





BMJ Open External validation and recalibration of an incidental meningioma prognostic model – IMPACT: protocol for an international multicentre retrospective cohort study

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ABSTRACT

Introduction Due to the increased use of CT and MRI, the prevalence of incidental findings on brain scans is increasing. Meningioma, the most common primary brain tumour, is a frequently encountered incidental finding, with an estimated prevalence of 3/1000. The management of incidental meningioma varies widely with active clinical-radiological monitoring being the most accepted method by clinicians. Duration of monitoring and time intervals for assessment, however, are not well defined. To this end, we have recently developed a statistical model of progression risk based on single-centre retrospective data. The model Incidental Meningioma: Prognostic Analysis Using Patient Comorbidity and MRI Tests (IMPACT) employs baseline clinical and imaging features to categorise the patient with an incidental meningioma into one of three risk groups: low, medium and high risk with a proposed active monitoring strategy based on the risk and temporal trajectory of progression, accounting for actuarial life expectancy. The primary aim of this study is to assess the external validity of this model.

Methods and analysis IMPACT is a retrospective multicentre study which will aim to include 1500 patients with an incidental intracranial meningioma, powered to detect a 10% progression risk. Adult patients ≥16 years diagnosed with an incidental meningioma between 1 January 2009 and 31 December 2010 will be included. Clinical and radiological data will be collected longitudinally until the patient reaches one of the study endpoints: intervention (surgery, stereotactic radiosurgery or fractionated radiotherapy), mortality or last date of follow-up. Data will be uploaded to an online Research Electronic Data Capture database with no unique identifiers. External validity of IMPACT will be tested using established statistical methods.

Ethics and dissemination Local institutional approval at each participating centre will be required. Results of the study will be reported through peer-reviewed articles and

Strengths and limitations of this study

- The first multicentre international study to investigate the prognosis of incidental intracranial meningiomas.
- The study will include a large cohort of 1500 patients.
- The longitudinal study design with serial collection of clinical and imaging data will provide a unique insight into meningioma behaviour and provide a platform for future investigation of novel biomarkers.
- The retrospective nature of the study may bias patient and information selection.
- Results of the study may be biased by clinician and patient management preference in each participating centre.

conferences and disseminated to participating centres, patients and the public using social media.

INTRODUCTION

Meningiomas have the highest incidence rate among all primary central nervous system tumours. Descriptive studies from Europe and North America suggest this rate is between 4.20 and 8.58 per 100 000 individuals.^{1 2} Wider access and increased use of MRI and CT have led to a marked rise in the number of incidental findings in clinical and research settings. Meningiomas comprise 15% of incidental findings on brain MRI and have a prevalence of 3 per 1000.³ A recent study of the Surveillance, Epidemiology, and End Results database demonstrated

a substantial increase in the detection of smaller, incidental tumours; between 2004 and 2012, the proportion of meningiomas <1 cm in diameter, diagnosed in a given year, increased in a linear fashion from 6% to 11%.⁴ Incidental, asymptomatic meningiomas cause patient anxiety and uncertainly around the need for future treatment and often prompt clinicians to commence long-term MRI and clinical follow-up. International consensus guidelines by the European Association of Neuro-Oncology and National Comprehensive Cancer Network suggest active monitoring with MRI as first line for managing these tumours,^{5 6} but data to advise on the optimal follow-up duration and screening intervals are currently lacking.⁷

Previous studies have identified prognostic radiological factors that are associated with the risk of meningioma growth and development of clinical symptoms; yet the timing of such progression is poorly defined.^{8–10} Moreover, clinical factors such as patient comorbidity and performance status remain unexplored in relation to prognosis but are highly relevant. The patient with an incidental meningioma wants to know whether their tumour will grow and become symptomatic such that it will require safe treatment within their healthy lifetime.

To this end, a recent retrospective cohort study of incidental meningioma patients in the UK was conducted to assess the utility of combining routinely available radiological and clinical factors to develop a prognostic model for the risk of incidental meningioma progression during active monitoring.¹¹ The model Incidental Meningioma: Prognostic Analysis Using Patient Comorbidity and MRI Tests (IMPACT) could be used as a tool to guide active monitoring strategies for patients with an incidental asymptomatic meningioma within the first 10 years of diagnosis, however, validation with external datasets is required.

The primary aim of this international retrospective cohort study of incidental meningioma is to externally validate and calibrate the prognostic model IMPACT, accessible using <https://www.impact-meningioma.com>. These data will provide insight into the incidence, epidemiology, presentation, management and long-term outcomes of incidental meningioma, which will inform the development of clinical guidelines and identify areas for future research.

THE IMPACT MODEL

The model, based on MRI parameters, stratifies patients with an incidental meningioma into three risk groups: low, medium and high risk. These MRI parameters are as follows: meningioma volume, meningioma hyperintensity, peritumoural signal change and proximity to critical neurovascular structures. The predictive function was built using an internally validated Cox regression model. Patients were also stratified in the model based on age, comorbidity and performance status using competing risk analyses.

OBJECTIVES

Primary objective

To externally validate the prognostic model IMPACT.

Secondary objectives

- ▶ To update the parameters of the prognostic model IMPACT if measures of external validation demonstrate a poor fit, and internally validate the updated model.
- ▶ To determine the growth patterns of incidental meningiomas.
- ▶ To examine the MRI and pathology features of meningiomas subject to surgical resection.
- ▶ To determine the risk of post-intervention complications and tumour recurrence/growth for meningiomas subject to surgery, stereotactic radiosurgery (SRS) or fractionated radiotherapy (fRT).
- ▶ Assess the economic implications of stratifying follow-up according to risk of disease progression.

METHODS AND ANALYSIS

Study design

This will be a retrospective, international multicentre cohort study. The study will include incidental meningioma patients managed at each participating centre. Cases will be identified by the local site research teams using existing patient medical records. Baseline clinical and radiological characteristics, tumour management, and clinical and radiological outcomes will be collected and recorded (anonymised data) on a secure database by the local investigators. Since this study falls within the remit of clinical outcomes audit, individual patient consent is not required. The study will collect data from the medical records for patients newly-diagnosed over a 2-year period between 1 January 2009 and 31 December 2010. This is an observational study and will not alter routine patient care.

Study population and eligibility criteria

The study will include adults (≥ 16 years of age) with a newly identified incidental intracranial meningioma, as per radiology report, diagnosed between 1 January 2009 and 31 December 2010. Radiological diagnosis is expected to be based on the presence of an extra-axial lesion with broad-based attachment along the dura showing contrast enhancement. The accepted definition of an incidental finding is 'a previously undetected abnormality of potential clinical relevance that is unexpectedly discovered and unrelated to the purpose of the examination'.

Exclusion criteria are as follows:

- ▶ History of cranial radiation >5 years before diagnosis.
- ▶ History of neurofibromatosis type 2.
- ▶ Surgical resection which revealed a different histopathological diagnosis.
- ▶ Unavailability of medical notes.

Patient identification

Eligible patients can be identified using local radiology information systems, for example the Computerised

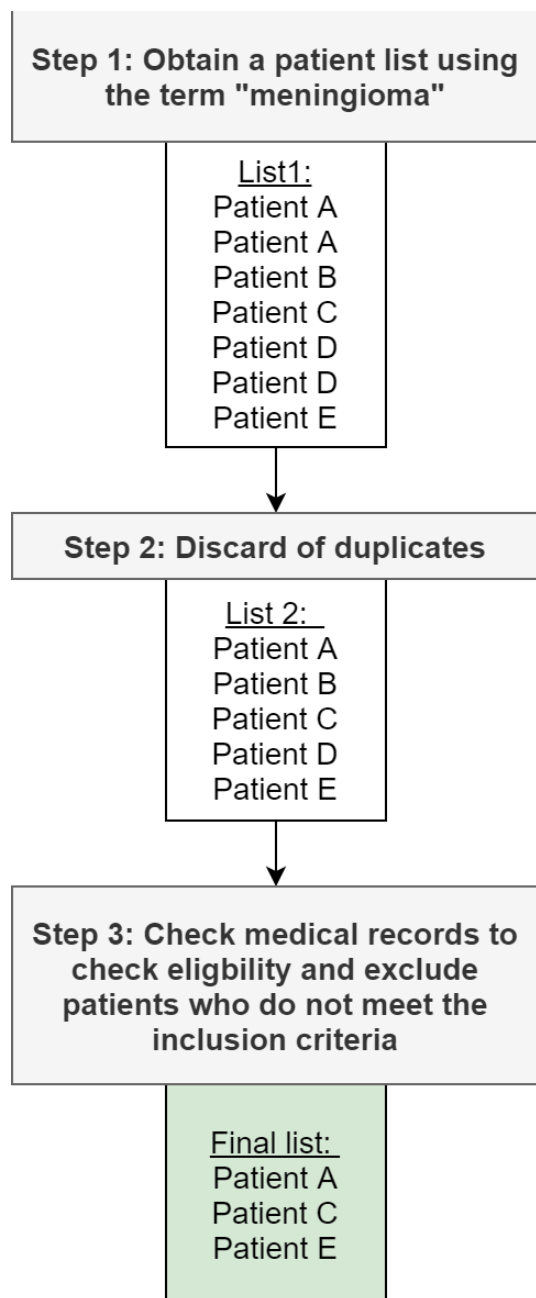


Figure 1 Process of creating a patient list at each study site.

Radiological Information System tool. The search strategy will involve review of the medical records of all patients managed with a meningioma at participating centres and exclusion of those that do not meet the selection criteria (figure 1).

Sample size

For external validation studies, a minimum of 100 events is required.¹² The risk of incidental meningioma progression is estimated to be 10%.¹¹ Based on this, data for 1000 patients will be required. To account for variability in the progression risk, follow-up regimens and loss to follow-up, we will aim to include a minimum of 1500 patients across participating centres. An interim analysis

will be conducted after data for 500 patients have been collected to assess for the risk of incidental meningioma progression and review the required number of patients.

Study endpoints

Primary endpoint

Disease progression will be defined using a composite endpoint comprising of new symptom development, meningioma-specific mortality, meningioma growth (absolute growth rate (AGR) $\geq 2 \text{ cm}^3/\text{year}$ or AGR $\geq 1 \text{ cm}^3/\text{year}$ + relative growth rate (RGR) $\geq 30\% / \text{year}$), development or increase of peritumoural brain oedema (defined as increased signal intensity on T2/fluid attenuated inversion recovery (FLAIR) MRI), venous sinus invasion and meningioma volume exceeding 10 cm^3 . The first two criteria denote clinical progression while the latter three are related to loss of window of curability. Venous sinus invasion and peritumoural oedema can prevent complete surgical resection.^{13 14} Peritumoural oedema and a meningioma volume $>10 \text{ cm}^3$ are relative contraindications to SRS.^{15 16}

Secondary endpoints

Intervention (surgery, SRS or γ RT) and mortality unrelated to the meningioma.

Data collection

Data will be collected at each centre by members of the local team. Data will be collected from the patient's medical and radiology records. All clinical and radiological information collected for this study by the local investigators should be available routinely and no extra patient assessment will be required. Data will be collected and stored online through a secure University of Liverpool server running the Research Electronic Data Capture (REDCap) web application and using the patient unique study number. Local investigators will be given secure REDCap project server login details. No patient identifiable information will be uploaded or stored on the REDCap database. The study number (site ID_patient ID) is generated by REDCap on creating a new patient record in the database. The clinical team can only view the records of patients from their own centre. All local investigators will store a copy of the link between the patient's unique study number and their patient identifiers on a secure password protected computer, using a blank link file provided by the study team.

REDCap database

REDCap is a secure web application for building and managing online databases. Access to REDCap will be provided by the Liverpool Clinical Trials Centre, University of Liverpool, a partner of the REDCap consortium. Database programmers will oversee the development of a data collection tool (online supplemental appendix 1) which can be accessed using any electronic device with internet access. The database will be built to comply with the UK's Data Protection Act 2018 and the European Union's General Data Protection Regulation (GDPR).

**Table 1** WHO performance status classification and the age-adjusted Charlson Comorbidity Index

WHO performance status classification		Age-adjusted Charlson Comorbidity Index		
Score	Description	Condition		Weight
0	Able to carry out all normal activity without restriction	Age (years)	<50	0
1	Restricted in strenuous activity but ambulatory and able to carry out light work		50–59	1
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours		60–69	2
3	Symptomatic and in a chair or in bed for greater than 50% of the day but not bedridden		70–79	3
4	Completely disabled; cannot carry out any self-care; totally confined to bed or chair.		≥80	4
5	Dead	Myocardial infarction		1
		Congestive heart failure		1
		Peripheral vascular disease		1
		Hemiplegia		2
		Cerebrovascular disease		1
		Pulmonary disease		1
		Diabetes		1
			With end-organ damage	2
		Renal disease		2
		Liver disease	Mild	1
			Severe	3
		Peptic ulcer disease		1
		Cancer		2
			Metastatic	6
		Dementia		1
		Connective tissue disease		1
		AIDS		6
		Hypertension		1
		Skin ulcers/cellulitis		2
		Depression		1
		On Warfarin		1

Quality assessment of the tool will be done over two phases. Phase 1 will involve local testing of the tool using pre-existing data.¹¹ Phase 2 will expand testing to three to five additional participating centres. After completion of phase 2, the data collection tool will be made live for use by the participating sites.

Recorded variables

Baseline clinical variables

Age at diagnosis, sex, ethnicity, World Health Organisation (WHO) performance status (PS) and the age adjusted Charlson Comorbidity Index (ACCI) (table 1).^{17–19} These factors will only be recorded at baseline.

Baseline radiological variables

Baseline imaging variables assessed will be:

- ▶ Single or multiple intracranial meningioma.

- ▶ Tumour signal intensity compared with the contralateral grey matter on FLAIR and T2-weighted (T2) MRI (hypo/iso/hyper) (figure 2).
- ▶ Peritumoural signal intensity in relation to tumour volume using the signal change present on FLAIR and T2 MRI (0%–5%/6%–33%/34%–66%/67%–100%; adapted from the Visually AcceSable Rembrandt Images MR features for gliomas²⁰).
- ▶ Meningioma volume using the ABC/2 formula on contrast-enhanced T1-weighted MRI/CT: (A) maximum meningioma diameter on axial plane, (B) diameter perpendicular to (A) and (C) maximum height on coronal/sagittal plane, not taking into the account the dural tail.
- ▶ Meningioma location classed into non-skull base and skull base and further subcategorised according to the International Consortium on Meningioma classification system (online supplemental appendix 2).

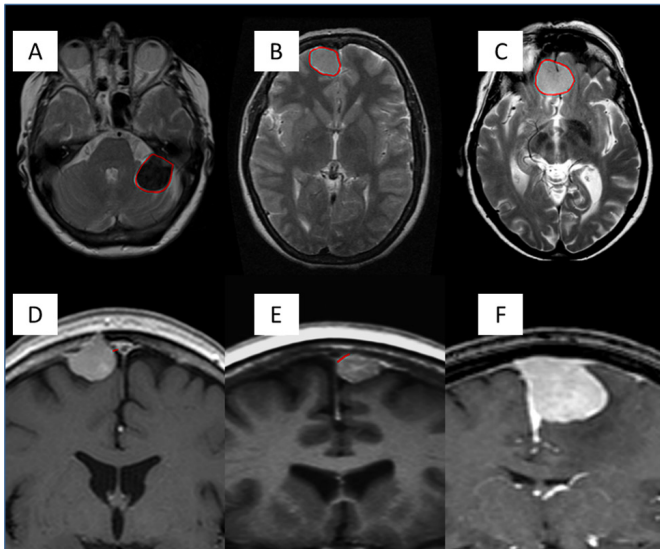


Figure 2 (A–C) T2 MR axial sequences showing the three levels of tumour intensity (circle). (A) Hypointense. (B) Isointense. (C) Hyperintense. (D–F) T1-weighted MR with gadolinium (contrast) showing the relationship between the meningioma and the nearby venous sinus (SSS). (D) Separate as there is no clear attachment to the sinus wall. (E) In direct contact with the lateral wall of the sinus. (F) Clear macroscopic distortion and invasion of the sinus. SSS, superior sagittal sinus.

- ▶ Proximity to major dural venous sinuses (superior sagittal sinus/transverse sinus/sigmoid sinus/cavernous sinus/the confluence of sinuses) categorised as separate (within 10 mm), in direct contact with its wall, or invading, excluding the dural tail (figure 2).
- ▶ Contact with critical neurovascular structures (ie, internal carotid artery and optic apparatus).

Meningiomas that fulfil one of the two previous categories are said to be in proximity to critical neurovascular structures. A video manual prepared by the study team will be made available to assist with standardisation and quality assurance of scan interpretation across participating centres.

Management strategy

Management strategies will include active monitoring, intervention (surgery, SRS and γ RT) or discharge from outpatient clinic care (figure 3). Active monitoring is defined as regular surveillance imaging and outpatient clinical observation. Recorded factors will include:

- ▶ Number of scans, and interval between them (months).
- ▶ For each scan: peritumoural signal intensity, venous sinus involvement and meningioma volume.
- ▶ Each scan will be examined alongside its corresponding outpatient clinic appointment for any evidence of meningioma-related symptoms (motor/sensory/language/cognitive/seizure/headache/other).
- ▶ The outcome of each clinical encounter (ie, outpatient appointment) will be recorded (resume follow-up/surgery/SRS/ γ RT/hospital discharge).

Intervention details; if performed, will also be recorded. These will include indication for intervention (clinical-radiological/clinical/radiological/patient preference) and time to intervention. For patients treated with clinical-radiological or clinical progression, status of meningioma-related neurological morbidity will be noted.

For surgery, the following will additionally be recorded:

- ▶ Simpson grade (as recorded by the surgeon in the operative notes).²¹

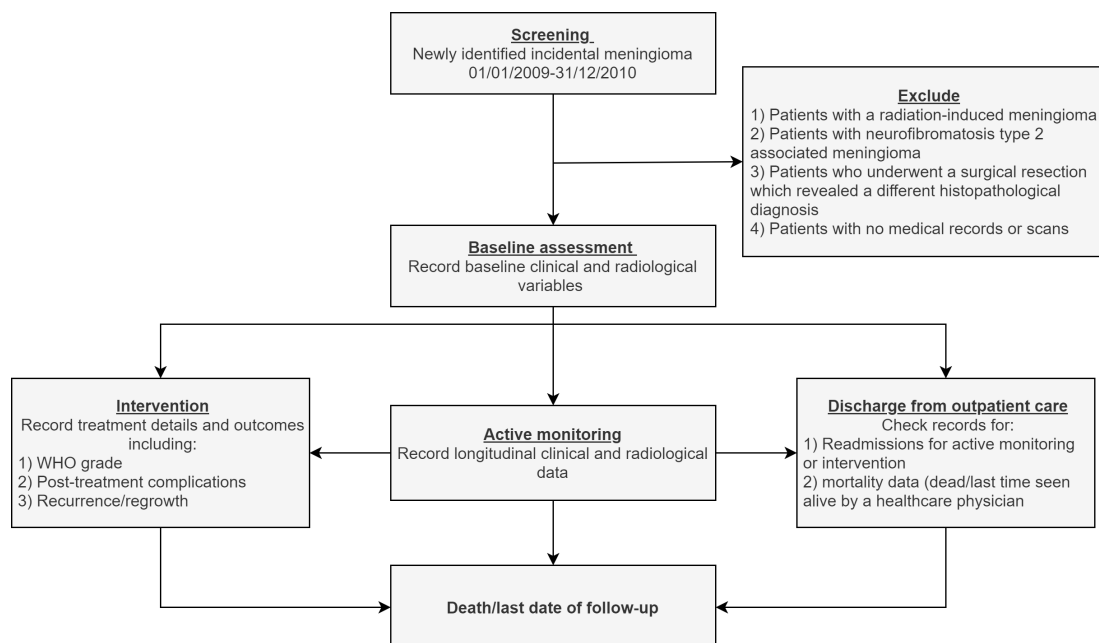


Figure 3 Study flow chart depicting the process of patient identification and possible management options within the study.

**Table 2** Landriel-Ibañez classification of neurosurgical complications

Grade 1	Any non-life-threatening deviation from normal postoperative course, not requiring invasive treatment
Grade 1a	Complication requiring no drug treatment
Grade 1b	Complication requiring drug treatment
Grade 2	Complication requiring invasive treatment such as surgical, endoscopic, or endovascular interventions
Grade 2a	Complication requiring intervention without general anaesthesia
Grade 2b	Complication requiring intervention with general anaesthesia
Grade 3	Life-threatening complications requiring management in an intensive care unit
Grade 3a	Complication involving single organ failure
Grade 3b	Complication involving multiple organ failure
Grade 4	Complication resulting in death
Surgical Complications	Adverse events that are directly related to surgery or surgical technique
Medical Complications	Adverse events that are not directly related to surgery or surgical technique
Suffix 'T' (Transient)	New neurologic deficit improving within 30 days of surgical procedure; can be added to each grade of complication
Suffix 'P' (Persistent)	New neurologic deficit extending beyond 30 days of surgical procedure; can be added to each grade of complication

- ▶ WHO grade (classified according to the WHO system in use at the time of surgery and updated according to the WHO 2016 classification dependent on pathologists' availability²²) and presence of any reported brain invasion (yes/no/not reported).
- ▶ Postoperative medical and surgical complications recorded at 30 days (Landriel-Ibañez classification (table 2).²³
- ▶ Follow-up duration (months).
- ▶ WHO PS preoperatively and postoperatively and at the last follow-up appointment.
- ▶ Recurrence on contrast-enhanced MRI during that time (yes/no) and if recurred then the time to recurrence.

For SRS and γ RT:

- ▶ Fractionated dose (γ RT), number of fractions (γ RT) and total dose (γ RT /SRS).
- ▶ Early and late (≥ 3 months) toxicity (assessed by CTCAE V.5.0, https://ctep.cancer.gov/protocoldevelopment/electronic_applications/ctc.htm).
- ▶ Duration of follow-up postradiation (months).
- ▶ WHO PS preradiation and post-radiation and at the last follow-up appointment.
- ▶ Progression/regrowth on contrast-enhanced MRI during that time (yes/no) and if progressed/regrew then the time to progression/regrowth.

For patients discharged from outpatient care, data sources will be checked for any readmissions/rescans thought to be attributed to the incidental meningioma within the study time frame; date of diagnosis up to the date of data entry. Outcome following readmissions/rescans will be noted.

Overall outcomes

Overall outcomes by the end of the study period (discharge from outpatient care/lost to follow-up/dead/under on-going active follow-up) and follow-up durations will be recorded. Any deaths encountered during follow-up will

be recorded. The medical records for patients who are discharged will also be examined for mortality data.

Data quality assurance

An e-learning module will be prepared by the study team. This will contain the data collection guides and video manual. On completion, each study investigator will need to undergo a five-item assessment. An iterative process in which investigators have to redo the assessment or module will dictate their progress as follows:

- ▶ An assessment percentage of 100% will indicate successful completion of the module, which will allow the investigator to collect data for the study.
- ▶ An assessment percentage less 100% will require repeating the assessment.
- ▶ Five attempts will be allowed.
- ▶ Subsequent failed attempts will entail review of the module components again.

Planned statistical analysis

Demographic differences across groups will be explored with the χ^2 test for categorical variable and the Mann-Whitney U test or Student's t-test for continuous variables. Correlation between baseline variables will be evaluated using the Pearson correlation coefficient. Normally distributed continuous variables will be expressed as mean (SD) whereas skewed variables as median (IQR). Differences will be considered statistically significant at $p < 0.05$.

External validation

Using IMPACT, the 5-year and 10-year estimated risk of disease progression for every patient included in this cohort study will be calculated. Kaplan-Meier method will be used to obtain the observed risks. The predictive performance of IMPACT will be assessed by examining measures of calibration and discrimination. Calibration refers to how closely the predicted 5-year and 10-year risk of progression agrees with the observed risk. A calibration

plot compares the observed and predicted rates of events for each group. A perfect match indicates accurate calibration. The Brier score for censored survival data will also be calculated, which is a measure of accuracy and is the average squared deviation between predicted and observed risk; a lower score represents greater accuracy. Discrimination is the ability of the risk score to differentiate between those patients who do and those who do not experience disease progression during the study time frame. This measure is quantified by calculating the C-statistic, D-statistic and Chambless and Diao's time-dependent area under the receiver operating characteristic curve which are tailored towards censored survival data. The proportional hazards assumption of the model will be tested by examination of Schoenfeld residuals, and influential observations will be examined using DFBETA panels.

The two competing risk analyses performed to build the IMPACT model will be repeated with the external dataset and plots of cumulative incidence rate (CIR) and 95% CIs will be compared with the original cohort.¹¹ Patients will be split based on WHO PS into two categories: 0–1 and 2–4 and stratified by ACCI (table 1) into three groups: 0–2, 3–5 and ≥ 6 . The first analysis will assess the CIR of primary intervention at different time points following diagnosis stratified by PS and ACCI groups and the second analysis will evaluate the CIR of disease progression. The competing event for the former will be non-meningioma-specific mortality either observed during follow-up or after being discharged from outpatient care. Patients who remain under follow-up will be censored at the last outpatient clinic appointment. Patients discharged alive from outpatient care will be censored at the last time they were seen by a healthcare physician up to the date of data entry. For the disease progression analysis, four events will be considered competing in nature, discharge from outpatient care, loss to follow-up, death during follow-up or an intervention before disease progression occurred with the first three grouped together. Censoring will only be done for patients who remain under follow-up at the last clinic appointment. To test the equality across CIR groups, the Fine and Gray test will be carried out.

Model recalibration

If calibration and discrimination measures of external validation demonstrate a poor fit, the model will be recalibrated and adjusted using the data of included patients. This will be done over four stages:

- ▶ Stage 1: The regression coefficients will be recalibrated. This will be done using a Cox regression model fitted with the linear predictor as the only covariate.
- ▶ Stage 2: The recalibrated model predictors will each be removed in a stepwise manner by a non-automated criterion-based procedure starting with the variable with a HR closest to 1. After removal of this variable, the aforementioned measures of discrimination of calibration and discrimination will be reassessed to detect model improvement. If the performance of the

model is unimproved or worsens, the variable will be reintroduced to the model. This step will be repeated in a staged manner until no further improvements are detected. Introduction of new predictive variables will be possible.

- ▶ Stage 3: The internal validity of the updated model will be assessed using a bootstrapping method.
- ▶ Stage 4: Adjusted stratification by ACCI and PS (table 1) will be performed to achieve statistically significant differences in equality across CIR groups, judged by the Fine and Gray test.

Additional analyses

We envisage that imaging protocols in the participating centres are varied and non-standardised and thus, the growth rate for each meningioma will be determined using a joint longitudinal and event-time outcomes model which does not require regularly spaced time points, and adjusts for informative follow-up, assuming a different intercept and slope for each meningioma.^{24 25} The sum of the regression coefficients of random and fixed effects for the slope estimated from the linear model will best represent the average growth rate for each meningioma. AGR will be defined as the increase in volume per year in cm^3 whereas RGR will be defined as the percentage increase in volume per year.

This statistical analysis plan will be reviewed prior to the final analysis of the study.

Health economic analysis

The health economic analysis will adopt the perspective of the National Health Service in the UK. Costs related to clinic appointments and MRI scans will be calculated for the study cohort's retrospectively performed follow-up plans and compared against two follow-up regimens:

- ▶ The follow-up regimen proposed by the National Institute for Healthcare Excellence of 2 scans at 12 months and 5 years.
- ▶ The follow-up regimen using the IMPACT model, stratified by risk of progression.

Patient and public involvement

Two patient research partners (PRPs) have been involved in the design of the study and are members of the steering committee. With the support of the Brain Tumour Charity, represented by a member of the steering committee, the aim is to engage with more PRPs and to build a partnership to be continued throughout delivery of the study and dissemination and presentation of results.

ETHICS AND DISSEMINATION

Study registration

It will be the responsibility of the research team at each unit to register the study as a clinical audit with their hospital's audit department in the UK, including Caldicott guardian or Information Governance approval as

required. Overseas sites will register with according to their local institutional policy.

Local investigator responsibilities

The investigator will be responsible for the overall conduct of the study at the site and compliance with the protocol. Responsibilities may be delegated to an appropriate member of the local research team. The investigator must also be familiar with the protocol and the study requirements and it is their responsibility to ensure that all staff assisting with the study are adequately informed about the protocol and the study requirement. The principal investigator at each centre is responsible for the quality of the data recorded in the database.

Confidentiality and data protection

No patient identifiable information will be uploaded or stored on the REDCap database. The clinical team can only view the records of patients from their own centre. All records must be identified in a manner designed to maintain patient confidentiality and must be kept in a secure storage area with limited access; all local investigators will store a copy of the link between the patient's unique study number and their patient identifiers on a secure password-protected computer, using a blank link file provided by the study team. The investigator and local research terms involved with this study may not disclose or use for any purpose other than performance of the study, any data, record, or other unpublished, confidential information. They also must comply with the requirements of the Data Protection Act 2018 and GDPR with regard to the collection, storage, processing and disclosure of personal information. Access to collated patient data will be restricted to individuals from the research team and representatives of the sponsor. Computers used to collate the data will have limited access measures via usernames and passwords. Published results will not contain any personal data that could allow identification of individual patients.

Ownership

Ownership of the complete dataset arising from this study resides with the steering committee (named authors in this protocol). Local data collected as part of this study belongs to the local team collecting that data. However, individual clinicians must not submit any part of their individual data for publication or presentation without prior consent from the study research team. Individual participant data, after deidentification, will be made available to researchers whose proposed use of the data is approved by the original study investigators. Proposals should be directed to the primary investigator.

Dissemination of results

The study results will be reported using the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis checklist. The results of this study will be presented at national and international

meetings and will be submitted for publication in peer-reviewed journals.

Authorship eligibility

The list of named authors will resemble this protocol's authorship. The contribution of all investigators captured via the REDCap database, will be recognised with PubMed Citable collaborator status authorship under the umbrella of the IMPACT study investigators.

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1 APPENDICES

1.1. Appendix. 1. Guide for REDCap database developers

Characteristic	Options	Notes
BASELINE CLINICAL CHARACTERISTICS (PAGE/SECTION 1)		
Age (years)	Free field	Required entry
Sex	Dropdown list/check box <ul style="list-style-type: none"> • Male • Female 	
Ethnicity	Dropdown list/check box <ul style="list-style-type: none"> • White • Mixed / Multiple ethnic groups • Asian / Asian British • Black / African / Caribbean / Black British • Other ethnic group • NA 	Required entry. Allow one option only. Other ethnic group prompts a free text box
Comorbidities	Check box <ul style="list-style-type: none"> • Hypertension - systolic > 140 or diastolic > 90 and patients on medical treatment • Previous myocardial infarction • Congestive heart failure • Peripheral vascular disease 	Required entry. Allow multiple options. Note to data collector: Age and comorbidities will be used to calculate the age adjusted Charlson comorbidity index. Each of these is defined in the guide provided

	<ul style="list-style-type: none"> • Previous stroke/TIA - If hemiplegia present, do not check • Hemi/paraplegia • Diabetes which requires medical treatment • Diabetes with end-organ damage - if so, do not check diabetes that requires treatment • COPD/Asthma • Renal disease • Mild liver disease - Hep B/C or cirrhosis without portal hypertension • Moderate to severe liver disease - cirrhosis with portal hypertension, jaundice, ascites • Peptic ulcer disease • Cancer - excluding basal cell carcinoma • Metastatic cancer - if so, do not check cancer • Rheumatic or connective tissue disease • HIV/AIDS • Skin ulcers/cellulitis • Depression • Dementia • On Warfarin 	
WHO Performance status	Dropdown list/check box <ul style="list-style-type: none"> • 0 • 1 • 2 	Required entry. Allow one option only

	<ul style="list-style-type: none"> • 3 • 4 	
Indication for scan	Dropdown list/check box <ul style="list-style-type: none"> • Headache • Cerebrovascular accident • Head injury • Audiovestibular symptoms • Visual symptoms • Psychiatric symptoms • Cognitive symptoms • Loss of consciousness • Other 	Required entry. Allow multiple options. Note to data collector: The meningioma must not be thought to be the cause of these symptoms. Other indications might include lethargy, research, sinusitis, anosmia...etc. Other prompts a free text box
NUMBER OF MENINGIOMAS ON 1ST DIAGNOSTIC SCAN (PAGE/SECTION 2)		
Initial scan date	DD/MM/YYYY	Required entry. YYYY can't be ≤ 2007 or ≥ 2011
How many meningiomas?	Check box <ul style="list-style-type: none"> • Single • Multiple 	Required entry If a single meningioma, direct to section/page 3. If multiple, prompt a new entry point (e.g. check box with options being 2-6) with number of meningiomas present. Each meningioma will then be treated as a separate entity with regards to the upcoming sections.
BASELINE IMAGING CHARACTERISTICS (SECTION/PAGE 3)		
Meningioma signal intensity on T2	Dropdown list/check box <ul style="list-style-type: none"> • Hypointense • Hyperintense • Isointense • NA 	Required entry. Allow one option only Note to data collector: In relation to the contralateral grey matter. If only baseline CT available, NA

Meningioma signal intensity on FLAIR	Dropdown list/check box <ul style="list-style-type: none"> • Hypointense • Hyperintense • Isointense • NA 	Required entry. Allow one option only Note to data collector: In relation to the contralateral grey matter. If only baseline CT available, NA
Peritumoural signal intensity on T2	Dropdown list/check box <ul style="list-style-type: none"> • 0-5% • 6-33% • 34-66% • 67-100% • NA 	Required entry. Allow one option only Note to data collector: In relation to tumour volume. If only baseline CT available, NA
Peritumoural signal intensity on FLAIR	Dropdown list: <ul style="list-style-type: none"> • 0-5% • 6-33% • 34-66% • 67-100% • NA 	Required entry. Allow one option only Note to data collector: In relation to tumour volume. If only baseline CT available, NA
Venous sinus nearby	Checkbox	Required entry. Note to data collector: Tick box if within 10 mm, in direct contact or invading one of: superior sagittal sinus (SSS), sigmoid sinus (SS), transverse sinus (TS), cavernous sinus (CS) and the confluence of sinuses (CoS)
If yes, specify	Dropdown list/check box <ul style="list-style-type: none"> • Superior sagittal sinus • Cavernous sinus • Sigmoid sinus • Transverse sinus • Confluence of sinuses 	Prompt entry if previous option (venous sinus nearby) has been ticked. Allow one option only.
Separate, direct contact or invaded?	Dropdown list/check box <ul style="list-style-type: none"> • Separate 	Prompt entry if previous option (venous sinus nearby) has been ticked. Allow one option only

	<ul style="list-style-type: none"> • Direct contact • Invaded 	
In contact with critical neuro-vascular structures?	Checkbox	Required entry
If yes, which	Dropdown list/check box <ul style="list-style-type: none"> • Internal carotid artery • Basilar artery • Vertebral artery • Middle cerebral artery • Anterior cerebral artery • Posterior cerebral artery • Optic apparatus (optic nerve and chiasm) • Trigeminal nerve • Facial nerve • Vestibulo-cochlear nerve • Other 	Prompt entry if previous option (In contact with critical neuro-vascular structures?) has been ticked
Major axis (mm)	Free field	Required entry Note to data collector: In mm to 1 dp. Measure on axial T1/CT + GAD
Minor axis (mm)	Free field	Required entry Note to data collector: In mm to 1 dp. Perpendicular to the major axis on axial T1/CT + GAD
Cor/sag major axis	Free field	Require entry Note to data collector: In mm to 1 dp. Maximum height
Location	Dropdown list/Check box <ul style="list-style-type: none"> • Convexity • Parasagittal • Parafalcine 	Required entry. Allow one option only Note to data collector: as per ICOM classification (appendix 2)

	<ul style="list-style-type: none"> • Sphenoid wing • Anterior midline • Post fossa-midline • Post fossa-lateral & posterior • Tentorial • Intraventricular • Pineal region 	
Location subcategory	<p>Dropdown list/Check box</p> <ul style="list-style-type: none"> • Anterior • Posterior • Falco-tentorial • Lateral • Medial (including ACP) • Cribriform plate/olfactory groove • Planum • Tuberculum/diaphragma sellae • Clival • Petro-clival • Anterior foramen magnum • Petrous • Squamous occipital • Posterior foramen magnum • Supratentorial • Infratentorial 	<p>Required entry. Allow one option only</p> <p>Note to data collector: ICOM classification (appendix 2)</p> <p>Appropriate subcategories will appear based on main category selected</p>
Side	<p>Dropdown list/check box</p> <ul style="list-style-type: none"> • Right • Left • Midline 	<p>Required entry. Allow one option only</p>
MANAGEMENT DECISION (PAGE/SECTION 4)		

Decision	Dropdown list/Check box <ul style="list-style-type: none"> • Active monitoring • Surgery • SRS • fRT • Discharge from outpatient care • <u>Lost to follow-up</u> • <u>Dead</u> 	Required entry. Allow one option only Note to data collector: You will be directed to the relevant page/section dependent on the choice. If the patient died or was lost to follow-up after this point in time, please choose one of the last two options, albeit the intention might have been to continue monitoring or intervene.
ACTIVE MONITORING (SECTION/PAGE 5)		
Scan date	DD/MM/YYYY	Required entry
Peritumoural signal intensity on T2	Dropdown list/check box <ul style="list-style-type: none"> • 0-5% • 6-33% • 34-66% • 67-100% • NA 	Required entry. Allow one option only Note to data collector: In relation to tumour volume on T2/FLAIR MRI. If only CT or T1 MRI available, NA
Peritumoural signal intensity on FLAIR	Dropdown list/check box <ul style="list-style-type: none"> • 0-5% • 6-33% • 34-66% • 67-100% • NA 	Required entry. Allow one option only Note to data collector: In relation to tumour volume on FLAIR MRI. If only CT or T1 MRI available, NA
Venous sinus nearby	Checkbox	Required entry. Note to data collector: Tick box if within 10 mm, in direct contact or invading one of: superior sagittal sinus (SSS), sigmoid sinus (SS), transverse sinus (TS), cavernous sinus (CS) and the confluence of sinuses (CoS)
If yes, specify	Dropdown list/check box	Prompt entry if previous option (venous sinus nearby) has been ticked. Allow one option only

	<ul style="list-style-type: none"> • Superior sagittal sinus • Cavernous sinus • Sigmoid sinus • Transverse sinus • Confluence of sinuses 	
Separate, direct contact or invaded?	Dropdown list/check box <ul style="list-style-type: none"> • Separate • Direct contact • Invaded 	Prompt entry if previous option (venous sinus nearby) has been ticked. Allow one option only
Any new meningioma-related symptoms?	Checkbox	Required entry
If yes, specify domain	Dropdown list/check box <ul style="list-style-type: none"> • Seizure • Headache • Motor • Sensory • Language • Cognitive • Other 	Prompt entry if previous option (Any new meningioma-related symptoms?) has been ticked. Allow multiple options
Major axis (mm)	Free field	Required entry Note to data collector: In mm to 1 dp. Measure on axial T1/CT + GAD if available
Minor axis (mm)	Free field	Required entry Note to data collector: In mm to 1 dp. Perpendicular to the major axis on axial T1/CT + GAD if available
Cor/sag major axis (mm)	Free field	Required entry Note to data collector: In mm to 1 dp. Maximum height

Outcome	Dropdown list/check box <ul style="list-style-type: none"> • Resume follow-up (active monitoring) • Surgery • SRS • fRT • Discharge • <u>Lost to follow-up</u> • <u>Dead</u> 	Required entry. Allow one option only Note to data collector: You will be directed to the relevant page/section dependent on the choice. If the patient died or was lost to follow-up after this interval scan, please choose one of the last two options, albeit the intention might have been to continue monitoring or intervene. If the option you choose is set to take place in the future, choose the option, save the data entered and exit the form with no further information required.
SURGERY (SECTION/PAGE 6)		
Surgery date	DD/MM/YYYY	Required entry
Indication for intervention	Dropdown list/checkbox <ul style="list-style-type: none"> • Clinical-radiological • Clinical • Radiological • Patient preference 	Required entry. Allow one option only
Preoperative WHO PS	Dropdown list/checkbox <ul style="list-style-type: none"> • 0 • 1 • 2 • 3 • 4 	Required entry. Allow one option only
Preoperative comorbidities	Check box <ul style="list-style-type: none"> • Hypertension - systolic > 140 or diastolic > 90 and patients on medical treatment • Previous myocardial infarction • Congestive heart failure 	Required entry. Allow multiple options. Note to data collector: Age and comorbidities will be used to calculate the age adjusted Charlson comorbidity index. Each of these is defined in the guide provided

	<ul style="list-style-type: none"> • Peripheral vascular disease • Previous stroke/TIA - If hemiplegia present, do not check • Hemi/paraplegia • Diabetes which requires medical treatment • Diabetes with end-organ damage - if so, do not check diabetes that requires treatment • COPD/Asthma • Renal disease • Mild liver disease - Hep B/C or cirrhosis without portal hypertension • Moderate to severe liver disease - cirrhosis with portal hypertension, jaundice, ascites • Peptic ulcer disease • Cancer - excluding basal cell carcinoma • Metastatic cancer - if so, do not check cancer • Rheumatic or connective tissue disease • HIV/AIDS • Skin ulcers/cellulitis • Depression • Dementia • On Warfarin 	
Simpson grade	Dropdown list/check box <ul style="list-style-type: none"> • 1-GTR • 2-GTR 	Required entry. Allow one option only

	<ul style="list-style-type: none"> • 3-GTR • 4-STR • 5-STR 	
WHO grade at the time of surgery	Dropdown list/check box <ul style="list-style-type: none"> • 1 • 2 • 3 	Required entry. Allow one option only Note to data collector: According to the WHO classification at the time of surgery
Microscopic brain invasion	Dropdown list/checkbox <ul style="list-style-type: none"> • Yes • No • Brain tissue absent • NA 	Required entry. Allow one option only Note to data collector: as described in the pathology report.
Updated WHO grade (2016)	Dropdown list/check box <ul style="list-style-type: none"> • 1 • 2 • 3 • NA 	Required entry. Allow one option only. Only to appear if date of surgery <2017 Note to data collector: For meningiomas operated prior to 2016, grading will have been done according to the 2007 classification. The 2016 version can upgrade WHO grade 1 meningiomas to grade 2 if microscopic brain invasion is present. This means that WHO grade 2 and 3 meningiomas remain unchanged. Grade 1 meningiomas on the other hand can be upgraded in the presence of brain invasion. This requires review by a pathologist and so if not feasible, choose NA. For meningiomas classed according to the 2016 WHO classification, grade remains unchanged.
Postoperative complications surgical	Checkbox	Required
Complication	Dropdown list/check box <ul style="list-style-type: none"> • Haemorrhage • Hydrocephalus • Surgical site infection - superficial and deep incisiona • Surgical site infection - intracranial (meningitis, ventriculitis and abscess) 	Prompt entry if previous option (Postoperative surgical complications) has been ticked Allow more the one option

	<ul style="list-style-type: none"> • Stroke • CSF leak • Other 	
New or worsening neurological impairment	Checkbox	<p>Prompt entry if previous option (Postoperative surgical complications) has been ticked</p> <p>Note to data collector: If symptoms present tick box. Note that some patients will have a radiological haemorrhage on postoperative imaging with no symptoms. Include these but don't tick clinical manifestation. On the other hand, some patients will have new symptoms such as seizure with no radiological cause, include these as well.</p>
Clinical manifestation	Dropdown list/checkbox <ul style="list-style-type: none"> • Seizure • Headache • Motor • Sensory • Language • Cognitive • Reduced GCS • Other 	<p>Prompt entry if previous option (New or worsening neurological impairment) has been ticked. Allow multiple options</p>
Pharmacological intervention	Checkbox	Prompt entry if previous option (Postoperative surgical complications) has been ticked
Surgical intervention	Dropdown list/checkbox <ul style="list-style-type: none"> • No • Without GA • Under GA 	Prompt entry if previous option (Postoperative surgical complications) has been ticked
ICU admission	Checkbox	Prompt entry if previous option (Postoperative surgical complications) has been ticked
Organ failure	Dropdown list/checkbox <ul style="list-style-type: none"> • None • Single-organ • Multi-organ 	Prompt entry if previous option (Postoperative surgical complications) has been ticked. Allow one option only

Persisted with no improvement beyond 30 days?	Checkbox	Prompt entry if previous option (Postoperative surgical complications) has been ticked
Postoperative medical complications	checkbox	Required
Complication	Dropdown list/check box <ul style="list-style-type: none"> • Myocardial infarction • Arrhythmia • Pneumonia • Pulmonary embolism • Deep venous thrombosis • Urinary tract infection • Acute kidney injury • Other 	Prompt entry if previous option (Postoperative medical complications) has been ticked Allow more than one option
Pharmacological intervention	Checkbox	Prompt entry if previous option (Postoperative medical complications) has been ticked
Surgical intervention	Dropdown list/checkbox <ul style="list-style-type: none"> • No • Without GA • Under GA 	Prompt entry if previous option (Postoperative medical complications) has been ticked
ICU admission	Checkbox	Prompt entry if previous option (Postoperative medical complications) has been ticked
Organ failure	Dropdown list/checkbox <ul style="list-style-type: none"> • None • Single-organ • Multi-organ 	Prompt entry if previous option (Postoperative medical complications) has been ticked. Allow one option only
Persisted with no improvement beyond 30 days?	Checkbox	Prompt entry if previous option (Postoperative medical complications) has been ticked
Postoperative WHO PS	Dropdown list/checkbox <ul style="list-style-type: none"> • 0 	Required. Allow one option only

	<ul style="list-style-type: none"> • 1 • 2 • 3 • 4 • 5 (dead) 	
Recurrence	Checkbox	Prompt entry if previous option (Postoperative WHO PS) is not 5
Scan date (at recurrence or last follow-up date if no recurrence)	DD/MM/YYYY	Prompt entry if previous option (Postoperative WHO PS) is not 5
WHO PS at time of recurrence/last follow-up	Dropdown list/checkbox <ul style="list-style-type: none"> • 0 • 1 • 2 • 3 • 4 	Prompt entry if previous option (Postoperative WHO PS) is not 5
SRS (SECTION/PAGE 7)		
Pre-radiation WHO PS	Dropdown list/check box <ul style="list-style-type: none"> • 0 • 1 • 2 • 3 • 4 	Required entry. Allow one option only
Pre-radiation comorbidity	Check box <ul style="list-style-type: none"> • Hypertension - systolic > 140 or diastolic > 90 and patients on medical treatment • Previous myocardial infarction • Congestive heart failure • Peripheral vascular disease 	Required entry. Allow multiple options. Note to data collector: Age and comorbidities will be used to calculate the age adjusted Charlson comorbidity index. Each of these is defined in the guide provided

	<ul style="list-style-type: none"> • Previous stroke/TIA - If hemiplegia present, do not check • Hemi/paraplegia • Diabetes which requires medical treatment • Diabetes with end-organ damage - if so, do not check diabetes that requires treatment • COPD/Asthma • Renal disease • Mild liver disease - Hep B/C or cirrhosis without portal hypertension • Moderate to severe liver disease - cirrhosis with portal hypertension, jaundice, ascites • Peptic ulcer disease • Cancer - excluding basal cell carcinoma • Metastatic cancer - if so, do not check cancer • Rheumatic or connective tissue disease • HIV/AIDS • Skin ulcers/cellulitis • Depression • Dementia • On Warfarin 	
Dose	Free field	Required entry
Early CTCAE toxicity (≤3 months)	Checkbox	Required entry

Toxicity	Free field	Prompt entry if previous option (Early CTCAE toxicity (≤3 months)) is ticked Note to data collector: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/ctc.htm Use the following format: System class organ (SOC)-CTCAE term-grade e.g. nervous system disorders-headache-1. Select the complication with the highest toxicity grade
Late CTCAE toxicity	Checkbox	Required entry
Toxicity	Free field	Prompt entry if previous option (Late CTCAE toxicity) is ticked Note to data collector: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/ctc.htm Use the following format: System class organ (SOC)-CTCAE term-grade e.g. nervous system disorders-headache-1. Select the complication with the highest toxicity grade
Meningioma progression/regrowth	Checkbox	Required
Scan date (at progression or last follow-up date if no progression)	DD/MM/YYYY	Required
WHO PS at time of progression/last follow-up	Dropdown list/checkbox <ul style="list-style-type: none"> • 0 • 1 • 2 • 3 • 4 • 5 (dead) 	Required. Allow one option only
fRT (SECTION/PAGE 8)		

Pre-radiation WHO PS	Dropdown list/check box <ul style="list-style-type: none"> • 0 • 1 • 2 • 3 • 4 	Required entry
Pre-radiation comorbidity	Check box <ul style="list-style-type: none"> • Myocardial infarction • Congestive heart failure • Peripheral vascular disease • Hemiplegia • Cerebrovascular disease • Pulmonary disease • Diabetes • Renal disease • Liver disease • Peptic ulcer disease • Cancer • Dementia • Connective tissue disease • AIDS • Hypertension • Skin ulcers/cellulitis • Depression • On Warfarin 	Required entry. Allow multiple options. Note to data collector: Age and comorbidities will be used to calculate the age adjusted Charlson comorbidity index. Each of these is defined in the guide provided
Number of fractions	Free field	Required entry
Fractionated dose	Free field	Required entry
Total dose	Free field	Required entry
Early CTCAE toxicity (≤ 3 months)	Checkbox	Required entry

Toxicity	Free field	Prompt entry if previous option (Early CTCAE toxicity (≤3 months)) is ticked Note to data collector: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/ctc.htm Use the following format: System class organ (SOC)-CTCAE term-grade e.g. nervous system disorders-headache-1. Select the complication with the highest toxicity grade
Late CTCAE toxicity	Checkbox	Required entry
Toxicity	Free field	Prompt entry if previous option (Late CTCAE toxicity) is ticked Note to data collector: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/ctc.htm Use the following format: System class organ (SOC)-CTCAE term-grade e.g. nervous system disorders-headache-1. Select the complication with the highest toxicity grade
Meningioma progression/regrowth	Checkbox	Required
Scan date (at progression or last follow-up date if no progression)	DD/MM/YYYY	Required
WHO PS at time of progression/last follow-up	Dropdown list/checkbox <ul style="list-style-type: none"> • 0 • 1 • 2 • 3 • 4 • 5 (dead) 	Required. Allow one option only
Discharge from outpatient care/Lost to follow-up (SECTION/PAGE 9)		

Date of data entry into the database	DD/MM/YYYY	Required entry
Rescanned during the time between discharge/loss to FU and the date of data entry	Checkbox	Required entry
Date of scan	DD/MM/YYYY	Prompt entry if previous option (Readmitted/rescanned during the time between discharge/loss to FU and the date of data entry) has been checked
Reason?	Dropdown list: <ul style="list-style-type: none"> • Seizure • Headache • Motor • Sensory • Language • Cognitive • Other 	Prompt entry if previous option (Readmitted/rescanned during the time between discharge/loss to FU and the date of data entry) has been checked. Allow multiple options
Peritumoural signal intensity on T2	Dropdown list/check box <ul style="list-style-type: none"> • 0-5% • 6-33% • 34-66% • 67-100% • NA 	Prompt entry if previous option (Readmitted/rescanned during the time between discharge/loss to FU and the date of data entry) has been checked. Allow one option only Note to data collector: In relation to tumour volume. If only baseline CT available, NA
Peritumoural signal intensity on FLAIR	Dropdown list: <ul style="list-style-type: none"> • 0-5% • 6-33% • 34-66% • 67-100% • NA 	Prompt entry if previous option (Readmitted/rescanned during the time between discharge/loss to FU and the date of data entry) has been checked. Allow one option only Note to data collector: In relation to tumour volume. If only baseline CT available, NA
Venous sinus nearby	Checkbox <ul style="list-style-type: none"> • Superior sagittal sinus • Cavernous sinus 	Prompt entry if previous option (Readmitted/rescanned during the time between discharge/loss to FU and the date of data entry) has been checked

	<ul style="list-style-type: none"> • Sigmoid sinus • Transverse sinus • Confluence of sinuses 	Note to data collector: Tick box if within 10 mm, in direct contact or invading one of: superior sagittal sinus (SSS), sigmoid sinus (SS), transverse sinus (TS), cavernous sinus (CS) and the confluence of sinuses (CoS)
If yes, specify	Dropdown list/check box	Prompt entry if previous option (venous sinus nearby) has been ticked. Allow one option only
Separate, direct contact or invaded?	Dropdown list/check box <ul style="list-style-type: none"> • Separate • Direct contact • Invaded 	Prompt entry if previous option (venous sinus nearby) has been ticked. Allow one option only
Major axis (mm)	Free field	Prompt entry if previous option (Readmitted/rescanned during the time between discharge/loss to FU and the date of data entry) has been checked Note to data collector: In mm to 1 dp. Measure on axial T1/CT + GAD
Minor axis (mm)	Free field	Prompt entry if previous option (Readmitted/rescanned during the time between discharge/loss to FU and the date of data entry) has been checked Note to data collector: In mm to 1 dp. Perpendicular to the major axis on axial T1/CT + GAD
Cor/sag major axis (mm)	Free field	Prompt entry if previous option (Readmitted/rescanned during the time between discharge/loss to FU and the date of data entry) has been checked Note to data collector: In mm to 1 dp. Maximum height
Verdict	Dropdown list/checkbox <ul style="list-style-type: none"> • Related • Unrelated 	Prompt entry if previous option (Readmitted/rescanned during the time between discharge/loss to FU and the date of data entry) has been checked. Allow one option only Note to data collector: Were the symptoms attributed to the meningioma?
Outcome	Dropdown list/Checkbox	Prompt entry if previous option (Readmitted/rescanned during the time between discharge/loss to FU and the date of data entry) has been checked. Allow one option only

	<ul style="list-style-type: none"> Resume follow-up (active monitoring) Surgery SRS fRT Discharge <u>Lost to follow-up</u> <u>Dead</u> 	<p>Note to data collector: You will be directed to the relevant page/section dependent on the choice. If the patient died or was lost to follow-up after this interval scan, please choose one of the last two options, albeit the intention might have been to continue monitoring or intervene. If the option you choose is set to take place in the future, choose the option, save the data entered and exit the form with no further information required.</p>
Overall outcome	<p>Dropdown list/Checkbox:</p> <ul style="list-style-type: none"> Dead Alive 	<p>Prompt entry if previous option (Rescanned during the time between discharge/loss to FU and the date of data entry) is not ticked.</p> <p>Allow one option only</p> <p>Note to data collector: You will be directed to section 10 if Dead is selected.</p>
Mortality (SECTION/PAGE 10)		
Date of death	DD/MM/YYYY	Required entry
Cause of death	<p>Dropdown list/checkbox</p> <ul style="list-style-type: none"> Meningioma-related Unrelated 	<p>Required entry. Allow one option only</p> <p>Note to data collector: An example of a meningioma-related death would be for example status epilepticus in a patient who manifested seizures but didn't have treatment. An unrelated death would be for example a community acquired pneumonia. For the purpose of the study, any death occurring from a morbidity, which did not necessitate neurosurgical input/opinion will be classified as unrelated</p>

1.2. Appendix. 2. ICOM classification of meningioma location

ICOM classification system of meningioma locations			
Main category	Subcategories		
Convexity	Anterior ¹	Posterior ¹	
Parasagittal	Anterior ¹	Posterior ¹	Falco-tentorial
Parafalcine	Anterior ¹	Posterior ¹	Falco-tentorial
Sphenoid wing	Lateral	Medial (including ACP)	
Anterior midline	Cribriform plate or olfactory groove ²	Planum ³	Tuberculum and diaphragma sellae
Posterior fossa - midline	Clival	Petro-clival	Anterior foramen magnum ⁴
Posterior fossa – Lateral & posterior	Petrous	Squamous occipital	Posterior foramen magnum ⁴
Tentorial	Supratentorial	Infratentorial	
Intraventricular			
Pineal region⁵			

¹ The main attachment is located anterior or posterior, respectively, to the coronal suture

² Arising between the crista galli and the fronto-sphenoid suture

³ Arising between the fronto-sphenoid suture and the limbus sphenoidale

⁴ The main attachment is located anterior or posterior, respectively, to the hypoglossal canal

⁵ No obvious tentorial attachment