of recurrence. Despite therapeutic advances, median survival remains between 12 and 18 months. Standard treatment (surgery followed by radiotherapy and temozolomide) offers limited benefits, while targeted therapies and immunotherapies face challenges linked to tumour heterogeneity and the blood–brain barrier. In Latin America and the Caribbean (LAC), inequalities in access and evidence generation hinder the development of regional recommendations. This scoping review mapped the available evidence on therapeutic strategies applied to non-recurrent GBM in LAC, identifying treatments under investigation, geographical distribution, clinical outcomes and methodological quality. Systematic searches were conducted in PubMed, the Cochrane Library, Virtual Health Library, SciELO and Redalyc (2015–2025), supplemented by a manual review. Quantitative studies and scoping or systematic reviews (SRs) evaluating therapeutic interventions in patients with non-recurrent GBM were included. Methodological quality was assessed using the risk of bias in non-randomised studies of interventions, Joanna Briggs Institute, and a measurement tool to assess SRs-2 tools. Of the 283 records identified, 34 studies met the inclusion criteria, with retrospective designs predominating; 14 comparative studies, three reviews and one qualitative study were identified. The studies originated from seven countries, with a predominance of Brazil. The median of medians for overall survival reported was 12.2 months (IQR, 9.48), and progression-free survival ranged from 7 to 22 months. Gaps remain in molecular characterisation, quality of life and the standardisation of the extent of resection and adjuvant protocols. The overall methodological quality was low to moderate. There is a need to strengthen multicentre networks, standardise definitions and promote the integration of biomarkers, functional and economic variables to improve the comparability and applicability of regional evidence on GBM in LAC.

Review

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Protocol Registration

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Background

Glioblastoma (GBM) is the most common and aggressive primary malignant brain tumour in adults, accounting for more than half of all malignant tumours of the central nervous system (CNS) [1]. According to the World Health Organisation (WHO 2021) classification, it is a grade 4 diffuse glioma [1]. It is characterised by rapid growth, extensive infiltration and a high recurrence rate; although it predominantly affects adults, it can also occur in children, with molecular and clinical differences [2]. Its incidence is higher in males and in the non-Hispanic white population; risk factors include previous cranial radiation and genetic syndromes such as neurofibromatosis or Li-Fraumeni syndrome, although the majority of cases are sporadic [1,2].

Molecularly, GBM is characterised by chromosome seven gain, epidermal growth factor receptor (EGFR) amplification, loss of chromosome ten and mutations in the Telomerase reverse transcriptase gene (TERT) promoter [3]. These alterations activate signalling pathways such as PI3K/AKT/mTOR, MAPK/ERK and Notch, which promote proliferation, invasion and resistance to treatment. Despite its local aggressiveness, it rarely metastasises outside the CNS [1–3]. Molecular complexity and the blood–brain barrier limit the efficacy of chemotherapy (CT), driving the development of targeted therapies [4].

Diagnosis is based on clinical presentation and contrast-enhanced magnetic resonance imaging (MRI); histopathological and molecular confirmation (Isocitrate dehydrogenase [IDH] status and O-6-methylguanine-DNA methyltransferase [MGMT] promoter methylation) has prognostic and predictive value with regard to temozolomide (TMZ) [5,6]. The standard treatment, described by Stupp *et al* [7] combines surgical resection with radiotherapy (RT) and concomitant and adjuvant CT with TMZ, demonstrating superiority over RT alone.

Despite surgical and pharmacological advances, median survival remains between 12 and 18 months, and the 5-year survival rate is <10% [1–3]. In high-income countries, the density of clinical trials and access to technology are greater, while regions with limited resources face gaps in availability and outcomes [8]. In Latin America and the Caribbean (LAC), evidence on the treatment of GBM is scarce and uneven: the estimated prevalence in Brazil is 6.04 per 100,000 inhabitants [9,10], and there are few consolidated data from Chile and other countries.

This scenario of fragmented and heterogeneous information hinders the formulation of regional recommendations and highlights the need to systematically map the evidence.

The aim of this scoping review (ScR) was to identify and characterise the treatment strategies applied to newly diagnosed GBM in LAC, describe their geographical distribution, analyse clinical outcomes and assess the methodological quality of the studies to guide future research and policies that promote equity in regional neuro-oncology.

Methods

Design

The ScR was designed and reported in accordance with the Preferred Reporting Items for Systematic Reviews (SRs) and Meta-Analyses extension for ScRs (PRISMA-ScR) guidelines [11]. The PRISMA-ScR checklist is available in Supplementary Table 1. The protocol can be consulted on the Open Science Framework (OSF; DOI: 10.17605/OSF.IO/HVBZ9) [12].

Search strategy

Systematic searches were carried out in the following electronic databases: PubMed, the Cochrane Library, the Virtual Health Library (BVS-LILACS), SciELO and Redalyc to ensure coverage of both international and regional literature. The searches were designed in a structured and independent manner, duplicated for each database, using a combination of controlled terms (MeSH) and free-text terms, adapted to the syntax and functionality of each platform [13]. An example of a search strategy carried out by a reviewer in the PubMed database was as follows: ('Glioblastoma'[MeSH] OR 'Glioblastoma'[Title/Abstract] OR 'GBM'[Title/Abstract]) AND ('Therapeutics' [MeSH] OR 'Treatment'[Title/Abstract] OR 'Therapy'[Title/Abstract] OR 'Management"[Title/Abstract]) AND ('Latin America"[MeSH] OR 'South America'[MeSH] OR "Central America'[MeSH] OR 'Argentina'[Title/Abstract] OR 'Brazil'[Title/Abstract] OR "Mexico'[Title/Abstract] OR 'Colombia'[Title/Abstract] OR 'Chile'[Title/Abstract] OR "Peru'[Title/Abstract] OR 'Ecuador'[Title/Abstract] OR 'Uruguay'[Title/Abstract] OR "Paraguay'[Title/Abstract] OR "Venezuela'[Title/Abstract] OR 'Bolivia'[Title/Abstract] OR 'Costa Rica'[Title/Abstract] OR 'Panama'[Title/Abstract] OR 'Honduras'[Title/Abstract] OR 'Guatemala'[Title/Abstract] OR 'El Salvador'[Title/Abstract] OR 'Nicaragua'[Title/Abstract])

Filters were applied based on study type and content (e.g. 'full text available'; 'Glioblastoma'), LAC countries (e.g. 'Brazil, Colombia, Argentina and Peru') and publication period ('Publication years 2015–2025"). In addition, a supplementary manual search was carried out, as well as a search of the reference lists of relevant articles, including SRs and original studies.

The search process took place between 25 February 2025 and 30 March 2025, with the most recent search date being 1 March 2025. The complete search strategies and the terms used in each database by each reviewer are presented in Supplementary Table 2.

Selection of evidence

All studies published between 2015 and 2025 that evaluated therapeutic interventions in patients with newly diagnosed, non-recurrent GBM, conducted in LAC countries, were considered eligible.

The inclusion criteria were as follows: (1) patients of any age with a diagnosis of non-recurrent GBM, confirmed by any diagnostic method in LAC countries, namely Antigua and Barbuda, Argentina, the Bahamas, Barbados, Belize, Bolivia, Brazil, Colombia, Costa Rica, Cuba, Chile, Dominica, Ecuador, El Salvador, Grenada, Guatemala, Guyana, Haiti, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay, Peru, the Dominican Republic, Saint Kitts and Nevis, Saint Vincent and the Grenadines, Saint Lucia, Suriname, Trinidad and Tobago, Uruguay and Venezuela [14], with no age restriction (paediatric and adult patients); (2) GBM-specific therapeutic interventions: surgery, CT (TMZ and cisplatin), RT, targeted therapies (anti-angiogenic agents and EGFR inhibitors), immunotherapy, genetic or epigenetic therapies, as well as experimental treatments such as oncolytic viruses, interstitial thermal therapy or alternating electric field therapy (TT fields) and other reported treatments; (3) study designs: quantitative, including randomised clinical trials (RCTs) and non-RCTs (NRCTs), observational studies (cohort studies, case-control studies, case series with no restriction on the number of participants, and case reports), quasi-experimental and pre-experimental studies, as well as SRs or ScRs that met the aforementioned regional and interventionist criteria; (4) context: public or private healthcare institutions in LAC or synthesis reviews that included at least one primary study conducted in that region and (5) language: no language restrictions.

The exclusion criteria were as follows: narrative reviews, preclinical or phase I studies, grey literature, conference abstracts, letters to the editor, and studies for full-text access was unavailable.

The study selection process was carried out in duplicate and independently by two reviewers, with any disagreements resolved by a third reviewer. The entire process of study identification, screening, eligibility assessment and inclusion was documented using a flow chart prepared in accordance with the PRISMA guidelines [15].

Methodological assessment of the evidence

The methodological quality of the studies was assessed independently and in duplicate by two reviewers, using the appropriate tool according to the study design. A third reviewer resolved any discrepancies. This process was applied to all the tools described below.

For comparative observational studies, the risk of bias in non-randomised studies of interventions (ROBINS-I) tool was applied, which assesses seven domains ranging from design to interpretation, classifying the risk of bias as low, moderate, serious, critical or unknown [16]. The overall assessment was based on these criteria, with a classification of low risk where methodological limitations were minimal and unlikely to affect the validity of the results; moderate risk when there were some methodological concerns without substantially compromising the interpretation of the findings; serious risk when one or more domains presented significant limitations with the potential to impact the estimation of effects; and critical risk when the limitations were severe enough to substantially compromise the internal validity of the study.

For non-comparative studies, the Joanna Briggs Institute (JBI) checklists were used, which allow for a qualitative assessment of methodological rigour and reporting quality [17]. The JBI checklists were applied to cohort studies, case series, qualitative research and diagnostic accuracy studies [18–21]. In these studies, the results were interpreted qualitatively, as these tools function as critical appraisal checklists rather than standardised instruments for classifying risk of bias. Consequently, their use was aimed at identifying relevant methodological strengths and weaknesses, rather than assigning rigid categories based on an aggregate score.

The SRs were analysed using 'a measurement tool to assess SRs-2' (AMSTAR-2), comprising 16 critical and non-critical items [22]. Quality was classified as high, moderate, low or critically low; in addition, a quality percentage was estimated using the formula: ([Total 'Yes' responses/Total items] + [Total 'Partially Yes' responses/Total items/2] × 100), to estimate a percentage score for the quality of the evidence. The overall quality was classified based on compliance with critical and non-critical domains: it was considered high when no critical weaknesses or only one non-critical weakness were identified; moderate when there was more than one non-critical weakness; low when one critical weakness was identified, with or without non-critical weaknesses; and critically low when multiple critical weaknesses were detected.

The ScRs were not formally assessed due to the lack of validated tools for this purpose. The results were summarised in tables according to the instrument used and were presented graphically using the RobVIS tool [23].

Data extraction

Two researchers independently reviewed the titles and abstracts of the identified records, removing duplicates prior to the full-text assessment. Full-text articles were screened against eligibility criteria, with any disagreements resolved by a third reviewer. Data were extracted in a standardised manner into a specially designed table, which included author, year of publication, country of origin, study design, sample size, reported therapeutic intervention and primary and secondary outcomes. A pilot test of the data extraction form was carried out on a random sample of articles to ensure consistency amongst reviewers. The data extraction form is attached in Supplementary Table 3.

The following were defined as primary outcomes: (1) types of treatment used for non-recurrent GBM; (2) outcomes reported in terms of overall survival (OS), progression-free survival (PFS), quality of life and adverse effects or complications and (3) knowledge gaps. Secondary outcomes included those reported in a supplementary manner.

Data analysis and synthesis

The results were summarised in a narrative and descriptive manner, in line with the review's objectives and the components of the research question. Tables and figures summarised the general characteristics of the studies, and subgroup analyses were carried out according to intervention type, country and outcomes. The geographical distribution map was created using Datawrapper [24], taking into account only primary studies. One author oversaw the synthesis and the resolution of discrepancies.

To summarise the evidence, a descriptive 'median of medians' approach was used to obtain a central estimate of the regional picture. We emphasise that this approach is purely descriptive, as we did not conduct a formal meta-analysis. The heterogeneity in the study designs analysed (as well as in the characteristics of their populations, therapeutic strategies and healthcare contexts) and the absence of data on the variance of medians or hazard ratios in the primary studies preclude weighted statistical aggregation; we therefore opted for this non-parametric method to provide a representative mapping of the regional landscape. For this calculation, only studies reporting OS medians for the total cohort or specifically for patients with non-recurrent GBM were included. RCTs were excluded to avoid double-counting of populations and to ensure the independence of the analysed data.

Where studies did not report a median OS, this was calculated where individual survival data for patients in the cohort were available. No study presented OS as a mean accompanied by a standard deviation; therefore, it was not necessary to use formulas to convert the mean to the median. Data extraction and calculation were carried out by one reviewer and independently validated by a second author. The studies used to calculate the median of medians, the formula used, and the studies excluded from the calculation (along with the reason for exclusion) are set out in Supplementary Table 4.

In cases where the original studies provided individual patient data but did not report a median specifically for the population of interest, a standardised three-step protocol was applied to calculate this value accurately. First, the sample was filtered and selected to extract only the survival times of patients diagnosed with non-recurrent GBM, ensuring the homogeneity of the data and explicitly excluding cases of recurrence or secondary tumours. Second, the positional median was calculated after sorting the data in ascending order; in samples with an odd number of patients (n), the median was defined as the value at position ($n + 1/2$), whilst in samples with an even number, the value was obtained by taking the arithmetic mean of the two central observations at positions ($n/2$) and ($n/2 + 1$).

Finally, in cases where survival data were originally provided in days, the result was converted to months using a conversion factor of 30.44 days/month (365.25/12) to account for leap years and ensure technical comparability and internal consistency in the regional quantitative synthesis. As a measure of dispersion of the median of medians, the interquartile range (IQR) was calculated as IQR = Q3–Q1. Data processing and the calculation of the median of medians were carried out using Microsoft Excel software (version 16.106.2; Microsoft Corp., Redmond, WA).

As most of the included studies did not report results stratified by age group, it was not possible to carry out a separate analysis for the adult and paediatric populations. For this reason, the results were analysed together in order to ensure that relevant studies were included and to maintain the integrity of the evidence synthesis.

Results

Study selection

A systematic search was conducted in the Cochrane databases (n = 111), PubMed (n = 91), the BVS-LILACS (n = 33) and Scielo (n = 11). In addition, a manual search (n = 31) and a search of reference lists (n = 6) were carried out. A total of 283 records were identified. Following an initial review, 192 were excluded for failing to meet eligibility criteria. The remaining 91 articles underwent screening for inclusion, resulting in the exclusion of 25 duplicates and 4 unretrievable articles or abstracts.

A total of 62 articles were assessed in full text. Of these, 28 studies were excluded on the basis of the following criteria: (1) narrative reviews (n = 7), (2) studies from non-LAC countries (n = 5), (3) studies not addressing therapeutic interventions (n = 5), (4) preclinical or experimental studies (n = 3), (5) studies focusing solely on recurrent GBM (n = 3), (6) other brain tumours or conditions other than GBM (n = 3), and (7) publications prior to 2015 (n = 2). Finally, 34 studies were included in the review. The studies excluded following the screening stage, together with the reasons for their exclusion, are detailed in Supplementary Table 5. The study selection process is presented in Figure 1, in accordance with the recommendations of the PRISMA-ScR statement.

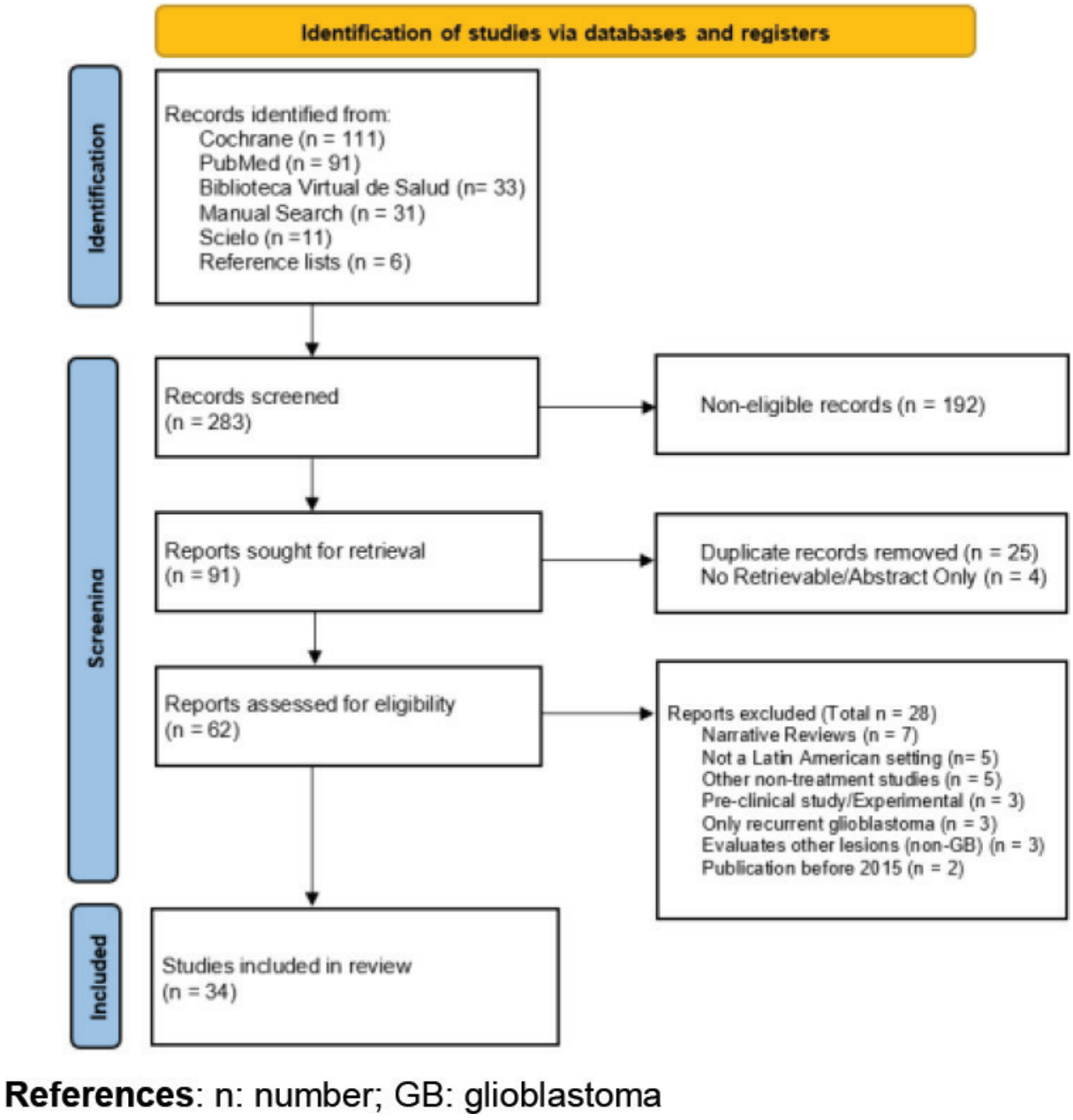

Figure 1. Flowchart of the study selection process. GB, glioblastoma; n, number.

General characteristics of the included studies

The general characteristics of the included studies are presented in Table 1, which details the lead author, year of publication, methodological design, country of origin (or countries included, in the case of synthesis or multicentre studies), population, total number of patients (*n*), intervention, follow-up period (months), primary outcomes and funding.

Table 1. Characteristics of the included studies.

Author/ID	Year	Design	Country	Population	*N*	Intervention	Follow-up	Results	Funding
Ciuffi [25] (ID 2)	2020	Retrospective cohort	Brazil	Patients diagnosed with GBM by biopsy and MRI and treated with postoperative RT and TMZ. Mean age 54 (36–78)	50	Surgery (total resection 26%, partial resection 64%, biopsy 10%) + RT 60 Gy/30 fractions + concomitant TMZ (75 mg/m²/day) and adjuvant TMZ (150–200 mg/m²/day for 5 days every 28 days, up to 6 cycles)	21 months	OS 17 months; PFS 9 months. Post-recurrence OS: 16 months with salvage therapy versus 4 months without salvage therapy ($p < 0.001$). Better OS associated with maximal resection, KPS > 70, metronomic TMZ, RPA-III, time to relapse >9 months	No funding reported. No conflicts of interest.
Sinning [9] (ID 3)	2021	Retrospective cohort	Chile	Adults with primary GBM (mean age 58, 24–79)	74	Primary: surgery (complete resection 59%, partial 26%, biopsy 15%) + RT 60 Gy/30 fractions + CT (concomitant and adjuvant TMZ, mean 6 cycles). 87% received the full Stupp regimen. 11% received palliative care only. Relapse: re-surgery 20%, second-line treatment (BEV ± irinotecan/LOM 49%; TMZ re-challenge 27%)	50 months	Median OS 13.9 months; PFS 10 months. In the Stupp regimen: OS 16.1 months, PFS 10 months. Median functional survival 11.8 months	Declares no funding. No conflicts of interest.
San Martin [26] (ID 4)	2021	Retrospective cohort	Chile	Adults aged over 18 with histologically confirmed GBM according to the WHO CNS classification	67	Surgery: total resection 45%, subtotal resection 55%. 3D conformal RT: 60 Gy/30 fractions (46 Gy + boost). CT: 54% received TMZ concomitantly with RT (Stupp protocol)	Median 10.3 months	Overall OS 11.4 months (95% CI, 9.7–14.6). OS at 1, 2 and 5 years: 48%, 15% and 3%. With concomitant TMZ: OS 14.6 months versus 9.7 months with RT alone (HR 0.39, $p < 0.001$)	Declares no funding. No conflicts of interest.
Prost [27] (ID 5)	2021	Retrospective cohort	Argentina	Adults aged over 18 with GBM, anaplastic astrocytoma or HGG (UBA)	63	Surgery: safe maximum resection 49%, incomplete resection 35%, biopsy 16%. Chemoradiotherapy with TMZ following surgery	–	Overall PFS 7 months (95% CI, 5.7–8.3). Start of chemoradiotherapy <5 weeks after surgery: PFS 10 months versus 7 months (5–8 weeks) and 4 months (>8 weeks), $p = 0.006$ (HR 2.18)	Declares no funding. No conflicts of interest.

Continued

Table 1. Characteristics of the included studies. *Continued*

Author/ID	Year	Design	Country	Population	*N*	Intervention	Follow-up	Results	Funding
Mansur Starling [28] (ID 6)	2024	Retrospective cohort	Brazil	Paediatric patients aged <18 years with gliomas (mean 7 years, range 0–17)	1,296	CT alone; RT alone; CT and RT alone; CT + RT; CT + RT and CT; RT + RT and CT; CT + RT + RT and CT; Other	Mean follow-up 135 m (95% CI, 128–142)	1-, 3- and 5-year OS: pilocytic astrocytoma 94%, 90% and 89%; grade II gliomas: 80%, 72% and 69%; grade III: 54%, 32% and 28%; GB: 53%, 29% and 25%, respectively. Brainstem tumours had poorer OS (p = 0.001). In non-brainstem HGG (n = 570): median OS 22 months (0–3 years) versus 13 months (4–18 years), p = 0.005. Combined treatments associated with better OS (surgery 11 months; Cx+Qt 16 months; Cx+RT+Qt 20 months; p = 0.005)	Declares no funding. No conflicts of interest.
Palacios [29] (ID 8)	2023	Retrospective case-control study	Mexico	Patients with GBM who underwent surgery between 2016 and 2019 (median age 56 years, range 6–83)	62	Cx + Rt + TMZ (cases: full regimen; controls: incomplete regimen)	24 months	Median OS 3.6 m (1–52); 73% <12 m. OS: cases 12 m versus controls 9 m (p = 0.08). PFS: 7 m versus 6 m (p = 0.12). Better OS associated with: adjuvant treatment (p < 0.001), good performance status (p = 0.001), absence of post-surgical complications (p = 0.034)	The authors declare no funding. No conflicts of interest.
Trevisan [30] (ID 9)	2019	Retrospective cohort	Brazil	Adults with GBM who underwent surgical resection (mean age 56.9 ± 12.3)	113	Clinical and genomic assessment (ROS1, NTRK1, KIT, PDGFRA, KDR, RB1) using multicolour FISH	Mean follow-up 5.8 months (3 days–7 years)	Mean OS 175 days. Rearrangements: NTRK1 and ROS1 (0.9% each). PDGFRA amplified in 20% (co-amplified with KDR >90% and KIT >60%). RB1 deleted in 16%. No association between molecular abnormalities and survival. Prognostic factors: advanced age, post-surgical complications, right-hemispheric tumours	Funding: NCI P30 CA046934 (USA), CNPq (Brazil), CAPES (Brazil). No conflicts of interest.
Figueredo [31] (ID 12)	2023	ScR	8 Latin American countries (BR, MEX, Chile, ARG, Peru, PGY, COL, Cuba)	Patients with a mean age of 43 years (11–92), mostly in public hospitals (70%)	258	Awake craniotomy (AC). Protocols: Asleep–Awake–Asleep 63%, Awake–Awake–Awake 15%	68 hours (24–168 hours)	Postoperative complications: epileptic seizures 14.6%, hemiparesis 8.4%, aphasia 3.6%, nausea 0.6%	Declares no funding. No conflicts of interest.

Continued

Table 1. Characteristics of the included studies. *Continued*

Author/ID	Year	Design	Country	Population	*N*	Intervention	Follow-up	Results	Funding
Jacobo [32] (ID 14)	2021	Retrospective cohort	Mexico	Adults who underwent decompressive craniectomy for refractory intracranial hypertension associated with a CNS tumour (mean age 48.8, 17–73)	61	Emergency decompressive craniectomy for uncontrolled oedema or intracerebral haemorrhage. Timing: intraoperative 34%, <72 hours 41%, >72 hours 25%	Median 18.9 m	Median OS 18.9 m. Mortality 65.5% (40/61). Worse OS with intracerebral haemorrhage (5 m) compared with intraoperative oedema (24.6 m) and postoperative oedema (21.2 m), $p = 0.04$	No funding declared. No conflicts of interest.
Garcia [33] (ID 17)	2015	Retrospective cohort	Peru	Adults with GBM who underwent surgical resection (mean age 51 years)	150	Microsurgical resection with (53%) or without (47%) FLS-Na. Total resection 54%, subtotal 46%. Adjuvant therapy: RT 63% (6,000–6,500 cGy), CT 53% (mainly TMZ)	Median 13 months	OS 13 months. With total resection: OS 17 months versus 7 months with subtotal resection ($p < 0.001$). Overall PFS 9 months	Self-funded. No conflicts of interest.
Villegas-Mejía [34] (ID 19)	2020	Retrospective cohort	Colombia	Adults with GBM treated with Cx, Rt and Qt (mean age 54.8 years, range 9–84)	193	Adjuvant CT with TMZ according to the Stupp protocol, assessing duration (6, 12, 18, 24 months)	Mean follow-up 24.4 months (4–104)	77% relapsed; 57% alive at the end of the study. Mean OS 26 m. OS by adjuvant therapy: 31 m (6 m), 30 m (12 m), not reached at 18–24 m; trend towards longer OS with more cycles	No funding declared. No conflicts of interest.
Barrera [35] (ID 22)	2024	Longitudinal descriptive cohort	Colombia	Adults aged 18–77 years (mean 50) with recent HGG, untreated	80	Survey of risk factors + analysis of genetic instability in peripheral blood (micronuclei in lymphocytes/ reticulocytes, sister chromatid exchanges)	Median 11 months	Median OS 784 days (26 months; 95% CI, 196–1,373). OS at 1,550 days: 43%. Better prognosis: young patients (83%, 95% CI, 62–93; $p = 0.001$) and grade 2 gliomas (92%, 95% CI, 77–99; $p = 0.015$)	Funding: Sustainability Strategy 2013/2014 (GRC Group), COI, Foundation for the Promotion of Research and Technology, Banco de la República. No conflict of interest.
Castellanos [36] (ID 24)	2022	RS	Cuba	Patients with cerebral astrocytoma	13 studies (n = 35–4,721)	Cx, Qt and Rt (alone or in combination, modalities unspecified)	-	Estimated SG: 14.3 m for high-grade tumours to 62.3 m for low-grade tumours. SG 31.5–14.5 m in patients with convulsive syndrome as an initial symptom	Declares no funding. No conflicts of interest.

Continued

Table 1. Characteristics of the included studies. *Continued*

Author/ID	Year	Design	Country	Population	*N*	Intervention	Follow-up	Results	Funding
Garcia [37] (ID 32)	2022	Retrospective cohort	Mexico	Patients with a histological diagnosis of high-grade primary CNS tumours. Mean age in paediatric patients: 8 years; mean age in adult patients: 51 years	114	54 (47.4%) received more than three therapeutic interventions (resection, CT , RT or placement of a ventriculoperitoneal shunt), whilst 3 (2.8%) received palliative treatment such as sedation, steroids for cerebral oedema and anticonvulsants	Not reported	Mortality: 52/114 patients (45.6%) died; among paediatric patients, 26/56 (46.4%) and among adults, 26/58 (44.8%). The tumours also associated with the longest hospital stay were medulloblastoma and GB	Declares no funding. No conflicts of interest.
Yamada [38] (ID 37)	2023	Retrospective cohort	Brazil	Adults aged over 18 with GBM	68	Assessment of MMR status (proficient versus deficient) by immunohistochemistry (MLH1, MSH2, MSH6, PMS2)	Not reported	15% dMMR (most commonly MSH6). No difference in OS: pMMR 19.8 m versus dMMR 16.9 m (p = 0.31). Better OS with total resection (30.7 versus 13.6 months, p = 0.02) and with methylated MGMT (29.6 versus 19.8 months, p = 0.049). 10 patients alive, all pMMR	Declares no funding. No conflicts of interest.
Koshiyama [39] (ID 41)	2017	Retrospective cohort	Brazil	Adults with histologically confirmed GBM (mean age 59.3; 41–83)	40	Surgery: total resection 48%, subtotal resection 43%. Molecular analysis (FISH: EGFR, PTEN, TP53, 1p/19q, chromosomes 7 and 10)	Median 4.8 months	Median OS 145 days (95% CI 128–162). Longer OS in younger patients (HR 1.04; 95% CI 1.00–1.08; p = 0.042)	No funding declared. No conflicts of interest.
Alert [40] (ID 42)	2016	Retrospective case series	Cuba	Paediatric patients (aged 3–18 years) with CNS tumours treated at INOR	98	RT with a linear accelerator (3D conformal/IMRT), 54–60 Gy depending on histology, with or without Qt or nimotuzumab	Minimum 18 months	5-year OS: 50% (median 64 months). Subgroups: 100% oligodendrogliomas/pineoblastomas; 88% grade I–II astrocytomas; 75% ependymomas; 67% germinomas; 71% craniopharyngiomas; 37% brainstem tumours; 34% medulloblastomas; 25% PNETs; 11% GB/grade III–IV astrocytomas	No funding declared. No conflicts of interest.

Continued

Table 1. Characteristics of the included studies. *Continued*

Author/ID	Year	Design	Country	Population	*N*	Intervention	Follow-up	Results	Funding
Loureiro [41] (ID 43)	2015	Retrospective cohort	Brazil	Adults aged over 18 with histologically confirmed GBM who underwent surgery and were treated with postoperative RT. Multicentre.	115	Cx (biopsy/subtotal or total resection) + 3D conformal RT (average 60 Gy/30 fractions). Some received adjuvant CT (TMZ or BCNU, depending on the year)	Median 12.9 months	OS 14.1 months (95% CI, 11.6–16.6). Factors associated with better OS: age <50 years, KPS ≥70, RT ≥60 Gy and adjuvant CT. In the multivariate analysis: KPS, extent of resection and adjuvant CT were independent predictors	No funding declared. No conflicts of interest.
JO review [42] (ID 44)	2022	Retrospective cohort	Brazil	Adults aged over 18 with primary or metastatic intracranial neoplasms, treated surgically	96	Intracranial resection (total or subtotal)	On hospital discharge	Postoperative mortality 41.7%. Severe neurological deficit 8.3%, mild 11.5%. Palliative care on discharge 18.8%, outpatient follow-up 19.8%. Complications in skull base meningiomas: CSF fistula and meningitis	No funding declared. No conflicts of interest.
Oliveira [43] (ID 47)	2018	Retrospective cohort	Brazil	Adults aged over 60 with histologically confirmed GBM (mean age 64.4 years)	42	Treatment: maximum possible resection 93%, stereotactic biopsy 5%. Standard protocol: RT 50–60 Gy/30 fractions + TMZ (75 mg/m² during RT, then 150 mg/m² every 5 days for 28 days for 12 months)	Range 4–24 m, mean 11.4 m	Median OS: < 60 years 191 days, 60–74 years 185 days, >75 years 147 days. Perioperative complications in 54% (infections, thromboembolism, etc.) reduced OS to 104 days versus 262 days without complications ($p = 0.001$)	No funding declared. No conflicts of interest.
Montgomery [44] (ID 51)	2015	Retrospective cohort	Brazil	Adults with primary or secondary GBM (mean age 59 years), treated at HC-UNICAMP 2008–2012	36	Surgery (total or subtotal resection) + initial CT with TMZ 200 mg/m² + RT 60 Gy	Median 7.6 m (4–11)	PFS 7.6 months, OS 7.1 months. Positive correlation between PFS, OS and OS ($p < 0.0001$). p53 expression was negatively associated with PFS ($p = 0.02$)	No funding declared. No conflicts of interest.
McBain [45] (ID 55)	2021	RS with MA	International multicentre (including Brazil)	Adults aged >16 years with recurrent or progressive GBM following standard treatment (Cx + Rt + TMZ)	5236	Qt: LOM, fotemustine, TMZ, regorafenib, PCV, combinations with BEV. Others: reoperation, reirradiation (hypofractionated or stereotactic), monoclonal antibodies, vaccines, cannabinoids, TTFields	Median 5.5–12.6 m	SG 5.5–12.6 m; SLP 1.5–4.5 m. BEV+LOM associated with higher EAG compared with LOM alone (RR 2.51; 95% CI 1.72–3.66), high-certainty evidence	No funding declared. No conflicts of interest.

Continued

Table 1. Characteristics of the included studies. *Continued*

Author/ID	Year	Design	Country	Population	*N*	Intervention	Follow-up	Results	Funding
Santos [46] (ID 57)	2017	ECNA	Brazil	Adults aged 27–61 years with recurrent GBM, KPS >70%, measurable lesions, with no other standard treatment options	32; 17 completed	Intervention group (*n* = 17): strict ketogenic diet + intranasal POH 220 mg/day × 3 months. Control group (*n* = 15): standard diet + POH. All had previously received conventional treatment	3 m	KD group: 78% partial response, 11% stable disease, 11% progression. Control group: 25% PR, 25% SD, 50% *P*. Significant tumour reduction in the KD group at 90 days ($p = 0.035$). Metabolic improvements (cholesterol, LDL-C, TG; $p < 0.005$) in the KD group	No funding declared. No conflicts of interest.
Méndez-Aguilar [47] (ID 58)	2020	Retrospective cohort	Peru	Adults aged over 18 with HGG treated at the institution	278	Assessment of prognostic factors for survival (10 variables). Analysis using Kaplan–Meier, log-rank and Cox models	-	Median PFS 22.7 months (range 5.6–80.3). Median OS 26.2 months (range 4–83.2). OS for grade IV: 15.7 months (95% CI 14.2–17.1), grade III: 38.4 months (95% CI 35.8–40.9). Associated factors: tumour grade (OS HR 15; SLP HR 25.1), surgery (OS HR 0.6; SLP HR 0.49), age (OS HR 1.47), adjuvant therapy (OS HR 0.6; SLP HR 0.58), Karnofsky score (OS HR 0.7)	Self-funded. No conflicts of interest.
Aguirre-Madrigal [48] (ID 59)	2022	Retrospective cohort	Mexico	Adults with GBM treated surgically (mean age 55.5; 20–83), who died within 30 days after surgery	50	Comparison of actual versus estimated mean OS using the GBM survival calculator (Harvard–Brigham and Women's)	-	Difference between estimated and actual mean OS: −1.37 months (95% CI −3.7 to +0.9). Within the equivalence interval (Lower Limit −3.8; Upper Limit +3.8). Conclusion: actual OS was equivalent to that calculated.	No funding declared. No conflicts of interest
Nader Marta [49] (ID 60)	2021	Retrospective cohort	Brazil	Adults aged >18 with GBM (18 to >70 years)	4,511	Survival analysis by age, treatment modality, public/private sector and educational level (national sample)	-	Median OS: 8 months in the public sector versus 17 months in the private sector ($p < 0.001$). By age: 22 months (18–40), 10 months (41–60), 6 months (61–65), 5 months (66–70), 4 months (>70). Combination therapies > monotherapy. Longer OS with higher educational attainment (4 months for illiterate patients versus 14 months for university graduates). Independent predictors: setting, education, age and treatment modality	Declares that it has no funding. No COI.

Table 1. Characteristics of the included studies. *Continued*

Author/ID	Year	Design	Country	Population	*N*	Intervention	Follow-up	Results	Funding
Sarria [50] (ID 61)	2020	Retrospective cohort	Peru; Germany; China	GBM patients from 5 centres treated with Cx + IORT	51	Tumour resection + IORT (10–40 Gy, low-energy X-rays) → followed by standard adjuvant chemoradiotherapy and maintenance Qt	Median 18 months (2–42)	Median OS 18.0 months (95% CI, 14.7–21.3); PFS 11.4 months (95% CI, 7.6–15.2); PFS-L 16 months (95% CI, 10.2–21.8); SLP-D 30 months (95% CI, 18.6–41.4). 1-, 2- and 3-year OS: 80%, 39%, 26%. Local progression: 35%. Grade 1 RN: 7.8%, grade 3: 17.6%. No grade 4 toxicity or related deaths	Declares no funding. Personal fees/grants received by authors, unrelated to the presented work. No conflicts of interest.
Gomes [51] (ID 62)	2021	Retrospective cohort	Brazil	Adults with GBM (mean 54 years, 29–75) treated with the Stupp protocol	112	Molecular analysis: IDH1 and ATRX by IHC, TERTp mutations by Sanger/pyrosequencing, MGMTp methylation by pyrosequencing, MGMT expression by nCounter® Vantage 3D™	Not reported	96/112 IDH1WT, 16 IDH1MUT. ATRX positive in 92% of IDHWT cases versus 44% of IDHMUT cases. TERTp mutated in 70% of IDHWT cases. MGMTp methylated in 56% of IDHWT cases and 85% of IDHMUT cases. MGMTp methylation → better response to TMZ. Low MGMT expression is associated with better OS. Combining methylation and expression improved prognostic value	Funding: Barretos Cancer Hospital, Campinas Public Labour Prosecutor's Office, FINEP (BioPlat 1302/13). No conflicts of interest.
Dy [52] (ID 63)	2022	RS with MA	Brazil; Turkey; China; Egypt; Tunisia; India; Ukraine	Adults aged 18 years and over with primary GBM in upper-middle- and lower-middle-income countries according to the WBIC	2552	Meta-analysis of OS (random-effects model). Subgroups: WBIC, pre/post Stupp protocol, treatment modality	Median 14 months (included studies)	Pooled OS: 14.2 months (95% CI 12.9–15.4; I^2 = 79). Subgroups: pre-Stupp 12.5 m (95% CI, 11.1–14.0; I^2 = 80; n = 1027) versus post-Stupp 15.6 m (95% CI 13.6–17.7; I^2 = 77; n = 1412), $p < 0.05$. WBIC and treatment modality showed no significant differences	No funding declared. No conflicts of interest.

Continued

Table 1. Characteristics of the included studies. *Continued*

Author/ID	Year	Design	Country	Population	*N*	Intervention	Follow-up	Results	Funding
Bennett [53] (ID 64)	2022	Prospective cohort	Chile	Adults (aged 18–72 years, mean 40) with supratentorial gliomas (high- and low-grade) undergoing AC	40	Preoperative fMRI + AC with DES. Functional maps visualised in 3D and compared with surgical mapping	Not reported	fMRI identified motor/linguistic areas in the majority of patients, including novel regions (e.g. 55b, SLF). Sensitivity/specificity for motor function in area 4: 100%/71%. Semantic protocols performed better in BA 55b/perisylvian (100%/20%), and word production protocols in BA 44–45 (70%/80%). Compensatory patterns were observed (e.g. postcentral activation in precentral gliomas)	Funding from *the National Agency for Research and Development, Health Research and Development Fund (FONIS) SA17I0124* (C.B., S.C., M.G., G.T., R.R., N.L., A.V.), and *FONDECYT Start-up 11201046* (A.V.).
Mamani [54] (ID 65)	2020	Retrospective cohort	Mexico	Adult patients (>18 years; mean 44.1; range 19–72) with CNS lesions in eloquent areas who underwent awake surgery with cortical-subcortical mapping using direct bipolar stimulation (*n* = 45)	45	Awake surgery with intraoperative mapping; analysis of IS and factors associated with MF	-	15.6% developed IS; 11.1% had partial motor seizures, 4.5% had secondary generalised seizures. One MF (14%) occurred due to an uncontrolled tonic-clonic seizure, requiring conversion to general anaesthesia. Larger tumour volume (>70 cc) was associated with a higher risk of IS (ROC curve, sensitivity/specificity >70 cc).	No funding declared. No conflicts of interest.
Magalhaes-Leal [55] (ID 66)	2017	Prospective qualitative	Brazil	Patients with supratentorial gliomas in language or sensorimotor areas, who underwent AC (*n* = 17; mean age 56, range 25–78).	17	Semi-structured interviews with open-ended questions.	-	Opinions grouped into 5 categories: (1) overall positive perception, not considered a bad experience; (2) variable recall of the procedure; (3) minimal negative sensations (some discomfort on the operating table); (4) postoperative recovery perceived as favourable; (5) preference among several patients for AC over general anaesthesia.	Declares no funding. No conflicts of interest.

Continued

Table 1. Characteristics of the included studies. *Continued*

Author/ID	Year	Design	Country	Population	*N*	Intervention	Follow-up	Results	Funding
Magalhaes-Leal [56] (ID 67)	2018	Retrospective cohort	Brazil	Patients with supratentorial gliomas near cortical language and/or sensorimotor areas, who underwent AC (mean age 56; range 25–78 years)	19	AC analysis of critical stages (preparation, positioning, anaesthesia, brain mapping, resection, management of seizures and pain)	-	New postoperative neurological deficit in 16%; intraoperative seizures in 24%, with no technical failures in the AC procedure.	Declares no funding. No conflicts of interest
Jiménez [57] (ID 68)	2018	Retrospective cohort	Chile	Patients with GBM (mean age 54.8 years; range 33–74) treated at the institution	30	Immunohistochemical (IH) staining and manual analysis of cells positive/negative for MGMT expression; a cut-off of ≥ 10% positive cells was applied.	-	Median number of cells counted per case 692 (IQR, 492–928); 52% MGMT-positive. Median OS 5.3 months (IQR, 3.4–12.8). The effect of MGMT on treatment response could not be assessed as only 3 patients received CT.	Declares no funding. No conflicts of interest.

"m", months; 1p/19q, combined deletion of the short arm of chromosome 1 and the long arm of chromosome 19; ATRX, X-linked alpha-thalassaemia/mental retardation; BA, Brodmann Area; BCNU, Carmustine; BEV, Bevacizumab; CAPES, Brazilian Agency for the coordination of the improvement of higher education personnel; CI, confidence interval; CLFS, clinical disease-free survival; CNPq, National Council for Scientific and Technological Development; CNS, central nervous system; COI, conflicts of interest; CSF, cerebrospinal fluid; Cx, surgery; DC, ketogenic diet; DES, direct electrical stimulation; dMMR, deficient); EGFR, epidermal growth factor receptor; FISH, fluorescence in situ hybridisation; FLS-Na, sodium fluorescein; fMRI, functional magnetic resonance imaging; GBM, glioblastoma; HGG, high-grade glioma; ID, Identification; IDH1, Isocitrate dehydrogenase 1; IDH1MUT, mutated isocitrate dehydrogenase 1; IDH1WT, wild-type isocitrate dehydrogenase 1; IHQ, Immunohistochemistry; IMRT, Intensity-Modulated Radiotherapy; IORT, Intraoperative Radiotherapy; IQR, Interquartile range; IS, Intraoperative seizures; KDR, Gene encoding the VEGFR-2 receptor (vascular endothelial growth factor receptor 2); KIT, Gene encoding the c-KIT tyrosine kinase; KPS, Karnofsky Performance Scale; LOM, Lomustine; MF, Mapping failures; MGMT, O-6-methylguanine-DNA methyltransferase; MGMTp, O-6-methylguanine-DNA methyltransferase gene promoter; MLH1, MutL Homolog 1; MMR, Mismatch Repair (pMMR, proficient; MSH2, MutS Homolog 2; MSH6, MutS Homolog 6; N, Number of patients; NCT, Non-randomised clinical trial; NTRK1, Gene encoding the TrkA receptor (tyrosine receptor kinase A); OS, Overall survival; PCV, (procarbazine, lomustine [CCNU] and vincristine); PD, Disease progression; PDGFRA, Gene encoding the receptor for platelet-derived growth factor α (PDGFRα); PFS, Progression-free survival; PMS2, Post-meiotic segregation increased 2; POH, perillyl alcohol; PR, Partial response; PTEN, Phosphatase and tensin homolog; Qt, Chemotherapy; RB1, Tumour suppressor gene encoding the retinoblastoma protein (pRB); RFS, Radiological Disease-Free Survival; ROC, Receiver operating characteristic; ROS1, proto-oncogene encoding a receptor tyrosine kinase (type 1 receptor); RPA, Recursive partitioning analysis; Rt, Radiotherapy; SD, Stable disease; SLF, Superior longitudinal fascicle; TERTp, Telomerase reverse transcriptase gene promoter; TG, Triglycerides; TMZ, Temozolomide; TP53, Tumour protein p53; TTFields, Tumour treatment fields; WBIC, World Bank Income Classification

Most of the included studies were retrospective observational studies (26) [9,25–30,32–34,37–44,47–51,54,56,57], with sample sizes ranging from 19 to 4,511 patients. Four prospective studies were identified: one qualitative study [55], two cohort studies (one descriptive longitudinal study [35] and one diagnostic accuracy study [53]) and one RCT [46]. Four synthesis studies were also included: three SRs [36,45,52] and one Latin American Scoping Review (ScR) by Figueredo *et al* [31]. The follow-up period ranged from 68 hours (decompressive craniectomy) to 135 months (11.2 years) [28].

The included SRs [36,45,52] provided relevant data on ALC. The Cochrane review (2021) on post-Stupp recurrent GBM [45] included a Brazilian RCT involving a ketogenic diet and perillyl alcohol (*n* = 32) [46]; another SR [36] analysed 13 studies (3,547–21,000 patients, ~2,674 GBM cases), from which a Peruvian cohort (*n* = 278 HGG, 144 GBM) was extracted [47]; the third, involving a meta-analysis [52], assessed

overall survival (OS) according to *the* World Bank Income Classification and identified a Brazilian multicentre cohort (*n* = 115) [41]. The Latin American ScR on Awake Craniotomy (AC) [31] compiled 27 reports, of which three cohorts and one retrospective qualitative study from Chile [53], Mexico [54] and Brazil [55,56] were included.

The study population had a mean age of 54–55 years (range, 0–86) [27,28,43], a predominance of males (55%–65%) [9,30,34] and a Karnofsky Performance Scale (KPS) score of 70–90 [26,41]. Most studies (27; 79.4%) included adults; two involved paediatric patients [28,40]; and five comprised mixed cohorts [27,33,35,37,50]. The most common comorbidities were identified as hypertension (20%–25%), diabetes mellitus (5%–10%) and smoking (15%–20%) [25,29]. The operational definitions of key clinical variables, such as extent of resection (EOR), RT and QT, varied across the included studies and are summarised in Supplementary Table 6. Detailed population data and additional results (univariate and multivariate analyses) are presented in Supplementary Table 7.

Methodological assessment of the evidence

Of the 34 studies included, 14 (41.2%) were assessed using the ROBINS-I tool [9,25–29,32–34,38,41,47,49,51]. In the overall assessment of risk of bias, seven reports (50%) were categorised as having moderate risk [9,25,33,34,38,47,49], four (28.6%) were classified as having serious risk [26–29] and three (21.4%) as having critical risk [32,41,51]. None were categorised as having a low overall risk. The domains (D) with the poorest performance were D1 (confounder bias), with a serious risk in four studies [27–29,51] and a critical risk in two [32,41]; and D5 (missing data bias), with a serious risk in three studies [26–28] and a critical risk in one [32]. The results of the ROBINS-I analysis are shown in Figure 2.

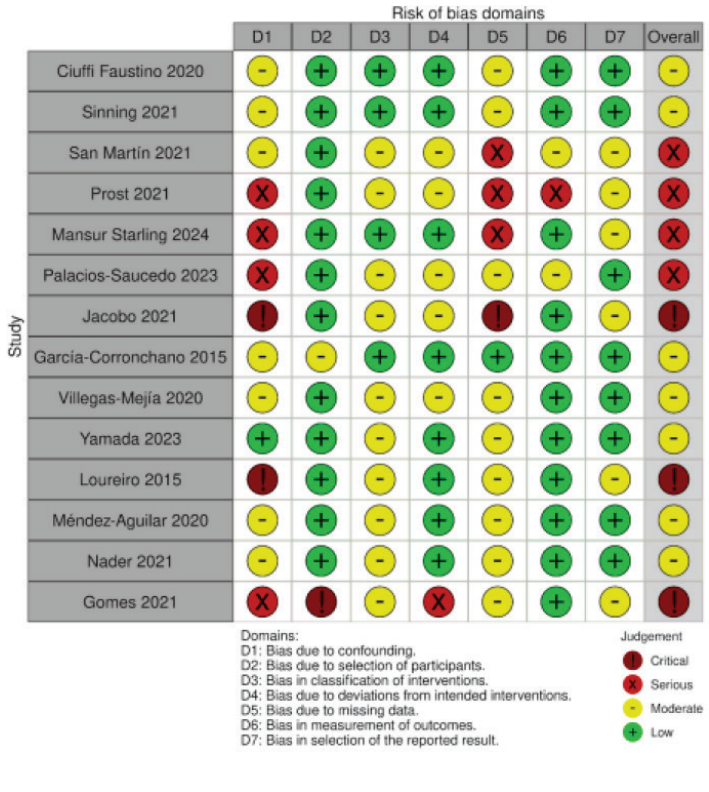

Figure 2. Results of the risk of bias assessment using the ROBINS-I tool.

AMSTAR-2 was applied to the three included SRs. None of them were rated as high or moderate quality: one (33.3%) was classified as low [45] and two (66.7%) as critically low [36,52]. The main shortcomings were linked to the absence of a registered protocol (item 2), the failure to incorporate risk of bias into the interpretation of results (item 13) and insufficient assessment of risk of bias (item 9). Two SRs lacked a registered protocol [36,52], and all showed limited incorporation of bias analysis into their conclusions. The summary is presented in Table 2.

Table 2. Results of the methodological quality assessment according to AMSTAR-2.

ID	**Author**	**I1**	**I2**	**I3**	**I4**
24	Castellanos-Bertot 2022	Yes	No	No	Partial Yes
		I5	I6	I7	I8
		No	No	No	No
		I9	I10	I11	I12
		No	Yes	N/A	N/A
		I13	I14	I15	I16
		N/A	No	N/A	Yes
ID	**Author**	I1	I2	I3	I4
55	Mc Bain 2021	Yes	Yes	Yes	Partial Yes
		I5	I6	I7	I8
		Yes	Yes	Yes	Partial Yes
		I9	I10	I11	I12
		Yes	Yes	Yes	No
		I13	I14	I15	I16
		Yes	Yes	No	Yes
ID	**Author**	I1	I2	I3	I4
63	Dy 2022	Yes	No	No	Partial Yes
		I5	I6	I7	I8
		Yes	No	No	Partial Yes
		I9	I10	I11	I12
		No	No	No	No
		I13	I14	I15	I16
		Yes	Yes	Yes	No
%Quality: (total 'Yes' / total items) + (total 'Partial Yes' / items / 2) × 100					
Critical Domains: I2, I4, I7, I9, I11, I13, I15.					
High	0CD	1NCD			
Moderate	0CD	2NCD or more			
Low	1CD	with or without NCD			
Critically Low	2CD	with or without NCD			

Continued

Table 2. Results of the methodological quality assessment according to AMSTAR-2. *Continued*

ID	Author	I1	I2	I3	I4
Analysis	YES	PARTIAL YES	NO		
	3	1	8		
	12	2	2		
	5	2	9		
	Total	% Quality	CD		
	12	29%	2		
	16	81%	1		
	16	37.5%	3		
	NCD	Qual. Assess.	ID		
	6	Critically Low	24		
	1	Low	55		
	6	Critically Low	63		

CD, critical domain; ID, identifier; N/A, Not applicable; NCD, Non-critical domain; Qual Assess, Quality assessment; I: item.

The JBI checklists were applied according to study design: nine case series [37,40,42,44,48,50,54,56,57], one diagnostic accuracy study [53], one qualitative research study [55] and five cohort studies [30,35,39,43,46]. The results of the checklists are presented in Supplementary Table 8. The case series were characterised by an adequate clinical description and clear diagnostic criteria, but nevertheless exhibited shortcomings in consecutive inclusion and follow-up. The diagnostic accuracy study appeared to comply with the application of tests, although it did not detail the final selection of patients; the qualitative study showed apparent methodological consistency without explicitly stating its theoretical framework. The cohorts suggested acceptable levels of validity and comparability, although limitations were identified in the control of confounders and follow-up. Overall, the JBI assessment revealed marked methodological heterogeneity, with some internal consistency but recurring weaknesses in follow-up and case inclusion.

The rationale for the score assigned to each item/domain of the quality assessment tools applied to the included studies is presented in Supplementary Table 9.

Results from individual sources of evidence

Overview and geographical distribution

The geographical distribution of the included studies is shown in Figure 3, which facilitates the observation of the origin and concentration of the identified regional scientific output.

In total, 30 studies published between 2015 and 2025 were identified, originating from seven LAC countries. The highest concentration of publications was found in Brazil (14 studies; 46.7%) [25,28,30,38,39,41–44,46,49,51,55,56], followed by Mexico (5; 16.7%) [29,32,37,48,54], Chile (4; 13.3%) [9,26,53,57], Peru (3; 10.0%) [33,47,50], Colombia (2; 6.7%) [34,35] and, to a lesser extent, publications from Cuba (1; 3.3%) [36] and Argentina (1; 3.3%) [27].

Darker shades indicate a higher concentration of studies; intensity is proportional to the number of publications per country.

Figure 3. Geographical distribution of studies in LAC.

Therapeutic interventions reported

Standard regimen (Stupp) and variations

Of the 34 studies included, 24 (70.6%) referred to the Stupp protocol in their cohorts or reviews [9,25–29,32-37,40,41,43–47,49–52,57]. Most of these studies were characterised by a retrospective design (19; 79.1%), with moderate quality and a moderate to serious risk of bias [9,25–29,32–34,37,40,41,43,44,47,49–51,57]. Three SRs (12.5%) were categorised as being of low quality [45] or critically low quality [36,52], while two prospective studies [46,55] suggested greater methodological rigour.

Thirteen studies (54.2%) described the protocol in general terms without specifying doses or regimens for RT or TMZ [27–29,32,35–37,45,46,49,51,52,57], while eleven (45.8%) specified surgical procedures and RT/QT parameters [9,25,26,33,34,40,41,43,44,47,50].

Among the most detailed studies, a Brazilian cohort [25] reported three-dimensional conformal radiotherapy (3D-CRT; 43%) and intensity-modulated radiotherapy (IMRT; 57%), with volumes defined according to guidelines from the Radiation Therapy Oncology Group and the European Organisation for Research and Treatment of Cancer. A dose of 44 Gy in 22 fractions was delivered to the oedematous volume and 60 Gy in 30 fractions to the tumour volume, combined with concomitant (75 mg/m²/day) and adjuvant (150–200 mg/m²/day in 5/28-day cycles) TMZ.

In two retrospective cohorts (RC) from Chile [9,26], 3D-CRT delivered 60 Gy in 30 fractions, with an average of six cycles of TMZ. In two RCs from Peru [33,47], RT ranged from 40 to 65 Gy with concomitant TMZ at half the standard dose and adjuvant TMZ at 200 mg/m² for 4–6 cycles; in one RC from Colombia [34], between 30 and 82 Gy (mean 59.2 Gy) with prolonged adjuvant TMZ (>24 months). In a retrospective case series from Cuba [40], 3D-CRT (59.4–60 Gy) was reported in paediatric patients; in Brazil [41,43,44], RT at 50–60 Gy with TMZ 200 mg/m² was identified as the replacement for the historical regimen with carmustine (BCNU).

Finally, an international multicentre cohort (Peru, Germany, and China) [50] described the use of intraoperative radiotherapy (IORT) with 50 kV X-rays (10–40 Gy) applied to the surgical margin, followed by external RT (IMRT or volumetric modulated arc therapy [VMAT]) at 60 Gy in 20 fractions, with concomitant and adjuvant TMZ under the Stupp protocol.

Neurosurgical treatment

Surgical tumour resection was described in the 34 included studies as part of the diagnostic and therapeutic approach to GBM. Twenty (58.8%) provided details on the extent of resection (EOR) using categories such as gross total resection (GTR), subtotal resection (STR), partial resection (PR) or biopsy [9,25–27,29–31,33,34,37–41,43,44,47,48,51,57]. Six retrospective studies (five cohorts and one case-control study) specified these criteria; these were found to have a moderate-to-serious risk of bias [9,27,29,47] or to have partially met the Joanna Briggs Institute (JBI) standards [30,39]. Four cohort studies [9,27,30,39] defined GTR as >90% of tumour volume, one case-control study [29] as 100%, and another cohort study [47] as post-surgical residual tumour <5%. Definitions of STR/PR varied across reports: Argentina (10%–50% residual) [27]; Mexico (STR, 90%–99%; PR <90%) [29]; Brazil (10%–90%) [30,39]; and Chile (>80%) [47].

Only four studies (20%) detailed the method used to estimate resection: postoperative MRI [9], a combination of clinical and radiological reports [34], computed tomography (CT) or MRI within 48 hours [41], and specialised radiological assessment [47].

Eight studies (23.5%) described the use of specialised surgical techniques [31–33,37,53–56]. AC was identified as the most common (five studies, 62.5%), including one ScR [31], six CRs (moderate-to-critical risk of bias [32,33]; adequate rigour according to the JBI [37,53,54,56]) and one prospective qualitative study [55]. The ScR by Figueredo *et al* [31] compiled 27 Latin American reports on high-grade gliomas (HGG), describing the use of 'Awake–Awake–Asleep' (63%) or 'Awake–Awake–Awake' (14.8%), with intraoperative stimulation in 85.2% of cases and sedation using propofol, remifentanil and dexmedetomidine.

Other reported interventions included decompressive craniectomy, mentioned in a Mexican cohort [32] in 39.2% of patients during surgery and in 47.8% within the first 72 hours, primarily associated with the management of intraoperative cerebral oedema. A Peruvian cohort [33] reported the use of sodium fluorescein (FLS-Na) in 80 out of 150 patients (53.3%), with a dose of 20 mg/kg prior to dural opening; in this specific group, higher rates of GTR were observed (77.5% versus 27.1%; $p < 0.001$) compared with the group without contrast. Finally, a Mexican cohort [37] recorded the placement of ventriculo-peritoneal shunts in 26% of 114 patients with GGB, including 39 GBM cases.

Other interventions

Of the total number of studies, 12 (35.3%) (including 10 retrospective cohorts (RC), one RCT-NA and one prospective qualitative study) described the use of interventions in addition to the Stupp protocol, RT or QT [9,25,28,37,41,46,49,50,53–56]. These studies were categorised as having a moderate to critical risk of bias according to ROBINS-I, and considerable methodological rigour was identified according to JBI.

Six studies reported symptomatic management with corticosteroids ([25,46]; dexamethasone) and antiepileptic drugs ([25,46,54,56]; phenytoin, levetiracetam and valproic acid). Two cohorts (one from Chile [9] and another from Mexico [37]) also described the implementation of palliative care in patients with rapid disease progression or a low KPS score, associating this approach with the use of corticosteroids, sedatives and antiepileptics.

In the context of AC, three studies (two RC and one qualitative study), linked to the ScR by Figueredo *et al* [31], documented the intraoperative management of seizures using cold-water irrigation, followed by propofol (30–40 mg or 1 mg/kg) and intravenous phenytoin or

levetiracetam, including advanced airway management in cases reported as refractory [54–56]. Finally, two Brazilian cohorts referred to other interventions without specifying the type of approach [28,49].

Clinical outcomes

Progression-free survival

Six studies (17.6%) were identified that provided quantitative data on PFS; all were retrospective [9,25,27,33,47,50]. Most of these reports were categorised as having moderate methodological quality [9,25,33,47], followed by a classification of serious risk [27] and an 'outstanding' rating according to JBI criteria [50]. The reported medians ranged from 7 to 22.7 months, with a tendency to cluster between 9 and 11 months. Some studies reported annual rates: 36.5%–18.9% [9], while others recorded figures of 46.2%, 29.4% and 5.9% at 1 to 3 years, respectively [50].

Various cohorts analysed the SLP according to specific clinical and therapeutic variables. In a cohort from Chile [9], the median was reported as 10 months (with rates of 32.8% and 14% at 1 and 2 years, respectively, within the subgroup identified as Stupp). In a cohort from Argentina [27], the overall PFS was estimated at 7 months (6 months in GBM), with possible variations reported in association with the QT-RT interval (<5 weeks: 10 months; 5–8: 7; >8: 4; $p = 0.014$) and to the extent of surgery (total: 8; subtotal: 5; biopsy: 3; $p = 0.001$). In a Peruvian cohort [33], higher SLP figures were associated with functional-guided surgery (10 versus 7; $p = 0.001$), total versus subtotal resection (15 versus 7; $p = 0.001$) and in patients aged <50 years (11.5 versus 7; $p = 0.002$). Sarria *et al* [50] described differences between local progression (16 months; 95% CI 10.2–21.8) and distal progression (30; 95% CI 18.6–41.4). Another Peruvian cohort [47] reported differences in SLP linked to tumour grade (GBM: 13.3; HGG grade III: 32.8; $p < 0.001$), EOR (total: 28.3; subtotal: 20.4; $p < 0.001$) and the adjuvant regimen received (RT + QT: 30.4; RT alone: 14.9; no treatment: 9; $p < 0.001$).

Overall survival

Seventeen studies (50%) provided data on the median OS for GBM: 14 RC (identified as having moderate to critical risk of bias and acceptable quality according to JBI) [9,25,26,30,33–35,38,39,41,47–50,57], one retrospective case-control study (serious risk) [29] and a SR of critically low quality [52]. Excluding the SR, the reported medians ranged from 3.6 months (case-control study from Mexico [29]) to 19.07 months (cohort study from Colombia [35]), with a calculated median of medians of 12.2 months (IQR 9.48), a value that falls within a range close to that reported in the SR by Dy *et al* [52] (14.17 months across 24 studies, including Brazilian data [41]).

OS by year

Seven studies (20.6%) reported annual OS figures: at 1 year, 79.5% [50], 52.9% [28], 48% [26] and 27% [29]; at 2 years, 38.7% [50], 37.7% [25], 31% [9,43] and 15% [26]; at 3 years, 28.7% [28] and 25.6% [50]; and at 5 years, 25.2% [28] and 3% [26]. A Brazilian cohort (primary/secondary GBM) reported OS at 1 year = 23% and at 5 years = 3.4% [30]; the Cuban series reported figures of 50.2% for GBM and 11.1% for HGG [40].

OS according to EOR

Seven cohorts [9,33,34,38,39,41,47] analysed OS in relation to the extent of surgery: Chile reported a median of 16.3 months for GTR, 12.5 months for PR and 5.2 months for biopsy ($p < 0.0001$) [9]; Peru reported figures of 17 versus 7 months (GTR versus STR; $p < 0.001$), as well as an association between longer OS and the use of FLS-Na (15 versus 8 months; $p = 0.002$) [33]; one of the reports from Brazil recorded 30.7 GTR versus 13.6 STR/biopsy ($p = 0.020$) [38], while two reports from Colombia and Brazil found no statistically significant differences ($p = 0.2902$; $p = 0.096$) [34,41]; and a Peruvian cohort recorded values of 30.8, 20.6 and 7.3 months for GTR, STR and biopsy, respectively [47].

OS by adjuvant therapy

Nine studies (26.5%) examined OS in relation to other interventions; eight of these were retrospective in design [9,26,28,33,34,41,47,57], accompanied by a SR [52]. The risk of bias according to ROBINS-I was mainly classified as moderate (55.6%), followed by serious (22.2%). The SR was classified according to AMSTAR-2 as having critically low quality (11.1%), and the report assessed using JBI was classified as having moderate to high reporting quality (11.1%). Five studies linked OS to the Stupp protocol: a report from Chile described a median OS of 16.1 months (2-year OS 35.9%) [9] and 14.6 months with RT + TMZ versus 9.7 months with RT alone ($p < 0.05$) [26]. In a report from Colombia, medians of 22 versus 8 months were recorded ($p < 0.0001$) [34]. In another report from Brazil, figures of 17.7 versus 15.8 months were documented with BCNU ($p < 0.001$) [41]; and the RS [52] observed numerically higher OS values associated with the post-2005 period (15.6 versus 12.5 months; $p < 0.05$).

Two cohorts reported numerically higher OS figures associated with the use of RT and/or QT: Peru (15 versus 8 months with/without RT; $p = 0.016$, and 16 versus 8 months with/without QT; $p = 0.011$) [33] and Chile (13.1 versus 6.9 months with/without QT; $p < 0.001$) [57]. With regard to RT doses, a cohort from Colombia found no differences between <54 and >64 Gy, although it reported a longer median OS associated with the use of prolonged adjuvant TMZ (27 versus 15 months; $p < 0.0001$) [34]. Meanwhile, a cohort from Brazil identified a favourable trend in OS associated with doses >60 Gy (16.2 versus. 11 months; $p = 0.042$) [41]. Two mixed cohorts described an apparent relationship between increased OS and greater therapeutic complexity in Brazil (11 months with surgery alone, 16 months with surgery + CT, 20 months with surgery + CT + RT) [28] and reported higher OS values associated with the use of adjuvant treatment in Peru (32 months with RT + QT, 26.4 months with RT alone, 12.6 months without RT; $p < 0.001$) [47].

Complications

Ten studies (29.4%) provided data on the occurrence of treatment-related complications [9,25,29–31,34,43,54–56]. Most of these reports were linked to RC (80.0%) and were identified as having a moderate to serious risk of bias [9,25,29,34]; the remainder were categorised as having acceptable methodological quality according to the JBI, although limitations were noted in the control of confounders and follow-up [30,43,54,56]. One ScR [31] and one prospective qualitative study [55] were also included.

Reported rates of post-surgical complications ranged from 13.7% to 54% in Brazilian cohorts [30,43], with events such as infections, haemorrhages, hydrocephalus, thromboembolism and neurological deficits being identified. In Mexico, a case-control study [29] recorded the occurrence of complications in 24% of its sample (severe cerebral oedema 11%, infection 6% and cerebrospinal fluid fistula 3%). In Brazil, one cohort described an association between the presence of complications and higher mortality (HR, 2.69; $p = 0.003$) [30], while another report linked the presence of adverse events to a numerically lower OS (104 versus 262 days; $p = 0.001$) and a lower rate of initiation of adjuvant therapy (25% versus 75%) [43].

With regard to surgical techniques, the ScR by Figueredo *et al* [31] on AC documented the presence of limited neurological complications (aphasia 3.6%, hemiparesis 8.4%, with no mortality). Two Brazilian cohorts [54,56] reported the occurrence of intraoperative seizures (15%–21%) and mild or transient neurological deficits.

In terms of treatment-related toxicity, a Brazilian cohort [25] reported the discontinuation or reduction of the Stupp protocol in 12% of cases, attributing this phenomenon primarily to disease progression or haematological toxicity (thrombocytopenia 12%, anaemia 6%, neutropenia 5%–6%). In a RC from Chile [9], grade 3–4 haematological toxicity was documented in 17.2% of cases and infections in 7.8%, alongside reports of hepatotoxicity and mild cutaneous reactions.

Knowledge gaps, gaps in evidence and inequalities in the region

Mapping of regional evidence revealed consistent gaps in coverage, detail and quality of reporting. A significant proportion of studies mentioning the Stupp protocol lacked key information on RT dose and fractionation, QT phases with TMZ, concomitant interventions (corticosteroids and antiepileptics), local variations (such as IORT) and criteria for the application of advanced surgical techniques, such as AC or the use of FLS-Na.

The surgical descriptions were characterised by marked heterogeneity in the categories and thresholds for EOR (GTR, STR and PR) and, in particular, in the methods of verification using postoperative MRI or CT, centralised reading and volumetry, which limits comparability between series.

Outcomes were primarily identified as SLP and SG, with varying timeframes and limited assessment of quality of life, neurocognitive function or symptoms. Reports of toxicity were incomplete or non-standardised, with no reference to the Common Terminology Criteria for Adverse Events, and with inconsistent recording of losses to follow-up and missing data.

Biomolecular characterisation was reported inconsistently, with possible under-reporting of IDH status, MGMT methylation and other markers, which could influence the accuracy of analyses by biological subgroups in the region.

A predominance of RC was identified, with limited control of confounders and small sample sizes, and a scarcity of prospective or multicentre studies. Scientific output was characterised by geographical concentration and heterogeneous access to technologies (IMRT, VMAT, neuronavigation and FLS-Na), as well as by the identification of omissions in operational indicators (surgery–RT/QT intervals, duration of adjuvant therapy and interruptions due to toxicity).

Finally, there was a lack of representation of vulnerable populations (paediatric patients, frail older adults or those with a low KPS score) and limited availability of economic evaluations and interoperable data structures (such as prospective registries, centralised radiological reading or biobanks with clinical annotation), which is linked to the fragmentation of the available evidence in LAC.

Discussion

This ScR synthesises regional evidence on the treatment of newly diagnosed GBM in LAC, highlighting a concentration of scientific output in a few countries and marked methodological heterogeneity. The Stupp protocol was the most frequently reported approach, although its application showed variability and a lack of detail regarding doses, techniques or cycles of RT and QT, which could hinder comparability between studies.

Surgery remains the mainstay of treatment according to international guidelines [7], but studies show considerable variability in the definition and assessment of EOR, with no standardised volumetric criteria [58,59]. Despite this, the apparent association between greater EOR and prolonged OS remains consistent [60]. Advanced techniques, particularly AC, suggest a trend towards the progressive adoption of connectomic approaches that are associated with a possible increase in EOR, without appearing to increase morbidity [31,53–56,61,62], although the studies present a moderate–high risk of bias and small sample sizes, requiring these results to be confirmed through prospective studies [9,25–57].

The use of FLS-Na was associated with higher rates of complete resection, in line with international evidence [33,63]. Anatomical factors, such as ependymal invasion or ventricular opening, appear to be linked to a lower EOR and a poor prognosis, which emphasises the need for anatomical–functional surgical planning supported by imaging and tractography [64]. The combined use of cortical/subcortical mapping, neurophysiology and intraoperative imaging was associated with extensive resections with functional preservation [65,66], although its implementation remains restricted to high-complexity centres [31–33,37,53–56].

Inequalities in access and resources may help to explain some of the observed variability: a Brazilian analysis reported differences in overall survival associated with the type of practice, educational level and availability of combined therapies [49]. Overall, the literature appears to reflect significant technical advances, but persistent structural limitations that could restrict their impact on the general population.

The evidence analysed presents common methodological limitations: a predominance of single-centre retrospective designs, heterogeneity in surgical and adjuvant definitions and a lack of multicentre studies that facilitate the analysis of therapeutic effect independently of the healthcare context. It is important to note that the definitions of key clinical variables, such as EOR, RT regimens and QT regimens, varied across the included studies. This methodological heterogeneity may influence the comparability of the reported results and must be taken into account when interpreting the findings of this review. In particular, differences in the definition of EOR and in treatment protocols could impact the clinical outcomes assessed, limiting the possibility of making direct comparisons between studies. There is a need to consolidate regional databases and prospective studies that integrate clinical, molecular and treatment access variables.

Among the limitations of this review, the lack of age-stratified reporting in the included studies prevented a separate analysis between the adult and paediatric populations, which limits interpretation specific to each age group. Furthermore, there is a risk of selection bias due to the eligibility criteria and the availability of articles in the databases consulted, which may have influenced the inclusion of certain types of studies or populations. For operational and time-related reasons, grey literature, such as conference abstracts, was excluded; while this decision ensured that detailed methodological information was available for the quantitative and descriptive analysis, it does not rule out publication bias due to the possible under-representation of negative or non-significant findings.

Regional oncological neurosurgery is making progress towards international standards, but would benefit from coordinated actions: (1) standardising EOR protocols with the support of neuroimaging and mapping; (2) expanding training in AC; (3) strengthening multidisciplinary teams to ensure timely adjuvant therapy; and (4) establishing population-based registries and multicentre collaborative networks. These measures, in line with global recommendations, could promote wide resection without compromising neurological function [67].

The observed trends are subject to methodological uncertainty due to the observational and retrospective nature of the evidence. Its quality – mostly low to moderate, with moderate to critical risks of bias according to ROBINS-I and AMSTAR-2 – prevents the establishment of causal relationships; the benefits represent potential clinical associations rather than statistical certainties. Furthermore, the survival synthesis is purely descriptive (median of medians) and not a conventional meta-analysis, given the marked methodological, contextual and population-level heterogeneity, coupled with the absence of comprehensive sensitivity analyses. This variability is reflected in the clinical definitions for EOR, RT protocols and TMZ regimens. Consequently, these findings are exploratory and hypothesis-generating in nature, requiring confirmation through future prospective, multicentre studies employing standardised and rigorous methodologies.

Despite these limitations, this ScR constitutes the first comprehensive synthesis of therapeutic strategies for GBM in LAC, integrating scattered information and highlighting gaps, inequalities and regional patterns. The application of validated methodological tools (PRISMA-ScR, ROBINS-I, AMSTAR-2 and JBI) facilitated a structured analysis and the identification of priorities: standardisation of reporting, inclusion of functional and quality-of-life outcomes, biomolecular integration and strengthening of regional prospective multicentre research.

Conclusion

This ScR SRs the available evidence on the treatment of newly diagnosed GBM in LAC. A predominance of single-centre retrospective studies was identified, with poor control of confounding factors and marked heterogeneity in the description of EOR, RT doses and QT regimens. Although the Stupp protocol was identified as the most common approach, its variable application and lack of methodological detail could limit comparisons between countries. Surgery remains the reported cornerstone of treatment, although disparate definitions of resection extent were observed. The adoption of advanced techniques (AC, intraoperative mapping and FLS-Na-guided resection) may suggest regional progress, although their implementation appears to remain uneven. The median of medians for overall survival (12.2 months [IQR, 9.48]) falls within ranges similar to those described in the international literature, but the differences observed may be linked to inequalities in access to combination therapies and specialist care.

Addressing methodological and structural gaps is identified as a key factor in strengthening research and optimising clinical outcomes. Standardising reporting, promoting multicentre studies, integrating biomarkers and ensuring equitable access to comprehensive therapies are proposed as priority courses of action towards precision medicine adapted to the LAC context.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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Author contributions

MAA, EJOC and MV were involved in the conceptualisation and design of the study; data collection, analysis and interpretation; drafting of the protocol and manuscript; critical review of the intellectual content; and overall supervision. CVG contributed to the conceptualisation, data analysis, drafting and critical review. MED contributed to the analysis and interpretation of data and the drafting of the manuscript. JAL, FEE, AMR and MCG were involved in data collection and analysis. AM, IMDD, JAS, LGD and MEE contributed to data collection and the critical review of the manuscript. All authors approved the final version and take responsibility for the published content.

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Supplementary material

Supplementary material can be viewed at https://doi.org/10.6084/m9.figshare.33148715