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Repeat ExCision Upon Recurrence: REthinking Neurosurgical Treatment of GlioBlastoma (Repeat surgery for recurrent glioblastoma)

Submission date
05/02/2026

Recruitment status
Recruiting

Registration date
25/02/2026

Overall study status
Ongoing

Last Edited
06/07/2026

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Glioblastoma (GB) is the most common type of brain cancer in adults, with around 3,200 new cases in the UK each year. Without treatment, average survival is less than 6 months. With surgery to remove as much cancer as possible, followed by radiotherapy and chemotherapy (temozolomide), survival can extend to 14-16 months. Despite this, the tumour inevitably grows back and is called a 'recurrent GB'. It is unclear what the most appropriate treatment for recurrent GB is. As a result, there is a wide variation in practice across the UK in whether or not patients are offered repeat surgery or whether to use only non-surgical treatments (chemotherapy and/or radiotherapy).

This study will determine if repeat surgery when a GB grows back, before further chemotherapy or radiotherapy, improves quality of life and survival. It was co-designed with UK-wide patient and relative advisory groups from the BrainsTrust charity, Brain Tumour Charity Research Involvement Network (BTC-RIN), Thames Valley Patient & Public Involvement (PPI) group, and specialist nurses who care for patients with GB.

Who can participate?
Adults will be recruited from at least 20 UK NHS hospitals who are aged 18 years and above, have previously undergone surgery to remove a GB, are now diagnosed with a recurrent GB, and have not experienced recurrence or progression within 6 weeks of completing radiotherapy (6-week or short course), with or without concomitant chemotherapy.

What does the study involve?
As part of routine NHS care, patients with recurrent GB will be discussed in a 'multi-disciplinary team' (MDT) meeting, where a group of medical specialists will discuss treatment options. If the MDT considers both repeat surgery and second-line chemotherapy reasonable, the patient will be invited to participate in this trial. If they agree to take part, they will be assigned at random to one of two groups:
Group 1: Offered repeat surgery followed by further chemotherapy and/or radiotherapy
Group 2: Offered further chemotherapy and/or radiotherapy without repeat surgery

Participants will be followed up weekly with three questions rating their general health and quality of life, plus additional questionnaires on various aspects of their health and quality of life every 6 weeks. Depending on participant preference, responses will be collected electronically via a smartphone app (RADAR-base) or via links to an online form sent by email/text, or via a telephone interview. If participants choose to complete questionnaires using the RADAR-based app, they will also be invited to provide optional short speech samples, which may offer insights into aspects of well-being.

The study also requires participants to nominate a 'proxy', ideally who will be their primary carer* /support through their treatment (family member/friend), to complete similar questionnaires about the participant's quality of life, as they may not always feel well enough to respond and at three timepoints, their own quality of life. Nominated proxies will be provided with a Proxy Information Sheet and invited to give their consent to complete questionnaires on behalf of the participant. The follow-up period of the trial is up to 12 months post-randomisation. Due to the natural history of recurrent glioblastoma, some participants may pass away prior to this time point.

In addition to the health and quality of life questionnaires described above, participants will be invited to take part in an optional component of the trial, which aims to measure their physical activity levels using a smartwatch. Participants who wish to participate in this part of the trial will be provided with a complimentary smartwatch and asked to wear it for a minimum of 7 days every six weeks, to coincide with when they fill out their 6-weekly questionnaires. Physical activity data (e.g. activity levels, sleep patterns and, where supported by the device, time spent at home) will be collected remotely by researchers.

No additional blood tests or hospital visits are required from participants.

The trial will also look at the costs involved in treatment of recurrent glioblastoma to determine which treatment combination offers the best value for money to the NHS.

What are the possible benefits and risks of participating?
Benefits and risks not provided at time of registration

Where is the study run from?
John Radcliffe Hospital, Headington, UK.

When is the study starting and how long is it expected to run for?
April 2026 to June 2030.

Who is funding the study?
1. National Institute for Health and Care Research, UK.
2. BrainStorm Charity (Smartwatches for Substudy), UK.

Who is the main contact?
Recurrent GB team, recurrentgb@nds.ox.ac.uk

Contact information

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Principal investigator, Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
358925

Central Portfolio Management System (CPMS)
62049

Study information

Scientific Title
RECURRENT-GB: Repeat ExCision Upon Recurrence: REthinking Neurosurgical Treatment of GlioBlastoma

Acronym
RECURRENT-GB

Study objectives
Primary Objective: In participants with a recurrent GB, does repeat tumour resection surgery improve quality of life and survival when added to second-line medical therapy?

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 28/05/2026, Wales REC 7 (Health and Care Research Wales Castlebridge 4 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; no telephone number provided; Wales.REC7@wales.nhs.uk), ref: 26/WA/0086

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Open (masking not used)

Control
Active

Assignment
Parallel

Purpose
Treatment

Study type(s)

Health condition(s) or problem(s) studied
Repeat surgery for patients with recurrent glioblastoma

Interventions
This is a two-arm, pragmatic randomised controlled trial in adults with recurrent glioblastoma (GB). Participants will be followed for a maximum of 12 months from randomisation.

Intervention arm: Repeat maximal safe resection followed by second-line medical therapy
Participants randomised to the intervention arm will undergo repeat surgical resection of recurrent GB in the hospital. The aim of surgery is maximal safe resection and it is expected that the operating surgeon will use pre-operative MRI with diffusion tensor imaging (DTI) tractography for neuronavigation, as well as 5-aminolevulinic acid (5-ALA) intra-operative fluorescence. The operating surgeon may additionally use other adjuncts at their discretion to maximise safe resection, including intra-operative neuromonitoring, awake craniotomy with neuropsychological assessment, intra-operative ultrasound, or intra-operative MRI. Post-operative care will follow routine NHS practice, including a brain MRI with gadolinium contrast within 48–72 hours to assess the extent of resection. Following recovery from surgery, participants will receive all appropriate second-line medical therapies as determined by their multidisciplinary team (MDT), in accordance with national guidance and local NHS policy. There are no protocol-imposed restrictions on systemic therapy.

Comparator arm: Standard of care (SOC) alone
Participants randomised to the control arm will receive second-line treatment as recommended by their neuro-oncology MDT and in line with national guidance and local NHS practice. As there is no single standard treatment for recurrent GB, management may include chemotherapy, radiotherapy, re-irradiation, and repeat surgery if clinically indicated. No trial-mandated surgical intervention is delivered in this arm. All other aspects of clinical care will be as per routine NHS practice.

Follow-up and assessments
All participants will receive standard NHS follow-up. Participants will be asked to complete patient-reported outcome questionnaires during follow-up, which may be completed remotely via an online link (sent via email or SMS), via a trial-specific app, or by phone with the research team. Participants will be followed for up to 12 months from randomisation.

Randomisation
Participants will be randomised in a 1:1 ratio to either repeat maximal safe resection followed by second-line medical therapy or second-line medical therapy alone. Randomisation will take place after confirmation of eligibility, informed consent, and completion of baseline assessments. Allocation will be performed by authorised site research staff using a secure, web-based REDCap system hosted by the Oxford Clinical Trials Research Unit (OCTRU). Minimisation with a random component will be used to ensure balance across treatment arms. A small number of initial participants will be allocated using simple randomisation to seed the minimisation algorithm.

Minimisation factors are: Baseline QLQ-C30 Global Health Status score (<10 vs ≥10), Age (<70 vs ≥70 years), Tumour location (eloquent vs non-eloquent), Timing of recurrence (before vs after 6th cycle of adjuvant temozolomide), Previous radiotherapy (≤3-week vs standard 6-week course), MGMT methylation status (unknown grouped with unmethylated), Recruiting centre.

Intervention Type
Procedure/Surgery

Primary outcome(s)
1. Deterioration-free survival (DFS): Time from randomisation to either a ≥10-point deterioration from baseline in Global Health Status (GHS) without subsequent recovery, or death measured using Q29 & Q30 of EORTC QLQ-C30 questionnaire and mortality data from hospital records /NHS Spine at baseline, then weekly up to 12 months

Key secondary outcome(s)
1. Overall survival (OS): Time from randomisation to death, up to 12 months measured using hospital records/NHS Spine at one time point for data collection at the end of the study

2. Progression-free survival (PFS): Time to radiological tumour progression or death (MRI/MDT), up to 12 months measured using hospital records/NHS Spine at one time point for data collection at the end of the study

3. Health-related quality of life (HRQoL) measured using the EORTC QLQ-C30 and QLQ-BN20 at baseline and 6-weekly

4. Physical/social functioning, motor and communication deficits measured using domains of QLQ-C30/BN20 at baseline and 6-weekly

5. Performance status and Activities of Daily Living (ADLs) measured using WHO ECOG + QLQ-C30 items at baseline and 6-weekly

6. Seizure frequency and neurocognitive/physical symptoms measured using QLQ-C30/BN20 at baseline and 6-weekly

7. Surgical complications: Incidence/type within 31 days post-op (intervention arm) measured using hospital records/NHS Spine at one time point

8. Completion of adjuvant therapy: Proportion starting/completing therapy, up to 12 months measured using hospital records/NHS Spine at one time point

9. Extent of resection: Residual tumour volume on MRI within 72 hours post-op (intervention arm) measured using hospital records/NHS Spine at one time point

10. Health economics measured using QALYs via EQ-5D-5L, resource use from hospital records at baseline and 3-monthly; incremental cost per QALY modelled over lifetime

11. Carer QoL measured using EQ-5D-5L (proxy) at baseline and 6-monthly

Completion date
30/06/2030

Eligibility

Key inclusion criteria
1. Aged 18 years or above
2. First recurrence/progression of IDH wild-type GB following previous maximal safe resection (attempted gross total resection of contrast-enhancing tumour) as confirmed by local Neuro-oncology Multidisciplinary Team (MDT)
3. WHO Performance Status 0-2
4. Neuro-oncology MDT feels that the patient should be offered the trial and confirms that repeat maximal safe resection (>90%) is feasible and a reasonable treatment option
5. Able to give informed consent
6. Able to provide a proxy who is willing to complete the trial questionnaires

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
120 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Recurrence/progression of GB within 6 weeks of completion of radiotherapy (6 weeks or short course), with or without concomitant chemotherapy (See note* below)
2. Multifocal recurrence/progression of GB
3. Contraindication to MRI
4. Glioblastoma located in the brainstem, basal ganglia or the thalamus
*In the UK, standard treatment for operable glioblastoma consists of surgery followed by radiotherapy (with or without concomitant chemotherapy), then a short treatment break before starting adjuvant chemotherapy. The exclusion criterion refers to recurrence or progression occurring within 6 weeks of completing radiotherapy. Patients are therefore only eligible for RECURRENT GB once they have completed radiotherapy and reached the point at which adjuvant chemotherapy would normally begin, or are further along in their treatment pathway.

Date of first enrolment
20/07/2026

Date of final enrolment
30/06/2029

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
Barts Health NHS Trust
The Royal London Hospital
80 Newark Street
London
England
E1 2ES

Study participating centre
Belfast Health and Social Care Trust
Trust Headquarters
A Floor - Belfast City Hospital
Lisburn Road
Belfast

England
BT9 7AB

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
England
B15 2GW

Study participating centre
North Bristol NHS Trust
Southmead Hospital
Southmead Road
Westbury-on-trym
Bristol
England
BS10 5NB

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Cambridge Biomedical Campus
Hills Road
Cambridge
England
CB2 0QQ

Study participating centre
Cardiff & Vale University Lhb
Woodland House
Maes-y-coed Road
Cardiff
Wales
CF14 4HH

Study participating centre
University Hospitals Coventry and Warwickshire NHS Trust
Walsgrave General Hospital
Clifford Bridge Road

Coventry
England
CV2 2DX

Study participating centre
NHS Lothian
Waverley Gate
2-4 Waterloo Place
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EH1 3EG

Study participating centre
Hull University Teaching Hospitals NHS Trust
Hull Royal Infirmary
Anlaby Road
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England
HU3 2JZ

Study participating centre
Imperial College Healthcare NHS Trust
The Bays
St Marys Hospital
South Wharf Road
London
England
W2 1BL

Study participating centre
King's College Hospital NHS Foundation Trust
Denmark Hill
London
England
SE5 9RS

Study participating centre
Leeds Teaching Hospitals NHS Trust
St. James's University Hospital
Beckett Street
Leeds

England
LS9 7TF

Study participating centre
The Walton Centre NHS Foundation Trust
Lower Lane
Fazakerley
Liverpool
England
L9 7LJ

Study participating centre
Northern Care Alliance NHS Foundation Trust
Salford Royal
Stott Lane
Salford
England
M6 8HD

Study participating centre
South Tees Hospitals NHS Foundation Trust
James Cook University Hospital
Marton Road
Middlesbrough
England
TS4 3BW

Study participating centre
Nottingham University Hospitals NHS Trust - Queen's Medical Centre Campus
Nottingham University Hospital
Derby Road
Nottingham
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NG7 2UH

Study participating centre
University Hospitals Plymouth NHS Trust
Derriford Hospital
Derriford Road
Derriford
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PL6 8DH

Study participating centre
Lancashire Teaching Hospitals NHS Foundation Trust
Royal Preston Hospital
Sharoe Green Lane
Fulwood
Preston
England
PR2 9HT

Study participating centre
Barking, Havering and Redbridge University Hospitals NHS Trust
Queens Hospital
Rom Valley Way
Romford
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RM7 0AG

Study participating centre
University Hospital Southampton NHS Foundation Trust
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Tremona Road
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Study participating centre
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OX3 9DU

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
BrainStorm Charity

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available