Adjustment, psychological functioning and health-related quality of life in adults with primary malignant brain tumours

A thesis submitted to The University of Manchester for the degree of
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SCHOOL OF PSYCHOLOGICAL SCIENCES
Section for Clinical and Health Psychology
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Word count: 21,254
(excluding contents, tables, figures, references and appendices)
1. Thesis abstract

Adjustment, psychological functioning and health-related quality of life in adults with primary malignant brain tumours

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The University of Manchester
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The thesis has been prepared in a paper-based format and includes three papers: Paper 1, a systematic review; Paper 2, an empirical study; and Paper 3, a critical appraisal and reflection on the work.

Paper 1 has been prepared for submission to Neuro-Oncology. The paper presents a systematic review of 21 studies concerning the relationships of demographic, clinical and mental health factors on health-related quality of life (HRQoL) and psychological functioning in adults with primary malignant brain tumours. The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) principles. Methodological qualities of studies included were appraised using a checklist based on the Newcastle-Ottawa Scale (Wells et al, n.d.). Findings were synthesised narratively adhering to published guidelines (Popay et al, 2006). The review identified evidence for factors relating to HRQoL and psychological functioning, offered several considerations for clinical practice, and outlined recommendations for improving the methodological rigour of future research.

Paper 2 has been prepared for submission to Psycho-Oncology and presents the findings of a qualitative study of patients’ psychological adjustment to glioblastoma, the most aggressive and most common form of brain tumour in adults. Semi-structured interviews were conducted with 10 participants 3.3-5.1 months post-diagnosis. Data were analysed using a constructivist grounded theory methodology (Charmaz, 2014). Analysis yielded three theoretical categories describing processes of maintaining continuity with the past, reframing the present and changing to accommodate an uncertain future. The implications of these findings on current supportive interventions are discussed.

Paper 3 is not intended for publication. It offers a critical appraisal of the individual papers and the research process overall, considering their strengths and limitations. The paper also discusses issues of reflexivity encountered during the empirical study, and considers the implications of this research for the author’s professional development as a clinical psychologist.
2. Declaration

No portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.
3. Statement of copyright and ownership

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4. Acknowledgements

I would like to thank my supervisors, Dr Jacki Bambrough, Dr John Fox and Dr Simon Kyle, for their support and guidance over the past three years. Their collective enthusiasm, insight and expertise have been vital to the completion of this thesis and in containing my uncertainty. It has been a privilege to have worked with you on this project.

I am grateful for the clinicians whom have assisted with the development of the study, particularly Liz Molloy for her advice and assistance with participant recruitment. I am also thankful for the individuals whom gave their valuable time to participate in the qualitative study, who were prepared to share their experiences for the benefit of others.

I would like to thank my family and friends for supporting me throughout the ClinPsyD, for whom I am grateful for reminding me that there is a world outside of clinical psychology. In particular, I am endlessly thankful for the comradeship of Cohort 2012, for whom I owe much of my sanity.

Lastly, an immense thank you to my wife, Bex. Your faith and encouragement have kept me going whenever I have not believed in myself, and your patience and understanding have grounded me when I have felt overwhelmed. Thank you for everything – I hope I haven’t been too much of a nightmare!
5. Paper 1: Systematic Review

Health-related quality of life and psychological functioning in patients with primary malignant brain tumors: A systematic review of clinical, demographic and mental health factors

Paper 1 is a systematic review of the qualitative literature pertaining to factors associated with health related quality of life and psychological functioning in adults with primary malignant brain tumours (PMBT), published between 1984 and 2014. The findings of 21 quantitative studies were synthesised in accordance with published guidance on narrative synthesis to identify key factors underlying the wellbeing of patients with PMBT. The methodologies of these 21 studies were assessed using a checklist adapted from a previously validated quality assessment tool.

This systematic review has been prepared for submission to Neuro-Oncology in accordance with the guidelines for contributors (appendix 1). As such the paper is written in US English and adheres as closely as possible to the style guidelines of the AMA Manual of Style, 10th edition, while ensuring compliance with the University of Manchester Presentation of Theses Policy. Tables and figures have been incorporated into the text to aid readability and reference; for the version submitted to Neuro-Oncology, tables and figures were submitted as separate sheets as per the guidelines for contributors. Footnotes that cross-reference other sections of this thesis were not included in the journal copy. Permission was sought from the editor-in-chief of Neuro-Oncology prior to submitting the manuscript for peer review.

Word count: 6740

(including references and captions; excluding abstract, figures and tables)
5.1. Abstract

**Background:** The impact of primary malignant brain tumors (PMBT) on patient quality of life and psychological functioning is poorly understood, limiting the development of an evidence base for supportive interventions. We conducted a thorough systematic review and quality appraisal of the relevant literature to identify correlates of health-related quality of life (HRQoL) and psychological functioning (depression, anxiety and distress) in adults with PMBT.

**Method:** Twenty-one articles met pre-defined inclusion criteria from a pool of peer-reviewed literature published between January 1984 to April 2014 (n=2289). Methodological quality of included studies was assessed using an adapted version of the Newcastle-Ottawa Scale.

**Results:** The overall methodological quality of the literature was moderate. Factors relating consistently with HRQoL and/or psychological functioning were cognitive impairment, corticosteroid use, current or previous mental health difficulties, fatigue, functional impairment and motor impairment.

**Conclusions:** Practitioners should remain alert to the presence of these factors as they may indicate patients at greater risk of poor HRQoL and psychological functioning. Attention should be directed towards improving patients’ psychological functioning and maximizing functional independence to promote HRQoL. We outline several areas of future research with emphasis on improved methodological rigor.
5.2 Introduction

Health-related quality of life (HRQoL), has become increasingly important throughout the health sciences with the widespread recognition that objective improvements in clinical presentation rarely correlate with patient-reported satisfaction.\(^1\) Defined as a measurement of the “radiating impact of pathology on the patient’s wider world,”\(^2\) HRQoL has been present in medical oncology literature from the 1990s, and is an increasingly important endpoint in treatment trials.\(^3\) Comprehensive assessment in patients with brain tumors has however lagged behind that of other cancers.\(^4-6\)

Patients’ experiences of primary malignant brain tumor (PMBT) can vary depending on the size, location and specific variant of tumor.\(^7\) Seizures persist in at least 30% of patients throughout disease duration.\(^8\) Approximately 50% of patients experience headaches due to raised intracranial pressure,\(^9\) as well as nausea, vomiting, drowsiness and visual disturbances.\(^10\) Progressive neurological deficits and cognitive impairments are also common, with many patients experiencing hemiparesis and hemisensory loss, dysphasia, memory impairment, confusion, and difficulties with the regulation of emotion and behavior.\(^11-13\) Symptoms can be triggered or exacerbated by treatment; radiotherapy can lead to radiation encephalopathy, causing significant neurological and cognitive impairment,\(^11,14\) and chemotherapy is associated with a high frequency of neurotoxic complications affecting peripheral and central nervous systems.\(^15\)

Psychological distress is also prevalent amongst patients with PMBT. Studies utilizing brief univariate measures, such as the Distress Thermometer,\(^16\) vary widely in their estimations with prevalence rates between 30% and 73%.\(^17-19\) Approximately one-third of patients experience clinically significant levels of depression and anxiety.\(^20-22\) It is highly likely that the reported incidence of emotional problems is not representative
of reality: patients typically under-report psychological concerns and such difficulties can go undetected by clinicians.23,24

Despite advances in detection and treatment of brain tumors over the previous three decades, there has been limited improvement in the survival rate of PMBT25,26; at present, one-year and five-year survival rates in the UK are 40% and 18% respectively, 27 although this varies significantly with tumor morphology.26 It is important, therefore, that protection and maintenance of HRQoL for patients with PMBT remains central to care, as per national guidelines.28,29 Unfortunately, much still remains unknown about the impact of the illness experience on patients’ HRQoL, psychological functioning and overall adjustment to PMBT, which consequently limits supportive interventions.5

Previous reviews have attempted to describe and delineate factors related to HRQoL in patients with malignant and non-malignant brain tumors5,6,30,31; however none have focused exclusively on PMBT. As illness experiences differ substantially between patients with malignant and non-malignant disease,6 we aim to improve on existing evaluations with a specific orientation towards patients with PMBT.

The present report describes a systematic review of evidence for factors associated with HRQoL and psychological functioning in adults with PMBT published over the previous three decades. The quality of the evidence is assessed and findings synthesized narratively. We endeavor to make tentative suggestions as to which subgroups of patients may be at greater risk of impaired HRQoL or psychological functioning. The review concludes with recommendations for clinical care and the ongoing research agenda.
5.3. Method

5.3.1. Search strategy\textsuperscript{i}

A systematic search of electronic databases (CINAHL, PsycInfo and PubMed), covering the period from 1 January 1984 to 30 April 2014, was conducted to identify articles investigating HRQoL and/or psychological functioning outcomes in patients with PMBT. The search was restricted to English language, peer-reviewed studies. Conference abstracts, case reports and grey literature were omitted. The search terms for this review are listed in the supplemental material. The review was completed in accordance with the PRISMA statement\textsuperscript{ii,32}

Studies were considered for review if they: (a) aimed to delineate independent variables that may be related to HRQoL and/or psychological functioning outcomes; (b) investigated samples where greater than 75\% of the participants had a diagnosis of PMBT; (c) recruited adult patients (\geq 18 years old) exclusively; (d) utilized at least one validated outcome measure; and (e) reported statistics in sufficient detail to describe the relationship between the independent variables and the outcomes under consideration. All study designs were considered for inclusion.

The electronic database search returned 2289 articles, excluding duplicates. The titles and/or abstracts of these articles were screened and 2207 were rejected. The majority of these articles were excluded as they were not relevant to the research question, such as reports of the findings of biochemical, neuropathological and epidemiological studies. Approximately 330 articles identified were excluded as they were not peer-reviewed research, despite the limitations specified in the search query, and 52 were excluded as they reported qualitative findings. Full versions of the remaining 81 articles were obtained and reviewed against the inclusion criteria above. The bibliographies of these 81 articles were examined to identify further potential

\textsuperscript{i} See also section 7.2.2.  
\textsuperscript{ii} See appendix 3.
studies for inclusion, yielding 18 additional papers. Manual searches of the four journals in which the most identified articles had been published returned no additional articles. Of these 99 studies, 21 fulfilled all inclusion criteria and 78 were excluded (see figure 5.1). Data extraction was conducted by the lead author.

5.3.2 Quality assessment

All studies selected for inclusion were assessed by the lead author and a randomly selected subset of ten studies was assessed independently by two post-graduate level researchers with experience conducting quality assessments but who were unfamiliar with the field. Studies were assessed against an 8-item quality assessment tool based on the Newcastle-Ottawa Scale\textsuperscript{iv} 33 and tailored to the requirements of this review. Assessment criteria were consistent with published recommendations.\textsuperscript{v} The overall methodological quality of a study was defined in terms of the following: clarity of the research aim; validity of outcome measures; clarity of sampling methodology; exclusivity of diagnoses; specificity of diagnoses; representativeness of the sample; justification for sample size; and clarity of statistical tests\textsuperscript{v}. Each criterion was scored on a three-point rating scale (2 points = fully met; 1 point = partially met; 0 = not met), yielding a range of scores of 0-16. All studies, regardless of score, were retained for review.

5.3.3. Synthesis\textsuperscript{vi}

Due to considerable heterogeneity amongst the methodologies and outcomes of the studies included, meta-analysis was considered neither viable nor appropriate. In

\textsuperscript{iii} See also section 7.2.3.
\textsuperscript{iv} See appendix 4.
\textsuperscript{v} See appendix 5.
\textsuperscript{vi} See also section 7.2.4.
Figure 5.1. Flowchart of the selection process for the review.
answering the research question, the authors conducted a narrative synthesis, as per guidance developed by Popay and colleagues,\textsuperscript{35} in which a theory of effect was established, a preliminary synthesis developed, relationships explored and robustness of the synthesis assessed.
5.4. Results

The following sub-sections report an overall review of the 21 studies selected for inclusion, which are summarized in table 5.1.

5.4.1. Description of studies

Studies included in the review used cross-sectional (n=12) or cohort designs (n=9). Sample sizes varied substantially; seventeen studies featured a sample between 50 and 186 participants, two reported results for less than 50 participants and two recruited 363 and 598 participants, respectively. The majority of studies recruited participants opportunistically from routine treatment clinics (n=19), whereas one recruited patients as part of a companion protocol of a clinical trial and one recruited solely using advertisements on a website for patients with brain tumors.

Fourteen studies recruited patients with PMBT exclusively with the remaining 7 including participants with other diagnoses. The mean participant age across the 13 studies providing sufficient information was 47.17±13.25 years. Of the 19 studies with adequate demographic information, males comprised greater than 50% of the sample in 18 cases.

5.4.2. Study evaluation and assessment

The overall quality ratings of included studies varied (mean: 10.67; SD: 1.36; range: 9-14, out of 16). The intra-class correlation between raters for a randomly-selected subset of ten studies was 0.72 (95% CI: 0.40-0.91), suggesting satisfactory inter-rater reliability for the assessment tool.36 Strengths of the included papers were
Table 5.1. Description of studies included in the review of factors associated with HRQoL and psychological functioning in patients with PMBT.

<table>
<thead>
<tr>
<th>Study (quality score)</th>
<th>Methodology</th>
<th>Participants</th>
<th>Independent variables (measures)</th>
<th>Outcomes of interest (measures)</th>
<th>Summary of relevant findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arnold et al., 2006 (9/16)</td>
<td>Cross-sectional</td>
<td>288 with PMBT 75 with other brain tumor diagnoses</td>
<td>Tumor grade; TFD; Tumor site; Recurrence; Sex; Age; Marital status; Education; Ethnicity; Previous psychiatric illness</td>
<td>Depression (mPHQ) Generalised anxiety (mPHQ)</td>
<td>Anxiety (mPHQ): Greater in females cf. males (p=0.03), low cf. high grade (p=0.0013) and people with a history of psychiatric illness (0=0.082). Greater risk in females cf. males (OR: 0.665; 95% CI: 0.432-1.022), low grade cf. high grade (OR: 0.665; 95% CI: 0.432-1.022), and previous psychiatric difficulties cf. no difficulties reported (OR=2.78; 95% CI: 0.96-8.07). NS for age, marital status, education level, TFD, tumor site, recurrence or ethnicity.</td>
</tr>
<tr>
<td>Brown et al., 2005 (10/16)</td>
<td>Prospective cohort</td>
<td>124 with newly diagnosed high-grade gliomas</td>
<td>Fatigue (POMS-SF, SDS); Excessive daytime somnolence (ESE); Extent of resection; AED use; Depression (POMS-SF)</td>
<td>QoL (LASA, FACT-Br) Depression (POMS-SF)</td>
<td>QoL at follow-up (LASA): Negative association with baseline POMS-SF fatigue, (OR=0.96; 95% CI: 0.93-0.98, p=0.0004), ESE (OR=0.91; 95% CI: 0.87-0.95, p&lt;0.0001) and POMS-SF depression (OR=0.95; 95% CI: 0.92-0.99, p=0.002). QoL at follow-up (LASA): Improved with STR cf. biopsy only (OR=21.88; 95% CI: 7.78-172.45, p=0.0003) and AED use (OR=5.83; 95% CI: 1.28-26.61, p=0.02). Depression at follow-up (POMS-SF): Greater with biopsy only cf. GTR (OR=0.10; 95% CI: 0.03-0.38, p=0.0008) and cf. STR (OR=0.11, 95% CI: 0.03-0.38, p=0.0008)</td>
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<td>Study (quality score)</td>
<td>Methodology</td>
<td>Participants</td>
<td>Independent variables (measures)</td>
<td>Outcomes of interest (measures)</td>
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<tr>
<td>Daigle et al, 2013&lt;sup&gt;23&lt;/sup&gt; (10/16)</td>
<td>Prospective cohort</td>
<td>35 with newly diagnosed GBM</td>
<td>Tumor volume; Extent of resection</td>
<td>QoL (SNAS)</td>
<td>QoL (SNAS): Generally decreased over time for biopsy group, generally stable for craniotomy group (apart from digestive symptomatology (Z=2.23, p=0.01, η²=0.39). Tumor volume at time 1 associated with decreased social support/acceptance of disease (r=0.43, p=0.009) and pain (r=0.41, p=0.015), NS for symptom severity/fear of death, functional wellbeing, autonomy in personal care, digestive symptomatology, neurocognitive function or global QoL. Extent of resection associated with changes in functional wellbeing (r=0.313, p=0.005), neurocognitive function (r=0.51, p=0.026) and global QoL (r=0.68, p=0.001) NS for symptom severity/fear of death, social support/acceptance, autonomy in personal care, digestive symptomatology, or pain.</td>
</tr>
<tr>
<td>Fox et al, 2007&lt;sup&gt;22&lt;/sup&gt; (12/16)</td>
<td>Cross-sectional</td>
<td>73 with high-grade gliomas (median TFD: 46 months)</td>
<td>Fatigue (BFI); Sleep quality (GSDS); Cognitive function (COGMOS); Pain (BPI); Functional status (FACT-Br); QoL (FSQoLS)</td>
<td>Depression (HADS); QoL (FSQoLS)</td>
<td>Depression (HADS): Correlated with BFI (r=0.561, p&lt;0.01), GSDS (r=0.490, p&lt;0.01), COGMOS (r=0.539, p&lt;0.01), FACT-Br (r=0.757, p&lt;0.01) and QoL (r=0.511, p&lt;0.01). NS correlation with BPI (r=0.197). QoL (FSQoLS): Correlated with HADS depression r=0.511, p&lt;0.01), BFI (r=0.407, p&lt;0.01), GSDS (r=0.281, p&lt;0.05), COGMOS (r=0.346, p&lt;0.05) and FACT-Br (r=0.705, p&lt;0.01). NS correlation with BPI (r=0.197)</td>
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<tr>
<td>Study (quality score)</td>
<td>Methodology</td>
<td>Participants</td>
<td>Independent variables (measures)</td>
<td>Outcomes of interest (measures)</td>
<td>Summary of relevant findings</td>
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<tr>
<td>Giovagnoli et al, 1996 (10/16)</td>
<td>Cross-sectional</td>
<td>90 with PMBT (mean TFD: 24.59±30.75 months); 11 with other brain tumor diagnoses; 90 non-clinical participants</td>
<td>Performance status (KPS); Functional independence (ADLS); Tumor site; Tumor grade; Extent of resection; Age; Education; Sex; Marital status; Anxiety (STAI); Depression (SRDS); Cognitive function</td>
<td>QoL (FLIC); Anxiety (STAI); Depression (SRDS)</td>
<td>QoL (FLIC): Correlated with KPS (r=0.40, p&lt;0.001), ADLS (r=0.26, p&lt;0.01), STAI state anxiety (r=-0.36, p&lt;0.001), STAI trait anxiety (r=-0.36, p&lt;0.001) and SRDS (r=-0.45, p&lt;0.001). NS for age (as covariate, p=0.36). Regression model: years of education (B=0.13, p=0.035, exp(B)=1.14), location in anterior right hemisphere (B=1.37, p=0.0038, exp(B)=3.96) or diencephalon (B=1.43, p=0.046, exp(B)=4.18. NS for age, sex, marital status, or extent of resection.</td>
</tr>
<tr>
<td>Giovagnoli, 1999 (11/16)</td>
<td>Cross-sectional</td>
<td>57 with PMBT (mean TFD: 37.05±54.36 months (range: 3-84 months)); 24 with other chronic neurological diseases</td>
<td>Tumor site; Tumor type; TFD; Performance status (KPS); Age; Education; Anxiety (STAI, STAI-2); Depression (SRDS); Functional independence (ADLS); Cognitive function</td>
<td>QoL (FLIC); Anxiety (STAI, STAI-2); Depression (SRDS)</td>
<td>QoL (FLIC): Correlated with STAI (r=-0.57, p&lt;0.001), STAI-2 (r=-0.63, p&lt;0.001), SRDS (r=-0.75, p&lt;0.001), KPS (r=-0.40, p&lt;0.001) and cognitive function (all p&lt;0.01). NS with age, education, tumor site, tumor type, sex, marital status or extent of resection.</td>
</tr>
<tr>
<td>Study (quality score)</td>
<td>Methodology</td>
<td>Participants</td>
<td>Independent variables (measures)</td>
<td>Outcomes of interest (measures)</td>
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<tr>
<td>Giovagnoli et al, 2008&lt;sup&gt;34&lt;/sup&gt; (9/16)</td>
<td>Cross-sectional</td>
<td>94 with recurrent high-grade glioma (mean TDF: 35.84±27.57 months); 24 with other chronic neurological diseases; 48 non-clinical participants</td>
<td>Tumor site; Cognitive function; Performance status (KPS); Sex; Marital status; Anxiety (STAI, STAI-2); Depression (SRDS); Functional independence (ADLS)</td>
<td>QoL (FLIC); Anxiety (STAI, STAI-2); Depression (SRDS)</td>
<td>QoL (FLIC): Higher in grade III cf. grade IV (p=0.023). NS for sex, marital status or tumor site. Anxiety (STAI, STAI-2): NS for sex or marital status. Depression (SRDS): NS for sex or marital status.</td>
</tr>
<tr>
<td>Hahn et al, 2003&lt;sup&gt;38&lt;/sup&gt; (10/16)</td>
<td>Cross-sectional</td>
<td>50 with newly diagnosed PMBT; 31 with other brain tumor diagnoses</td>
<td>Performance status (KPS); Lesion size; Tumor site; Steroid use; Cognitive function</td>
<td>Depression (BDI); QoL (LASA, MHS, HUS)</td>
<td>Depression (BDI): More symptoms present in left cf. right side tumor patients (p&lt;0.05). NS correlation between KPS and BDI. QoL (LASA, MHS, HUS): No correlation between KPS and QoL measures.</td>
</tr>
<tr>
<td>Kaplan &amp; Miner, 2000&lt;sup&gt;37&lt;/sup&gt; (9/16)</td>
<td>Cross-sectional</td>
<td>33 with newly-diagnosed PMBT</td>
<td>Sex; Problem list (CIPI) – includes: cognitive impairment, changes in physical appearance, sexual problems, inactivity, worries about body deteriorating, financial worries, marital difficulties</td>
<td>Depression (BDI, MAS); Anxiety (BAI, STAI)</td>
<td>Depression (BDI, MAS): Correlated with CIPI reported problem with sex (r=0.66, p&lt;0.01), inactivity (r=0.64, p&lt;0.01), bodily deterioration (r=0.60, p&lt;0.01), finances (r=0.58, p&lt;0.01), cognition (r=0.54, p&lt;0.01), physical appearance (r=0.54, p&lt;0.01) and marital relationships (r=0.46, p&lt;0.01). NS correlation with sex. Rates of depression higher in married cf. single participants (no statistics reported). Anxiety (BAI, STAI): NS correlation with sex. Rates of anxiety higher in single cf. married participants (no statistics reported).</td>
</tr>
<tr>
<td>Study (quality score)</td>
<td>Methodology</td>
<td>Participants</td>
<td>Independent variables (measures)</td>
<td>Outcomes of interest (measures)</td>
<td>Summary of relevant findings</td>
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<tr>
<td>Keir et al, 2008&lt;sup&gt;17&lt;/sup&gt; (13/16)</td>
<td>Cross-sectional</td>
<td>83 with PMBT (&lt;18 months: 41; &gt; 18 months: 42; median TFD: 1.3 years (range: 10 days-14 years))</td>
<td>TFD; Sex; Problem list (DT)</td>
<td>Distress (DT)</td>
<td>Distress (DT): Correlated with psychosocial concerns reported on DT problem list in longer-term patients (r=0.424, p&lt;0.02) and physical concerns reported on DT problem list in both longer (r=0.363, p&lt;0.05) and shorter term patients (r=0.325, p&lt;0.05). Greater in females cf. males (p&lt;0.01). NS trend for greater distress with more physical concerns (p=0.07). NS association with TFD.</td>
</tr>
<tr>
<td>Kilbride et al, 2007&lt;sup&gt;26&lt;/sup&gt; (9/16)</td>
<td>Prospective cohort</td>
<td>42 with PMBT; 9 with other brain tumor diagnoses</td>
<td>TFD; Age; History of mental health problems; Marital status</td>
<td>Anxiety (HADS); Depression (HADS)</td>
<td>Anxiety (HADS): NS correlations with TFD, age, history of mental health problems or marital status. Depression (HADS): NS correlations with TFD, age, history of mental health problems or marital status.</td>
</tr>
<tr>
<td>Klein et al, 2001&lt;sup&gt;50&lt;/sup&gt; (11/16)</td>
<td>Cross-sectional</td>
<td>68 with newly-diagnosed high-grade gliomas; 50 with non-small cell lung cancer; 118 non-clinical participants</td>
<td>Functional independence (BADLI); Tumor site; AED use; Steroid use; Extent of resection; Neurological function (NFSS); Cognitive function (COGMOCS); Performance status (KPS)</td>
<td>QoL (SF-36, QLQ-BN20)</td>
<td>QoL (SF-36, QLQ-BN20): Lower in biopsy cf. GTR (p&lt;0.05) and steroids cf. no steroids (p&lt;0.05). NS difference in left cf. right tumor sites or AED cf. no AED.</td>
</tr>
<tr>
<td>Study (quality score)</td>
<td>Methodology</td>
<td>Participants</td>
<td>Independent variables (measures)</td>
<td>Outcomes of interest (measures)</td>
<td>Summary of relevant findings</td>
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<tr>
<td>Kvale et al., 2008(^{18}) (12/15)</td>
<td>Cross-sectional</td>
<td>50 with PMBT (mean TFD: 13.88±13.6 months (range: 2-57 months))</td>
<td>QoL (FACT-Br); Age; Sex; Ethnicity</td>
<td>Distress (DT); QoL (FACT-Br)</td>
<td>Distress (DT): Correlation between FACT-Br social wellbeing (r=0.46, p=0.001) and FACT-Br emotional wellbeing (r=0.56, p=0.001). NS correlation with FACT-Br physical and FACT-Br functional wellbeing. NS difference for age, sex, race, or TFD.</td>
</tr>
<tr>
<td>Lin et al, 2013(^{11}) (11/16)</td>
<td>Cross-sectional</td>
<td>143 with PMBT; 43 with other brain tumor diagnoses</td>
<td>Performance status (KPS); Stage in treatment; Uncertainty (MUIS-BT)</td>
<td>Depression (POMS-SF); Anxiety (POMS-SF)</td>
<td>Depression (POMS-SF): Correlation with uncertainty (r=0.48, p&lt;0.001). NS relationship with performance status.</td>
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<td>Anxiety (POMS-SF): Correlation with uncertainty (r=0.56, p&lt;0.001) and performance status (r=0.17, p&lt;0.05)</td>
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<tr>
<td>Study (quality score)</td>
<td>Methodology</td>
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<td>Litofsky et al, 2004&lt;sup&gt;24&lt;/sup&gt; (11/16)</td>
<td>Prospective cohort</td>
<td>598 with newly-diagnosed high-grade gliomas</td>
<td>Performance status (KPS); Sex; Age; Ethnicity; Tumor site; Steroid use; Presenting symptoms (consciousness, headache, memory loss, nausea, language deficits, personality change, progressive motor deficits, seizures, cognitive changes, sensory symptoms, papilledema, visual problems)</td>
<td>Depression (SF-36, 3-item binary measure, physician report);</td>
<td>Significant discordance between physician and patient-reported depression (baseline $\kappa=0.02$, 3 month follow-up $\kappa=0.01$, 6 month follow-up $\kappa=0.05$) – physicians under report. Depression (physician report): Depression associated with lower KPS score ($p=0.0193$), multifocal cf. one tumor site ($p=0.0277$), larger tumor sizes ($p&lt;0.005$), steroid use cf. no steroids ($p&lt;0.002$, at 6 month follow-up), consciousness problems ($p=0.0168$), headaches ($p=0.0073$, memory loss ($p=0.0148$), personality changes ($p&lt;0.0001$), progressive motor deficits ($p&lt;0.0004$), cognitive changes ($p&lt;0.0011$) and papilledema ($p=0.0001$). Skewed data for ethnicity. NS difference for sex, age, steroid use (at 3 month follow-up), frontal lobe site cf. non-frontal site, extent of resection, nausea, language deficits, seizures, sensory symptoms or visual problems</td>
</tr>
<tr>
<td>Osoba et al, 1997&lt;sup&gt;31&lt;/sup&gt; (11/16)</td>
<td>Prospective cohort</td>
<td>105 with high-grade gliomas (recently diagnosed: 41; recurrent disease: 64)</td>
<td>Functional independence (BADLI); Recurrence; Dysphasia; Motor deficits; Confusion; Performance status (KPS)</td>
<td>QoL (QLQ-C30)</td>
<td>QoL (QLQ-C30): Global QoL greater in independent cf. dependent ($p&lt;0.001$), recently diagnosed cf. recurrence ($p&lt;0.01$), no motor deficit cf. motor deficit ($p&lt;0.001$). NS for dysphasia, confusion. Emotional subscale only significant for no motor deficit cf. motor deficit ($p&lt;0.01$), all others NS. Role subscale significant for all. Social only significant for independent cf. dependent ($p&lt;0.01$), no dysphasia cf. dysphasia ($p&lt;0.001$), no motor deficits cf. motor deficits ($p&lt;0.01$)</td>
</tr>
<tr>
<td>Study (quality score)</td>
<td>Methodology</td>
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<td>Independent variables (measures)</td>
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<tr>
<td>Raysi Dehordi et al. 2012(12/16)</td>
<td>Prospective cohort</td>
<td>58 with newly-diagnosed GBM</td>
<td>Tumor site; Tumor laterality; Age; Sex; Performance status (KPS)</td>
<td>Depression (BDI)</td>
<td>Depression (BDI): Significantly greater in frontal lobe cf. other tumor site (p=0.01), KPS ≤70 cf. &gt;70 (p=0.001 at 6 months, p=0.005 at 12 months). NS difference for tumor laterality, sex or age.</td>
</tr>
<tr>
<td>Rooney et al. 2011(14/16)</td>
<td>Prospective cohort</td>
<td>133 with newly-diagnosed high-grade gliomas; 22 with other brain tumor diagnoses</td>
<td>Performance status (KPS); Steroid use; AED use; Cognitive impairment (ACE-R); Tumor type; Tumor grade; Tumor laterality; Tumor site; Extent of resection; Radiotherapy schedule; Chemotherapy schedule; Age; Sex; Marital status; Previous diagnosis of MDD; Epilepsy</td>
<td>Depression (SCID)</td>
<td>Depression (SCID): Significantly greater in previous depression cf. none (p=0.004), KPS ≤70 cf. &gt;70 (p=0.007 at start of radiotherapy), steroid use (dexamethasone) (p=0.001) and cognitive impairment cf. none (p=0.048). NS with age (p=0.610), sex (p=0.802), marital status (p=0.447), tumor type (p=0.233), tumor laterality (p=0.697), tumor grade (p=0.570), tumor lobe (p=0.445), extent of resection (p=0.662), radiotherapy schedule (p=0.75), chemotherapy schedule (p=0.901), AED use (p=0.552) or epilepsy (p=1.0). In multivariate regression model, independent predictors were KPS ≤ 70 (OR: 3.9, 95% CI: 1.5-10.8, p=0.006) or previous depression (OR: 2.7, 95% CI 0.99 - 7.3, p=0.053), NS for cognitive impairment.</td>
</tr>
<tr>
<td>Study (quality score)</td>
<td>Methodology</td>
<td>Participants</td>
<td>Independent variables (measures)</td>
<td>Outcomes of interest (measures)</td>
<td>Summary of relevant findings</td>
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<tr>
<td>Rooney et al, 2013*10 (10/16)</td>
<td>Prospective cohort</td>
<td>132 with newly-diagnosed high-grade gliomas; 22 with other brain tumor diagnoses</td>
<td>Performance status (KPS); Steroid use; AED use; Cognitive impairment (ACE-R); Functional impairment; Tumor type; Tumor grade; Tumor laterality; Tumor site; Extent of resection; Radiotherapy schedule; Chemotherapy schedule; Age; Sex; Marital status; Previous diagnosis of MDD, Epilepsy</td>
<td>Distress (DT)</td>
<td>Distress (DT): Significantly greater in patients with MDD (p&lt;0.001, at 8 weeks post-surgery and 3 months, NS at 6 months), functional impairment (p&lt;0.02 at 3 months and 6 months, NS at 8 weeks post-surgery), AED use (p=0.038 at 8 weeks post-surgery, NS at 3 months and 6 months), biopsy cf. resection (p=0.047 at 6 months, NS at 8 weeks post-surgery and 3 months). Significant relationship with age (r=-0.197, p=0.014, 8 weeks post-surgery, NS at 3 months or 6 months). NS with marital status, tumor type, tumor grade, tumor laterality, tumor site, radiotherapy schedule, chemotherapy schedule, steroid use, epilepsy or cognitive function. In logistic regression model, independent predictors were MDD, functional impairment and young age (χ²=39.682, R²=0.312, p&lt;0.001)</td>
</tr>
<tr>
<td>Study (quality score)</td>
<td>Methodology</td>
<td>Participants</td>
<td>Independent variables (measures)</td>
<td>Outcomes of interest (measures)</td>
<td>Summary of relevant findings</td>
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<tr>
<td>Weitzner et al, 1996&lt;sup&gt;46&lt;/sup&gt; (9/16)</td>
<td>Cross-sectional</td>
<td>42 with PMBT (mean TFB: 30.7 months; range: 1-154 months); 8 with other brain tumor diagnoses</td>
<td>Tumor type; Tumor laterality; TFB; Age; Education; Marital status</td>
<td>QoL (FP-QLI, PAIS-SR)</td>
<td>QoL (FP-QLI): QoL significantly lower in divorced cf. married (p&lt;0.03) and bilateral cf. unilateral tumors (p&lt;0.04). NS for age, educational level, tumor type and TFB.</td>
</tr>
<tr>
<td>Yavas et al, 2012&lt;sup&gt;47&lt;/sup&gt; (11/16)</td>
<td>Prospective cohort</td>
<td>118 with newly-diagnosed high-grade glioma</td>
<td>Tumor laterality; Sex; Age</td>
<td>QoL (QLQ-C30, QLQ-BN20); Anxiety (HADS); Depression (HADS)</td>
<td>QoL (QLQ-C30, QLQ-BN20): Significantly greater in males cf. females with grade III tumors (p=0.049), NS for males cf. females with grade IV tumors. NS with age or laterality. Anxiety (HADS): Not reported. Depression (HADS): Not reported.</td>
</tr>
</tbody>
</table>

ACE-R: Addenbrooke’s Cognitive Examination-Revised; ADLS: Activities of Daily Living Scale; AED: Anti-epileptic drug; BADLI: Barthel Activities of Daily Living Index; BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; BFI: Brief Fatigue Inventory; BPI: Brief Pain Inventory; CIPI: Chronic Illness Problem Inventory; COG MOS: Cognitive Functioning subscale of the Medical Outcomes Scale; DT: Distress Thermometer; ESE: Epworth Sleepiness Scale; FACT-B: Functional Assessment of Cancer Therapy - Brain; FLIC: Functional Living Index - Cancer; FP-QLI: Ferrans and Powers Quality of Life Index for Cancer; FSQoLS: Fox Simple Quality of Life Scale; GBM: Glioblastoma multiforme; GTR: Gross total resection; GSDS: General Sleep Disturbance Scale; HADS: Hospital Anxiety and Depression Scale; HUS: Hassles and Uplifts Scale; KPS: Karnofsky Performance Scale; LASA: Linear analogue scale assessment; MAS: Mood Assessment Scale; MDD: Major Depressive Disorder; MHS: Miller Hope Scale; mPHQ: Modified Patient Health Questionnaire; MUIS-BT: Mishel Uncertainty in Illness Scale - Brain Tumor; NFSS: Neurological Function Status Scale; NS: Not significant; PAIS-SR: Psychosocial Adjustment to Illness Scale - Self Report; POMS-SF: Profile of Mood States - Short Form; QLQ-C30: Quality of Life Questionnaire for Cancer-30; QLQ-BN20: Quality of Life Questionnaire for Cancer – Brain Cancer Module; SCID: Structured Clinical Interview for DSM-IV Disorders; SDS: Symptom Distress Scale; SF-36: Short Form (36) Health Survey; SNAS: Sherbrooke Neuro-oncology Assessment Scale; SRDS: Zung Self-Rating Depression Scale; STAI-1: State Trait Anxiety Inventory; STAI-2: State Trait Anxiety Inventory-2; STR: Subtotal resection; TFD: Time from diagnosis; VAMS: Visual Analog of Mood Scales.
that all but one used appropriate statistical tests and reported them sufficiently (one study used descriptive statistics only), and that 20 studies used validated measures exclusively, with a further study using a combination of validated and non-validated measures. Weaknesses included the lack of demonstrable representativeness of the sample to a wider population of patients with PMBT and lack of a priori or post hoc justification for sample sizes. As the aim of the present report was to review factors pertinent to patients with PMBT, the findings of seven papers were weakened in specificity by their inclusion of small numbers of patients diagnosed with low-grade brain tumors.

5.4.3. Independent variables and outcomes

The principal study outcomes considered in this review were HRQoL (12 studies), depression (14 studies), anxiety (8 studies) and distress (3 studies). Multiple outcomes were reported in 13 studies. In reporting HRQoL outcomes, we acknowledge that HRQoL and QoL (quality of life) are often used interchangeably (and erroneously) by a number of authors; as such we have considered all findings reported for QoL as HRQoL outcomes. A wide range of validated measures (n=23) were used to quantify these outcomes (see table 5.2).

Due to the nature of the review question, a large number of independent variables were considered relevant for inclusion. These variables were grouped into three thematic categories: demographic factors, clinical factors and mental health factors.
**Table 5.2.** Validated measures used to quantify outcomes of interest in studies selected for inclusion.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Times used (n)*</th>
<th>Outcomes measured</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAI</td>
<td>1</td>
<td>Anxiety[^37]</td>
</tr>
<tr>
<td>BDI</td>
<td>3</td>
<td>Depression[^37-39]</td>
</tr>
<tr>
<td>DT</td>
<td>3</td>
<td>Distress[^17,18,40]</td>
</tr>
<tr>
<td>FACT-Br</td>
<td>2</td>
<td>HRQoL[^18,41]</td>
</tr>
<tr>
<td>FLIC</td>
<td>3</td>
<td>HRQoL[^42-44]</td>
</tr>
<tr>
<td>FP-QLI</td>
<td>1</td>
<td>HRQoL[^45]</td>
</tr>
<tr>
<td>FSQoLS</td>
<td>1</td>
<td>HRQoL[^12]</td>
</tr>
<tr>
<td>HADS</td>
<td>5</td>
<td>Depression[^12,46,47]; anxiety[^46,47]</td>
</tr>
<tr>
<td>HUS</td>
<td>1</td>
<td>HRQoL[^38]</td>
</tr>
<tr>
<td>LASA</td>
<td>2</td>
<td>HRQoL[^38,41]</td>
</tr>
<tr>
<td>MAS</td>
<td>1</td>
<td>Depression[^37]</td>
</tr>
<tr>
<td>MHS</td>
<td>1</td>
<td>HRQoL[^38]</td>
</tr>
<tr>
<td>mPHQ</td>
<td>2</td>
<td>Depression[^48]; anxiety[^48]</td>
</tr>
<tr>
<td>PAIS-SR</td>
<td>1</td>
<td>HRQoL[^45]</td>
</tr>
<tr>
<td>POMS-SF</td>
<td>3</td>
<td>Depression[^41,49]; anxiety[^49]</td>
</tr>
<tr>
<td>QLQ-BN20</td>
<td>2</td>
<td>HRQoL[^47,50]</td>
</tr>
<tr>
<td>QLQ-C30</td>
<td>2</td>
<td>HRQoL[^47,51]</td>
</tr>
<tr>
<td>SCID</td>
<td>1</td>
<td>Depression[^52]</td>
</tr>
<tr>
<td>SF-36</td>
<td>2</td>
<td>Depression[^24]; HRQoL[^50];</td>
</tr>
<tr>
<td>SNAS</td>
<td>1</td>
<td>HRQoL[^53]</td>
</tr>
<tr>
<td>SRDS</td>
<td>3</td>
<td>Depression[^42-44]</td>
</tr>
<tr>
<td>STAI</td>
<td>4</td>
<td>Anxiety[^37,42-44]</td>
</tr>
<tr>
<td>STAI-2</td>
<td>2</td>
<td>Anxiety[^42,43]</td>
</tr>
</tbody>
</table>

* Number of unique uses. If a study used one validated measure to quantify multiple outcomes, the measure is counted for each use.

BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; DT: Distress Thermometer; FACT-Br: Functional Assessment of Cancer Therapy - Brain; FLIC: Functional Living Index - Cancer; FP-QLI: Ferrans and Powers Quality of Life Index for Cancer; FSQoLS: Fox Simple Quality of Life Scale; HADS: Hospital Anxiety and Depression Scale; HUS: Hassles and Uplifts Scale; LASA: Linear analogue scale assessment; MAS: Mood Assessment Scale; MHS: Miller Hope Scale; mPHQ: Modified Patient Health Questionnaire; PAIS-SR: Psychosocial Adjustment to Illness Scale - Self Report; POMS-SF: Profile of Mood States - Short Form; QLQ-C30: Quality of Life Questionnaire for Cancer-30; QLQ-BN20: Quality of Life Questionnaire for Cancer – Brain Cancer Module; SCID: Structured Clinical Interview for DSM-IV Disorders; SF-36: Short Form (36) Health Survey; SNAS: Sherbrooke Neuro-oncology Assessment Scale; SRDS: Zung Self-Rating Depression Scale; STAI: State Trait Anxiety Inventory; STAI-1: State Trait Anxiety Inventory-1; STAI-2: State Trait Anxiety Inventory-2.
5.4.4. Demographic factors

Fourteen studies aimed to investigate the relationship between at least one demographic variable and HRQoL/psychological outcomes.

**Sex.** Patients’ sex was included as a variable in 11 studies of varied quality, in which evidence was mixed. Arnold et al’s evaluation of 363 patients with various brain tumors indicated that women were at a significantly higher risk of developing depression than men, and that generalized anxiety trended towards a similar relationship.48 This study however received a lower quality score, in part due to the mixed sample of high- and low-grade brain tumors. Furthermore, five studies concluded that sex was not significantly related to patient-reported (or, in one case, physician-reported) anxiety or depression.24,37,39,43,52 HRQoL was found to be significantly greater in men than women in one study of moderate quality, however only for patients with grade III tumors,47 and three further studies found no evidence of a significant effect of patient sex on HRQoL.42-44 In their study of 83 patients with PMBT, Keir et al found evidence for a significantly greater level of distress in women,17 however this finding was not replicated in a study of comparable quality by Kvale et al.18

**Age.** Eleven studies of mixed quality included age as an independent variable, with ten finding no evidence of a significant effect on levels of anxiety,46,48 depression,24,39,46,48,52 HRQoL,42,44,45,47 or distress.18,40 One study found evidence for a significant weak correlation between age and distress at baseline assessment eight weeks post-surgery, indicating greater distress for younger patients; this relationship was not significant at reassessment three and six months,40 however there was a substantial degree of attrition between the three assessment periods, which may indicate the withdrawal of patients with higher levels of distress from the study.
**Marital status.** Nine studies of mixed quality included marital status as an independent variable. Kaplan and Miner’s small study of patients with newly-diagnosed PMBT reported that married participants experienced higher levels of depression and lower levels of anxiety than non-married patients,\textsuperscript{37} although this finding was not evidenced statistically. Weitzner et al’s study of patients with varying brain tumor diagnoses found that divorced patients experienced lower HRQoL than married patients,\textsuperscript{45} although married patients accounted for a substantially greater proportion of the sample. The remaining seven studies found no relationship between marital status and anxiety,\textsuperscript{43,46,48} depression,\textsuperscript{43,46,48,52} HRQoL\textsuperscript{42-44} or distress.\textsuperscript{40}

**Education.** Giovagnoli et al demonstrated that years of education was significantly predictive HRQoL in their mixed sample of PMBT and other brain tumor patients\textsuperscript{44}, with higher-educated patients reporting greater HRQoL; however no relationship was present in two further studies.\textsuperscript{42,45} Arnold et al reported that patients with graduate degrees were significantly less likely to experience distress than patients with less than a college education, although no effect was found on levels of anxiety.\textsuperscript{48}

**Ethnicity.** No effect of ethnicity was found for anxiety\textsuperscript{48} and distress.\textsuperscript{18} Litofsky et al demonstrated a significant role of ethnicity for levels of physician-reported depression,\textsuperscript{24} although these findings were highly skewed by small numbers of non-white participants. One further study found no link between depression and ethnicity.\textsuperscript{48}

### 5.4.5. Clinical factors

All studies included in the review investigated the relationship between HRQoL/psychological functioning and at least one factor relating to clinical presentation, tumor histopathology or treatment received.
**Site and laterality.** The location of the tumor was included as an independent variable in 12 studies, encompassing the full range of quality scores. Weitzner et al reported that HRQoL was significantly lower for patients with bilateral compared to unilateral tumors on account of greater symptomatic presentation\(^45\) and Hahn et al found that participants with left hemisphere tumors reported greater depressive symptoms.\(^38\) Five further studies found no evidence for an effect of laterality on depression,\(^39,52\) HRQoL\(^47,50\) or distress.\(^40\) Only two studies of moderate quality found an effect of tumor site on patient-reported outcomes. Giovagnoli et al reported that tumors located in the anterior right hemisphere or diencephalon were significantly predictive of higher HRQoL,\(^44\) and hypothesized that this was due to the comparatively reduced impact of the tumor in this area on overall cognitive function. Raysi Dehordi et al found that depression was significantly greater in patients with PMBT located in the frontal lobe compared to other sites, improving significantly following resection.\(^39\) Six studies found no evidence for a significant role of tumor site in predicting levels of anxiety,\(^48\) depression,\(^24,48,52\) HRQoL\(^42,43\) or distress.\(^40\)

**Grade and variant of tumor.** The role of tumor grade or type of PMBT was examined in six studies of varying quality. Arnold et al reported rates of depression and anxiety were lower in patients with high-grade tumors compared to low-grade, however reported no significant difference between grades III and IV.\(^48\) Rooney et al's high quality study reported no difference between tumor grade and rates of depression\(^52\); a subsequent study conducted by Rooney et al found no evidence for differences in levels of patient-reported distress and tumor grade.\(^40\) Patients with grade III tumors in Giovagnoli et al's study reported significantly higher HRQoL than those with grade IV tumors.\(^43\) Four studies of mixed quality considered differences between patients with different variants of PMBT, all finding no evidence for variation in levels of depression,\(^52\) HRQoL\(^42,45\) or distress.\(^40\)
**Tumor volume.** Three studies considered tumor volume as an independent variable. Litofsky et al observed significantly higher rates of physician-reported depression in high-grade glioma (HGG) patients with ‘larger’ (not quantified) tumor volume and multifocal tumors, although acknowledged that there was a significant discordance between physician and patient reports of depression at all intervals, which may limit the validity of these findings. A mid-quality study by Hahn et al of patients with a variety of brain tumor diagnoses, including PMBT, demonstrated that HRQoL or depression did not differ significantly between patients with lesions ≥5cm compared to those with smaller lesions. Daigle et al also found no evidence for a significant relationship between tumor volume and HRQoL in their small study of patients recently diagnosed with GBM.

**Recurrence.** Disease recurrence was considered in two studies. No significant difference in rates of anxiety or depression was identified by Arnold et al, whereas Osoba et al found that HRQoL was greater in patients recently diagnosed with HGG compared to patients with recurrent tumors.

**Time from diagnosis.** Five studies reported on the relationship between HRQoL or psychological functioning and the length of time from diagnosis. Across five studies, no significant relationship was demonstrated between time from diagnosis and HRQoL, anxiety, depression or distress.

**Treatment factors.** Extent of surgical resection was considered in eight studies of varying quality. Brown et al demonstrated that patients receiving gross total resection (GTR) reported greater HRQoL and reduced depression following surgery compared to patients receiving biopsy only. Evidence for significantly greater improvements in postoperative HRQoL for patients receiving GTR was also demonstrated by Daigle et al and Klein et al. GTR was not found to be significantly associated with post-surgery improvement in depression or HRQoL in three studies of
moderate quality\textsuperscript{24,42,44} and one of high quality.\textsuperscript{52} Rooney et al reported partial evidence for an effect of extent of resection on patient-reported distress, as patients who received resections (extent not specified) reported less distress than those receiving biopsy only at 6 months post-surgery, but not at 8 weeks or 3 months post-surgery.\textsuperscript{40}

Neither radiotherapy nor chemotherapy schedules were found to predict differences in psychological or HRQoL outcomes in two studies.\textsuperscript{40,52} Four studies of mixed quality examined whether corticosteroid use was associated with patients’ reports of HRQoL or psychological outcomes. Reasonable evidence for a relationship between increased depression and corticosteroid use was demonstrated in two studies of patients with newly-diagnosed brain tumors,\textsuperscript{24,52} and with HRQoL in one further study.\textsuperscript{50} No significant relationship was found between corticosteroid use and patient-reported distress in one study.\textsuperscript{40}

**Performance and functional status.** Eight studies of mixed quality examined Karnofsky performance status (KPS) as an independent variable. Significant relationships were found between low KPS and greater depression,\textsuperscript{24,39,52} greater anxiety\textsuperscript{49} and reduced HRQoL.\textsuperscript{42,44,50} Non-significant relationships were reported between KPS and depression in two studies\textsuperscript{38,49} and HRQoL in one study.\textsuperscript{38}

Functional impairment was included as a variable in four studies and was found to relate significantly to decreased HRQoL\textsuperscript{12,44,51} and increased depression.\textsuperscript{12} Rooney et al reported that functional impairment was not significantly related to greater distress eight weeks post-surgery, but was a significant correlate at reassessment three and six months later,\textsuperscript{52} suggesting an impact of persistent impairment.

**Symptoms:** Epileptic seizures were not found to be related to depression or distress.\textsuperscript{24,40,52} Evidence for anti-epileptic drug (AED) use was mixed. No significant relationship was apparent between AED use and depression.\textsuperscript{52} Rooney et al found
evidence for a significant relationship between AED use and greater distress shortly following surgery, but not at reassessment three and six month post-surgery. Brown et al reported that patients prescribed AED reported greater HRQoL than those not, whereas Klein et al found no significant difference between patients treated with AED and those not.

Impairments in self-reported cognitive functioning were found to be related to increased depression and reduced HRQoL. Cognitive impairment, as assessed using brief screening measures or formal neuropsychological assessment, was related significantly to decreased HRQoL and more depressive symptoms, but not distress. Confusion was not found to be related to patient-reported global HRQoL. Fatigue was significantly related to increased depression and poor HRQoL. Reduced sleep quality, daytime somnolence and decreased physical activity were similarly associated with significant impairments in HRQoL and greater depression.

Litofsky et al reported that physician-reported depression was significantly greater in HGG patients affected by problems with consciousness, headache, personality changes, papilledema and progressive motor deficits, but relationships to patient reports of dysphasia or sensory problems were not significant. Changes in appearance and sexual dysfunction were also related to depression. Osoba et al observed that a key predictor of reduced HRQoL is motor impairment, whereas language deficits were not significantly related. Fox et al found that pain was neither a significant correlate of depression nor HRQoL in HGG patients. Distress did not appear to be related to patients’ self-reports of neurological symptoms in three studies.
5.4.6. Mental health factors

Twelve studies examined the role of mental health factors on outcomes relating to HRQoL/psychological functioning.

**History of mental health difficulties:** Three considered whether previous mental health problems affected the likelihood of developing difficulties post-diagnosis. Arnold et al demonstrated that prior mental health problems significantly predicted post-diagnostic depression and trended towards significance for post-diagnostic anxiety,\(^48\) although in both cases numbers of participants disclosing previous difficulties were small. Rooney et al also identified a greater level of current depression in participants reporting previous depression,\(^52\) Inferential support could not be provided by Kilbride et al due to their small sample size, but descriptive analyses indicate greater levels of post-operative depression in patients with a history of mental health problems.\(^46\) However in these three studies it was unclear as to whether any participants reporting current depression or anxiety were experiencing significant mental health problems immediately before diagnosis, which would have persisted post-operatively, or whether prior experience of mental health problems predisposed participants to mood disturbances precipitated by diagnosis.

**Depression:** The relationship of current depression to HRQoL was examined in four studies, all providing evidence for a significant relationship between increased depression and decreased HRQoL.\(^12,41,42,44\) In addition, Rooney et al reported that a diagnosis of major depressive disorder was significantly related to patient-report distress at eight weeks and three months post-surgery, but not at six months.\(^40\)

**Anxiety:** Relationships between current anxiety and HRQoL were investigated in two studies, both reporting evidence of a significant correlation between heightened anxiety and reduced HRQoL.\(^42,44\) Kaplan et al. reported that specific worries about
finances, physical deterioration and marital difficulties were significantly related to greater patient-reported depression.\textsuperscript{37}

**Illness-related uncertainty**: Using structural equation modelling to explore mediating factors in a mixed sample of patients with varying grades of brain tumor, Lin et al identified that increased illness-related uncertainty was significantly related increased anxiety and greater depression.\textsuperscript{49} Uncertainty was not investigated as an independent variable in any other study.
5.5. Discussion

Our primary aim was to systematically review evidence for factors associated with HRQoL and psychological outcomes in adult patients with PMBT. A secondary, related aim was to assess the quality of the evidence in this field and provide recommendations to guide the ongoing research agenda.

5.5.1. Summary of findings

In conducting this synthesis, we have tentatively identified important factors that relate to patients’ HRQoL and psychological functioning. These factors are summarized in table 5.3. Where greater than two-thirds of studies provided significant evidence for a factor, we have identified this factor as potentially significant to patient functioning. Factors where less than one-third of studies provided significant evidence were considered not significant. Where factors fall between these categories, or where factors have been investigated in only one study, we have considered these inconclusive.

Evidence for an effect of demographic differences was mixed. Although survival declines with age, variability in patient-reported outcomes remained comparable between age groups. One reason for this may be that patients’ resiliency increases with age, possibly offsetting the toll of increased deterioration. The lack of an effect of age is consistent with findings within the general population. Where significant demographic differences were found, these tended towards lower impairment in men, which may reflect greater resiliency or reduced tendency to report difficulties, and differences were consistent with gender differences observed in the general population. Some evidence indicated a general trend towards greater functioning in patients who were married, white or from higher educational backgrounds; reliability of these associations is limited by substantial homogeneity within samples.
Table 5.3. Summary of factors relating to HRQoL/psychological functioning by degree of evidence.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Total studies (n)</th>
<th>Studies reporting significant evidence (n)</th>
<th>Studies reporting mixed evidence (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence of significant negative relationships to outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current level anxiety and worry</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Current level of depression</td>
<td>5</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Current level of functional impairment</td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Current level of motor impairment</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Current use of corticosteroids</td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>History of mental health problems</td>
<td>3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Symptom: cognitive impairment</td>
<td>7</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Symptom: fatigue</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Evidence of significant positive relationships to outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KPS</td>
<td>8</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Evidence of no significant relationships to outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>11</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Current level of neurological function</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>3</td>
<td>1</td>
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</tr>
<tr>
<td>Marital status</td>
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<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Radiotherapy/chemotherapy schedules</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sex</td>
<td>11</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Symptom: language problems</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Symptom: seizures</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Time from diagnosis</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Tumor grade</td>
<td>6</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Tumor site/laterality</td>
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<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Tumor volume</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Inconclusive evidence of relationships to outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current use of AEDs</td>
<td>4</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Extent of resection</td>
<td>8</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Level of education</td>
<td>4</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Recurrence</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Evidence only available from one study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Changes in appearance</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Current level of physical inactivity</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Current level of sleep quality</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Current level of illness-related uncertainty</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Symptom: confusion</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Symptom: daytime sleepiness</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Symptom: headache</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Symptom: loss of consciousness</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Symptom: pain</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Symptom: papilledema</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Symptom: personality changes</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Symptom: sensory problems</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Symptom: sexual dysfunction</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

<sup>a</sup> One study reported descriptive statistics only
Findings concerning mental health variables were generally consistent. A history of mental health problems was related to the incidence of depression and poor HRQoL post-diagnosis; however this was only considered by three studies, of which one study could only provide descriptive support due to a small sample size. Given the apparent importance of previous mental health difficulties for patients with PMBT, it is necessary for further research to consider this factor. The experience of current depression or anxiety was related to impaired patient-reported HRQoL. Further research is necessary to determine the extent to which post-diagnosis depression is a consequence of illness-related metabolic or structural changes, or negative psychological reactions to the disease.

The nature of the relationship between clinical factors and HRQoL/psychological outcomes varied. Significant correlations between tumor characteristics and HRQoL/psychological outcomes appeared to be due to the uneven recruitment of participants across grades in study samples. Corticosteroid use was found to be related to increased depression and lower HRQoL. Recurrence appeared to be related to lower HRQoL, but not anxiety or depression. Low performance status and increased functional impairment were typically related to increased mental health problems and reduced HRQoL, particularly as patients progress further in the disease trajectory. Relationships between AED use and outcomes were inconclusive and were not sufficiently differentiated from the impact of seizures; when reported separately, seizure activity showed no significant relationship with HRQoL or psychological functioning. With regards to specific symptoms, conclusions are limited by lack of evidence with many only investigated in one study. Where more than one study provided evidence, HRQoL/psychological outcomes were significantly related to the experience of cognitive difficulties (both as formally assessed and self-reported), fatigue and motor impairment.
5.5.2. Quality of the literature\textsuperscript{vii}

The overall quality of the literature was generally moderate, with substantial variability between studies. In general, the majority of studies used validated psychometric tools to assess outcomes of interest. However, as described in table 2, a broad range of outcome measures were used to assess similar constructs; for example, we identified twelve separate measures of QoL/HRQoL. The quality of the literature would be vastly improved, and allow for comprehensive meta-analysis, if there were greater consistency in the choice of outcome measures.

Our review aimed to focus exclusively on findings for patients with histologically-confirmed diagnoses of PMBT. The number of relevant studies where patients with PMBT were recruited exclusively was low (n=14). By including studies where at least 75% of participants recruited were diagnosed with PMBT (n=7), we broadened the scope of the review at the expense of some specificity. Studies combining PMBT and other brain tumor diagnoses compromise the methodological quality and validity of these findings for patients with PMBT. As such, the seven papers where small numbers of patients with non-PMBT diagnoses were recruited received lower quality scores. In all cases there was no clear rationale to justify why these patients were recruited.

The majority of authors did not demonstrate how their sample represented the wider population of patients with brain tumors, either by explicit statement or by similarity to published prevalence data.\textsuperscript{26} Most did not provide adequate justification for sample sizes and only four referenced a priori power calculations. Furthermore, the majority of literature included in our review reported correlations for cross-sectional data, reducing the strength of this evidence. These limitations may be evident of the

\textsuperscript{vii} See also section 7.2.4.
practicalities of conducting such research with critically ill patients, where investigators cannot afford to be highly selective during recruitment.\textsuperscript{58}

5.5.3. Considerations for further research

Our review has identified a number of methodological weaknesses in the current evidence base which limit our understanding of patients’ HRQoL and psychological functioning following diagnosis of PMBT.

**Exclusivity of sample.** Many studies identified during electronic database searches reported findings for a unified group of “brain tumor patients”, consisting of both patients with PMBT and those diagnosed with low-grade brain tumors. The findings of studies where diagnostic categories have been combined as such are limited, as prognoses, treatment options and disability varies widely between low and high grades of tumor.\textsuperscript{6} Although recruitment of both groups of patients has value, further research should endeavor to clearly delineate these groups in analysis.

**Greater consensus in choice of outcome measures.** The use of measures to assess identical or similar outcomes significantly limited comparisons between studies. Although different measures of depression or HRQoL may present with reasonable face validity, there can be subtle differences between validated and widely used outcome measures in their assessment of hypothesized contributing factors.\textsuperscript{59} As such it is possible that HRQoL or distress constructs vary significantly between instruments. Greater consensus in the choice of assessment instruments assessing HRQoL/psychological outcomes, guided by increased understanding of theoretical models underlying constructs of HRQoL, would lead to greater consistency in the literature and allow for more-rigorous comparison. The proliferation of studies within oncology using the Distress Thermometer\textsuperscript{16} may herald a movement towards such
standardization; however, such rapid screening measures are criticized for their questionable validity, limited specificity and oversimplification of a multifaceted patient experience.60

Attention to mediating factors: Although our review has demonstrated the complexity of factors relating to psychological functioning and HRQoL, the reliance of many studies on correlation limits our capacity to identify causal and directional relationships between factors and outcomes. Four studies included in the review used regression analyses to identify discrete predictors of HRQoL/psychological outcomes37,40,42,52; although increasing the predictive validity of the results, this does not account sufficiently for causality or simultaneous contributions of the myriad of patient and illness factors. Only one study used structural equation modelling to observe the concurrent interaction of variables mediating relationships between illness factors, psychological processes and patient functioning.49 In order to further our understanding of the patient experience of PMBT, we recommend that further research designs should aim towards mediation analysis, repeated sampling, or through treatment investigations targeting processes of change, rather than causal interpretation of findings from cross-sectional designs and correlations.

5.5.4. Potential implications for clinical practice

Promoting and maintaining patients’ HRQoL is central to clinical guidance.28,29 Based on the findings of this review, we advocate the following practice points:

i. Clinicians should ask patients directly about whether they have experienced mental health difficulties in the past and whether they currently feel depressed or anxious, referring patients for specialist support as appropriate.
ii. Patients reporting difficulties with cognition, functional independence, motor function or fatigue should be monitored closely, as they may more be more likely to experience greater impairments to their HRQoL and psychological functioning.

iii. Patients prescribed corticosteroids should be advised of possible side-effects relating to depression. Their mood should be monitored for the duration of this medication.

5.5.5. Limitations of the review

The wide range of methodologies and outcome measures included in this review limits the robustness of conclusions; and meta-analysis was neither possible nor appropriate. We elected pragmatically to not exclude studies on the basis of their methodological quality; although none were of such low quality as to invalidate findings, we acknowledge that the variance in quality can place undue value on conclusions drawn. We have tried to minimize bias and reporting error in our conclusions by adhering to published guidance on narrative synthesis35.

Although we used a validated assessment framework33 with adaptations compliant with published guidelines34, quality assessment is prone to subjectivity61. As independent assessment of a subset of studies yielded adequate inter-rater reliability, we can at least be confident that quality assessment was generally consistent within this review.
5.5.6. Conclusions

Our review has identified tentative evidence for a range of clinical and mental health factors that relate to HRQoL and psychological functioning in patients with PMBT, which could be used to identify individuals ‘at risk’ and to enhance frameworks of supportive interventions. These findings are however limited by a number of methodological flaws present throughout the literature. In order to advance this area of knowledge, the field would benefit from greater consensus on the choice of outcome measures. Investigators must also consider their research designs carefully, as further cross-sectional, correlational evidence in this field is unlikely advance our current understanding.
5.6. References


28. Lovely MP. *Care of the Adult Patient with a Brain Tumor.* Chicago, IL: American Association of Neuroscience Nurses; 2014.


6. Paper 2: Empirical study

Maintaining, reframing and changing: An exploratory qualitative study of psychosocial adjustment to glioblastoma

Paper 2 is a qualitative exploration of the processes of psychological adjustment as experienced by 10 patients diagnosed with glioblastoma who were receiving active treatment. Data were analysed in adhering to a constructivist grounded theory methodology. The paper concludes by discussing the implications for current supportive care and clinical practice.

This study has been prepared for submission to *Psycho-Oncology* in accordance with the guidelines for contributors (appendix 8). As such the paper is written in UK English and adheres as closely as possible to the style guidelines specified by the publisher, while ensuring compliance with the *University of Manchester Presentation of Theses Policy*. Tables and figures have been incorporated into the text to aid readability and reference; for the version submitted to *Psycho-Oncology*, tables and figures were submitted as separate sheets as per the guidelines for contributors. Footnotes that cross-reference other sections of this thesis were not included in the journal copy. Advice was sought from the editor-in-chief of *Psycho-Oncology* with regards to the suitability of the manuscript for publication.

Word count: 4033

(including abstract; excluding references, figures and tables)
6.1. Abstract

**Objective:** To explore psychosocial adjustment processes within patients (aged 18 years and above) with glioblastoma.

**Method:** Semi-structured interviews with patients (n=10) 3.3-5.1 months post-diagnosis were analysed using a constructivist grounded theory methodology.

**Results:** Three categories described participants' adjustments: maintenance processes (maintaining continuity with life before diagnosis); reframe processes (finding stability in the present); and change processes (promoting adaptation to an uncertain future, living with the effects of glioblastoma and treatment).

**Conclusions:** All participants described engaging in processes across all categories. Adjustment processes are homeostatic; by effectively balancing these processes, individuals can achieve a “healthy rebalance” of their emotional equilibrium. Findings provide a framework for supporting patients with an illness for which there remains limited psychological understanding.
6.2. Introduction

Glioblastoma (GBM) are the most common and aggressive variant of brain tumour in adults[1], with a median survival time of 15 months for patients receiving optimal treatment[2, 3]. Many patients experience mobility problems, debilitating fatigue, cognitive impairment, emotional dysregulation and behavioural changes, either as symptoms of progressive disease or as side effects of treatment[4-6]. Approximately one-third of patients experience clinically significant symptoms of depression and anxiety[7-10].

A diagnosis of cancer signifies a forceful departure from one’s expected life trajectory[11-13]. Adjustment describes the social-cognitive processes that occur within an individual, allowing them to manage, learn from and adapt to the multitude of changes precipitated by illness and treatment[14]. Rather than representing absence of distress or the end-point of coping[15], positive adjustment involves the modification of core assumptions and integration of illness into patients’ life narratives[16-18]. The processes and outcomes of positive adjustment are likely to differ between individuals and cancer diagnoses[19-21].

Much remains unknown about patients’ adjustment to GBM[8]. The neurocognitive sequelae of brain tumours and treatments can impair engagement with adjustment processes[22, 23], limiting the application of extant theory for other conditions[24, 25]. As clinical variables and cognitive impairment alone cannot account for adjustment[22], psychosocial variables are considered key mediators of patients’ adjustment outcomes.

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1 See also sections 7.3.1 and 7.3.2.
Maintenance of psychological wellbeing is central to clinical guidelines[26-28], yet limited empirical understanding of patients’ experiences restricts the provision of supportive interventions. Ownsworth et al[20] identified several processes adjustment processes in patients with malignant and benign brain tumours, concluding that common personal and social elements exist that require further exploration. Cavers et al[29] described the importance of reassurance, hope and effective communication in promoting adjustment to brain tumour, but did not focus on specific adjustment processes.

The present study aimed to extend previous work by exploring adjustment exclusively in patients with GBM. Semi-structured, individual interviews were analysed within a constructivist grounded theory methodology to identify specific processes facilitating or impeding adjustment.
6.3. Methods

6.3.1. Participants

Following NHS ethical approval, participants (aged ≥ 18 years) diagnosed with GBM were recruited from nurse-led consultation clinics covering a large, economically diverse area. Patients were eligible for participation if they were 3-7 months post-diagnosis, as patients may be most receptive to reflecting on psychological processes during this timeframe[30]. Restricting recruitment to this window ensured most patients were able to participate, and were not receiving treatment of such intensity to render participation excessively burdensome.

Patients were excluded if: their Karnofsky performance score at recruitment was below 40%; they were considered by their care team to be too unwell and/or distressed to provide informed consent or for participation to be appropriate (allowing for the wide range of emotional presentations common in this condition); or severe speech impairment rendered interview inappropriate.

Sampling was theoretical, in that the research team aimed to identify and recruit patients across the continuum of emotional distress, facilitated by the clinical judgement of the patients’ care team. Sampling continued in parallel with qualitative analysis, allowing construction of theory to influence recruitment, which continued until a point of theoretical sufficiency[31]. Of the 15 patients approached, 10 provided consent to participate. Of those declining participation, two deteriorated shortly after providing verbal consent, and three did not consider participation appropriate at present. Demographic data are presented in table 6.1.

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2 See also sections 7.3.3, 7.3.4 and 7.3.5.
Table 6.1. Clinical and demographic characteristics of participants

<table>
<thead>
<tr>
<th>Participant number</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Time since diagnosis (months)</th>
<th>Distress score (DT)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Depression score (DASS-21)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Anxiety score (DASS-21)&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Stress score (DASS-21)&lt;sup&gt;d&lt;/sup&gt;</th>
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</thead>
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<td>Pt08</td>
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<td><strong>Median</strong></td>
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<td>6</td>
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<td>5.0-7.0</td>
<td>2.3-7.00</td>
<td>1.3-8.8</td>
</tr>
</tbody>
</table>

<sup>a</sup> Caseness defined as score ≥6

<sup>b</sup> Normal range: 0-4; Mild range: 5-6; Moderate range: 7-10; Severe range: 11-13; Extremely severe: ≥14

<sup>c</sup> Normal range: 0-3; Mild range: 4-5; Moderate range: 6-7; Severe range: 8-9; Extremely severe: ≥10

<sup>d</sup> Normal range: 0-7; Mild range: 8-9; Moderate range: 10-12; Severe range: 13-16; Extremely severe: ≥17
6.3.2. Measures

**Distress Thermometer.** The Distress Thermometer (DT)[32] is a brief screening tool used throughout oncology settings[33], and is supported by UK and US clinical guidance[34, 35]. The DT consists of a visual analogue scale ranging from ‘0’ (“no distress”) to ‘10’ (“extreme distress”). Participants were asked to indicate the level of distress experienced over the previous seven days. Scores above five indicate clinically-significant levels of distress in patients with brain tumours[36]. Participants’ scores are presented in table 6.1.

**Depression Anxiety Stress Scale.** The 21-item version of Depression Anxiety Stress Scale (DASS-21)[37] consists of three subscales measuring anxiety, depression and stress. Participants were asked to consider their mood over the previous seven days and rate their responses to items on a 4-point scale from ‘0’ (“Did not apply to me at all”) to ‘3’ (“Applied to me very much, or most of the time”). The DASS-21 has been validated for use with patients with brain tumours[7]. Participants’ scores are presented in table 6.1.

6.3.3. Procedure

Eligible patients were approached by a clinical nurse specialist (CNS), with whom they had frequent contact throughout treatment. The CNS provided patients with the information sheet and sought verbal consent for the lead author (PDB) to contact them by telephone within three working days to discuss the study. If patients expressed interest in participation, PDB arranged an appointment to obtain written consent, conduct the interview and complete the measures above. All chose to be interviewed at home. As sampling was theoretical, the CNS was instructed to selectively approach
patients with characteristics required to further develop theory (e.g. female participants, or those experiencing acute distress.)

Semi-structured interviews were conducted by PDB. The interview schedule prompted participants to talk about the physical, cognitive, social and emotional impact of their illness; their understanding of ‘adjustment’ in relation to their own experiences; and external and internal facilitators and barriers to adjustment. The schedule was developed through consultation with members of a local patient support group and refined throughout recruitment through discussion with the research team. Interviews were audio-recorded and transcribed.

Interview data were analysed using a grounded theory framework\(^3\), which is an appropriate methodology for when there is little established theoretical understanding\(^{[38]}\). Analysis adhered to the principles of constructivist grounded theory to examine how and why participants construct meaning and action in response to the ongoing challenge of illness\(^{[39]}\). Following the process described by Charmaz\(^{[40]}\), the authors met regularly to discuss the ongoing coding and emergent analysis. This allowed the acknowledgement of subjectivity throughout data collection and analysis\(^{[41]}\). In adopting a reflexive stance towards this data\(^4\), the products of analysis represent interpretations grounded in context rather than objective observation\(^{[42]}\). The stages of analysis are described in table 6.2.

Although analysis was ‘grounded’ within the data, the authors were mindful of the need to be interpretive, particularly when participants used normative language to describe experiences\(^{[39, 43]}\). As analysis ran alongside data collection, the authors used later interviews to check and develop aspects of the constructed theory. Earlier

\(^3\) See also section 7.3.6.
\(^4\) See also section 7.3.7.
Table 6.2. Process of data analysis

<table>
<thead>
<tr>
<th>Stage</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Initial coding</td>
<td>Line-by-line coding and identification of in vivo codes</td>
</tr>
<tr>
<td>2. Memos</td>
<td>Memo writing to describe each case</td>
</tr>
<tr>
<td>3. Focused coding</td>
<td>Identifying patterns in initial coding and raising to focused coding using gerunds to describe action</td>
</tr>
<tr>
<td>4. Memos</td>
<td>Memo writing to compare and contrast incidents between cases using focused and initial coding</td>
</tr>
<tr>
<td>5. Refining topic guide</td>
<td>Using memos and focused coding to identify gaps in understanding, then revising the interview topic guide</td>
</tr>
<tr>
<td>6. Clustering and drafting conceptual maps</td>
<td>Grouping together focused codes that describe similar thematic concepts and drawing maps to demonstrate commonalities and contrasts in data</td>
</tr>
<tr>
<td>7. Theoretical sorting</td>
<td>Using memos, clusters of focused codes and conceptual maps to identify tentative theoretical categories</td>
</tr>
<tr>
<td>8. Theory construction</td>
<td>Memo writing to hypothesise the functions of and relationships between categories</td>
</tr>
</tbody>
</table>
interviews were revisited as new categories were developed to extend, refine and test the theory. Data and coding were organised and collated using NVivo 10 for Windows (QSR International, Version 10.0.138.0).
6.4. Results

Ten participants completed semi-structured interviews (median duration: 55 minutes; range: 42-65 minutes). Three scored above the clinical threshold for distress on the DT. Responses on the DASS-21 indicated scores above the ‘normal’ range (defined by the authors as scores above the 78th percentile) for depression in eight participants, anxiety in six participants and stress in four participants (see table 6.1).

A number of tentative, theoretical categories were constructed to describe and collate the products of initial and focussed coding, which helped to guide ongoing data collection. Categories were merged, separated and reconstructed to conceptualise data as analysis evolved. Three categories were identified as theoretical concepts of adjustment processes: maintaining connections to the past; reframing present experiences; and changing to face a future living with GBM. These categories are described separately, with attention to particular nuances within and between participants, and with consideration of whether participants engaged with processes as active agents or passive recipients.

6.4.1. Maintaining

In maintaining connections to the past, participants affirmed continuity of their existence, in spite of the impact of GBM. Much affirmation existed within discourses of “still leading a normal life”[Pt01] and “pottering along”[Pt02], emphasising continued familiarity of life. Through maintaining everyday activities, participants evidenced independence, despite their difficulties.

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5 See also section 7.3.6.
“I’m trying to get back to reading and doing things I used to [...] my daughter’s looking after me, but I can look after myself, I always have”[Pt06]

Participants’ maintenance of particular roles or positions present before diagnosis evidenced further efforts to maintain proximity to normality. Some described attempts to continue working, or fulfilling obligations within their family, at a reduced capacity; although described as ways to “keep going”[Pt07], they necessitated confrontation with activities that were no longer possible:

“I’ve been working part time. Could probably work a bit longer if I tried, but it’s taking it out of me[...] I try to do some things and sometimes it doesn’t work[...]I’ve got to come to terms with it”[Pt07]

For some, the prospect of not maintaining this level of independence was untenable, as relinquishing such control was synonymous with resignation. [Pt02] described appreciating the importance of rest, however this opposed his drive to live “what [time] I’ve got left”. This determination to maintain independence also conflicted with others’ intentions to help. Some perceived the sympathy of others as adverse or as a threat to this determination:

“I’ve been saying[...] ‘Don’t feel sorry for me,[...] I don’t want sympathy, I just want to have a normal, everyday, carefree life”[Pt03]

Many referred to the need to hold an awareness of the reality of their situation, while trying to maintain connections to the normalcy of life. None presented as in ‘denial’: all acknowledged the significance of their diagnosis and prognosis.
“I might be in denial, but I am aware of the seriousness of the sort of cancer I’ve got[...] I’m not sure that I’m strong enough to face it”[Pt04]

In order to maintain balance between these states, participants described acknowledging the limits of their capacity to cope. Some deployed this in anticipation of receiving distressing information. [Pt08] talked about needing to be proactive in instructing her consultant about the information she could receive:

“I’ve been careful not to hear what I don’t want. [The surgeon] said ‘Don’t ask me if you don’t want to know because I’m very blunt and will tell you the truth’”

However, quantifying the capacity of their coping resources required patients to confront and appraise the incoming ‘truth’ before deciding to enquire further, and risk receiving information beyond their coping limits, or remain safe in uncertainty. Some acknowledged this form of self-protection was limited. [Pt01] indicated her doubt about this strategy, but that it was her preferred way of managing her current predicament:

“I sometimes ask myself[...] “Am I just pretending?” I honestly don’t know, but I know the alternative would be worse”

Many invested in protecting those close to them from the impact of their illness. In some cases, attempts to support their loved ones bolstered participants’ resolve during times of vulnerability. For example, [Pt07] talked about his need to “be strong for my family[...] make it easier[...] show I’m not worried by this whole thing”; by doing this, he was able to maintain and reinforce a role in supporting his family. However, some acknowledged that supporting others required the suppression of their true emotional reactions, leading to unmet need:
“Still can’t speak with my husband, he just breaks down[...] There are things I want to discuss, or even just say how I’m feeling[...] I feel like I’ve always got to say ‘I’m fine’ even if I’m having a bad day” [Pt10]

6.4.2 Reframing

Participants described ways in which they attempted to manipulate their view of their ‘here and now’ circumstances. Many talked of the need to seek out sources of positivity to offset present challenges. For some, optimism came from perceptions of being cared for by their clinicians, noticing improvements following treatment, or taking comfort in positive messages. [Pt06] recalled a conversation when his consultant praised him for taking care of his health during chemotherapy, commenting “It’s nice knowing somebody believes in you so much.”

For others, finding positivity required an active stance of testing their abilities in these new circumstances. Rather than affirming that illness had not overcome their identity through the maintenance of roles and routines, as described previously, some talked about how proving some independence in spite of impairment was a source of self-esteem. [Pt01] reflected on her attempts to engage in normal activities and how, although taxing, they provided glimpses of hope despite her significant level of impairment.

“I’ve got to prove that I can still[...] make a difference. That I can do normal jobs and complete them [and say] ‘Oh! I’ve done that! There is still hope!’ But it’s more a battle than before”
Another construction of reframing described how participants made sense of the divergence of their life narratives from anticipated trajectories. In acknowledging disappointment, many took the opportunity for expressing their gratitude for life. Some were thankful for material gains and accomplishments: in talking about his house and his business successes, [Pt02] proudly proclaimed “I’m not being big headed but I worked[…] hard to get this.” [Pt07] declared “Nobody’s going to take these achievements away from me.” Most gave thanks for their relationships with others, or of raising families; in the face of a changed and uncertain future, participants found comfort in acknowledging their achievements of having been a good spouse or parent.

“That’s been one of the biggest adjustments, not seeing [granddaughter] as often[…] but we were lucky to have built up a lovely relationship with her over the years[…] I’ve just got to accept that we got that time”[Pt01]

Gratitude was also present in participants’ consideration that “things could be much worse [Pt07]. Some made comparisons to those they perceived as having symptoms worse than their own. [Pt02] reflected on his observations of the waiting room:

“Some people there are like cabbages, they’re just getting by[…] I thought ‘that could have been me’[…]There’s a lad with bowel cancer[…]and he looks like shit[…]All I had was constipation”

Participants spoke of the need to identify aims, to guide coping efforts and to exercise agency. [Pt01] spoke of how she was able to cope “better than perhaps I’m doing now” during her acute recovery from surgery because she had specific goals to meet:
“I had something to aim for. I had to get myself out of hospital [...] my grandchildren came in to see me and I had to [...] appear normal to them [...] so that kept me going”

Following her return home, she recalled struggling with her mood and motivation, until she was able to identify additional goals, such as regaining mobility and going shopping. Others referenced the need to identify aims, such as regaining or maintaining functional ability:

“Walking’s got to be the first thing [...] being able to get up and not be ended by the fact my knees are sore or shaky [...] learning that I’m able to get up and power through it”[Pt07]

A final theme of reframing concerned ways in which patients equated present difficulties with previous stressful events, drawing upon their guiding principles or ways of living, developed through prior experiences. For most, such principles were rooted in resilience, providing reassurance that current challenges could be surmounted as had others before. [Pt05] reflected on his previous triumphs over illness, motivated by his need to provide for his family:

“I don’t do sick. I had a heart attack twenty years ago [...] and I was straight back to work [...] The kids don’t eat so you’ve gotta get up and get on. And this is the same”

These principles were mostly optimistic, with participants emphasising attitudes of “[looking] on the bright side of life”[Pt06] or “I can solve this”[Pt03]. Some derived positivity from pessimistic or fatalistic ways of viewing the world. [Pt01] explained “I’ve always dreaded having a brain tumour. Now I’ve got it nothing worse can
happen!” [Pt02] described how a lifelong conviction with the prospect of dying from
lung cancer had prepared him for dealing with his brain tumour:

“I’ve always had that in the back of my mind, ‘Crack on with stuff because
you’ll be getting it’ [...] so this hasn’t come as a big shock [...] bit of a
positive thing ‘cos now I’m like ‘Yeah! I didn’t get lung cancer’ “

6.4.3. Changing

All described processes of tentatively creating new life narratives, incorporating
their illness and associated symptoms. On a practical basis, many spoke of developing
strategies mitigating the impact of symptoms on daily life. In managing her fatigue,
[Pt10] explained “I’ve learnt that it’s not worth pushing myself, it just gets worse. So I have
a cup of tea and get to bed for an hour”. [Pt01] and [Pt06] lamented that they were
unable to read books due to visual impairment, but were now using audiobooks instead.
[Pt02] described slowing his speech to manage his speech difficulties:

“I’m second-checking myself all the time [...] If I talk slow, I’ll talk
correctly [...] to give my brain a little time while it’s rejigging”

In accommodating illness, some attributed the cognitive and social changes
experienced since onset to their expected development in later life, or as consistent with
prior idiosyncrasies; changes associated with GBM were normalised, rather than
construed as aberrant. When describing his strategy for coping with memory
difficulties, [Pt02] commented “it wasn’t that great before!” [Pt06] attributed his
transient confusion and disinhibition to having “always been a silly grandad [...] [the
tumour] was just exaggerating it more.” In resolving her grief about being unable to care for her grandchildren, [Pt01] acknowledged this would be expected with age:

“I just can’t do everything that I used to do with [them][...] but when they get to nine or ten[...] that relationship gets a bit less close generally”

A diagnosis of GBM confronted all participants with a life-changing situation, and many spoke of how this provided them an opportunity to reprioritise their concerns. In some cases, reprioritisation allowed participants to focus on their “bucket lists”[Pt04] and to “get as much enjoyment as you can”[Pt01]. Participants used this opportunity to consider the utility of ongoing arguments with those close to them or involved in their care. In discussing ongoing family conflict, [Pt02] remarked “[cancer] focusses you in on what’s really important[...] most of the things we all fall out about are not.” [Pt08] admitted “I tend to neglect some people[...] because I’ve got more important things to worry about.” [Pt05] became tearful when recounting an adverse experience with his consultant. Later in the interview, he reflected:

“Why am I giving myself stress[...] thinking and worrying about what somebody said[...] when really I should be focussing on the biggest fight?”

In contrast to attempts to maintain continuity, participants described the need to modify their roles in order to adapt to a future changed by GBM. All talked about how their spouse or other family members had been required to take over various roles previously held by themselves, such as driving or managing finances. Some were able to take an active role in permitting such changes:

“My wife[...] has struggled at times[...][she’ll ask] ‘How do I do this?’ and I’ll say ‘I’ll show you, we’ll do it together the first few times’[...] she’s coped well with that” [Pt03]
Participants unable to take an active role in these transitions perceived such change as a substantial loss. [Pt05] recalled that when instructed by his consultant to surrender his driving license, he lost his ability to work and provide for his family without warning. [Pt08] talked of how her sudden onset of symptoms changed her from being “a mum[...] who people relied on[...] to very much reliant on other people.” For [Pt07], the shift in the dynamic of the relationship with his wife was a significant source of distress:

“You go from being a couple that looks after each other[...][to] where you’re worried about whether the other one’s going to die or not[...] you can’t set it back to what it was, because you know there could be an end to the relationship, and the life that you have”
6.5. Discussion

Patients with GBM were interviewed to explore processes of psychosocial adjustment. Participants’ emotional presentations were considered typical for this stage of treatment. Three theoretical categories captured processes participants engaged in to maintain connections to past identities, cope on a daily basis, and move towards uncertain futures. Analysis indicated that, despite heterogeneity between participants, all engaged in processes across each category.

Adjustment has been described as a means to regain emotional equilibrium[15] and resembles Cummin’s concept of subjective wellbeing homeostasis[44, 45], which posits that numerous processes are engaged to maintain stability of wellbeing. Within a model of optimal adjustment to GBM, it is plausible that individuals must balance maintaining, reframing and changing processes simultaneously to achieve a “healthy rebalance”[18] of homeostatic equilibrium (see figure 6.1). By extension, overinvestment or neglect of particular processes, particularly in response to new challenges, may lead to difficulties[17, 46].

The processes identified in this study supports the “maintaining” and “adapting” processes described by Ownsworth et al[20], illustrating how these are enacted by patients with GBM. The present study provides evidence for an additional process of reframing, which described participants’ attempts to mitigate threat in the ‘here and now’. Participants’ protection of themselves and others by maintaining normality while holding awareness of their objective reality closely resembled the concept of disavowal[47, 48]. In contrast to denial, disavowal represents an adaptive coping mechanism by which patients can simultaneously acknowledge and temper the
Figure 6.1 A conceptual model of patient’s adjustment to GBM

Maintaining
- Independent in activities
- Maintaining self and social status
- Protecting self and acknowledging limits
- Protecting others, meeting their needs

Changing
- Reprioritising concerns
- Accommodating change
- Normalising experiences of change
- Modifying roles and relationships

Reframing
- Finding positives
- Having goals and aims
- Being thankful
- Using guiding principles
significance of factual clinical information. Within dynamic models of adjustment, disavowal provides a mechanism by which patients ‘stall’ their processing of threatening information to regain equilibrium. By reframing or reconstructing their experience of present events, participants could attempt to manage acute episodes of distress, while making additional resources available to past and future-oriented processes of adjustment.

6.5.1. Limitations\(^6\)

The study reports on a small sample of patients, all whom identified as White British; the authors however sought to recruit a sample representative of the wider GBM population while maintaining homogeneity in terms of the ‘standard’ presentation and ‘standard’ treatment protocol in the United Kingdom. Findings may have been skewed by limited recruitment to patients above particular thresholds of function, therefore this analysis may not represent the views of those most distressed or impaired. Recruitment via one CNS may have increased selection bias, however the CNS was highly experienced in patient recruitment and was the sole neuro-oncology CNS for the region. The decision to recruit patients 3-7 months post-diagnosis was based on previous research and pragmatism, therefore findings may only be applicable to patients within this timeframe.

\(^6\) See also section 7.3.8.
6.5.2. Potential Implications

The findings of this research have important implications for clinical practice, particularly while there remains limited published evidence for brain tumour-specific supportive interventions[49]. Irrespective of psychological morbidity, these findings provide a tentative framework for reviewing patients’ progress and delivering targeted interventions to specific areas of need. Solution-focussed, skills-based approaches have been demonstrated to be beneficial to adjustment in patients with acquired brain injuries and their families[50-52], and may be of benefit to patients with GBM. Mindfulness-based approaches are effective in improving wellbeing and decreasing distress in numerous cancer populations [53-55], and may support adjustment to GBM.

The experience of cancer-related distress is contextual and in many cases may represent a normal reaction to illness[14, 56]. Screening programmes have been criticised for assuming distress equates to need, irrespective of context[57]. As such, the utility of screening within clinical settings is questionable[58]. The present findings advocate a multifaceted approach to understanding need, necessitating appreciation of the context of patients’ experiences.

Further work is necessary to clarify these adjustment processes and identify relevant barriers, facilitators and mediators within larger, more diverse samples. As adjustment does not necessarily correlate with distress or psychological morbidity[15], the challenge for future research is to identify sensitive methodologies to identify and quantify such heterogeneous, dynamic processes.
6.6. References


28. Lovely MP. Care of the Adult Patient with a Brain Tumor, 2014, Chicago, IL: American Association of Neuroscience Nurses.


7. Paper 3: Critical appraisal and reflection

Paper 3 is an evaluation and appraisal of the systematic review and the empirical study, and is not intended for publication. This paper also includes my reflections on this area of research, the process of completing this work within the context of the ClinPsyD thesis, and the implications of this work for my professional development.

This paper has been prepared in accordance with the guidelines for contributors to *Psycho-Oncology* (appendix 8), with the exception of the word count limit.

**Word count: 10,481**

(excluding references, figures and tables)
7.1. Introduction

In their review of the supportive needs of patients with high grade glioma, Catt and colleagues caution that conducting research with this population “is not for the faint hearted” [1]. In this paper I reflect on my attempts, faint heart notwithstanding, to explore and understand the experiences of patients with glioblastoma (GBM) and primary malignant brain tumours (PMBT). I review the process of developing research questions, conducting and analysing interview data, and completing a systematic review. There is an appraisal of how this body of work contributes to the evidence base and of limitations of the processes, methodologies and conclusions drawn. I have consider how the research can be developed further, and the degree to which conducting this work has facilitated my personal and professional development.
7.2. Paper 1: Systematic Review

7.2.1. Rationale for the topic

Despite improvements in the detection and treatment of PMBT, the evidence base for interventions designed to maximise psychological wellbeing and health-related quality of life (HRQoL) is limited. This is in part understandable considering the history of brain tumour treatment. Prior to the addition of adjuvant or concomitant systemic temozolomide to a multimodal therapy of surgical resection and radiotherapy in the late 1990s, median survival for patients with GBM was 8.1 months [2], with two-year survival at 7-9% [3]. Although advances in treatments have led to significant increases in survival, prognosis remains “unacceptably dismal” [4] and improvements across brain tumours in general are dwarfed in comparison to many other cancers [5]. Research funding into neurological cancers is significantly lower than other cancers that are less burdensome in terms of years of life lost [6], and neuro-oncology service configurations have traditionally struggled to support research other than treatment trials [7]. As HRQoL research appears more common in cancer types with higher research funding and media coverage [8], it is possible that restricted funding leads to a demotion of issues on the overall research agenda for a particular disease.

When meeting with a number of clinicians and patient representatives during the planning phase of this work, I was struck by their enthusiasm for my research. Although none denied the grim reality of high mortality rates and the debilitating impact of the tumour and treatment, all acknowledged the need for research to orientate towards issues of HRQoL as a standalone concept, rather than as an ancillary variable in clinical trials. Research has long upheld that patient-reported satisfaction rarely correlates with objective improvements in clinical presentation[9]; in the absence of significant improvements in treatment efficacy that completely mitigate the varied
sequelae of PMBTs, there is a strong rationale towards the investigation of methods to enhance patients HRQoL.

In developing a review question, I was initially guided by the aims of my empirical study. My first approach aimed to review evidence of interventions promoting psychosocial wellbeing or positive adjustment in PMBT, either within patients in general or specifically in those reporting distress and maladjustment. A wide range of quantitative literature has been published over the previous two decades reporting on trials or reviewing evidence for the promotion of adjustment and wellbeing for cancers of various aetiologies and prognoses [for examples, see 10, 11-19], yet neurological tumours have received little attention. Following initial probing searches of major electronic databases (CINAHL, Medline and PsycINFO), no relevant quantitative literature was found. When broadening the review criteria to include qualitative literature, a small number of studies were identified in which participants were interviewed about their needs for support [20, 21], however none evaluated supportive interventions.

My second attempt at developing a review question focused on the process of adjustment, rather than the facilitation of positive adjustment. As discussed in greater detail in the appraisal of my empirical paper, ‘adjustment’ as a concept appears to be widely acknowledged yet eludes comprehensive definition [22]. This was a significant barrier to developing a concise question and effective protocol. There are some established methods of assessing adjustment to cancer [23-25] and illness [26] however it appeared that none had been used extensively within neuro-oncology. Considering this review question from a qualitative perspective, I noted that Sterckx and colleagues had recently published a comprehensive review of qualitative literature of the needs and experiences of patients with high-grade glioma [27], and I did not consider that
sufficient new literature had been published to justify an additional qualitative review on this area at present.

In identifying my eventual review question, I returned to my initial driver for the thesis as a whole: to produce something of direct relevance to clinical practice, for use by clinicians who may not necessarily be attuned to the psychosocial processes of adjustment. I was inspired by Dennison et al’s systematic review of what they termed “psychological correlates of adjustment” in patients with multiple sclerosis [28], where they aimed to review quantitative evidence to identify markers of wellbeing or quality of life that may be amenable to change through intervention. There have been reviews using a similar approach in relation to patients’ experiences of brain tumour [29-32], however none had specifically focused on patients with PMBT. Of these reviews, the most recent was conducted by Ownsworth and colleagues in 2009, in which the authors had applied an a priori biopsychosocial framework to search protocol [31]. Although drawing some conclusions of interest, the authors presented findings for a homogenised group of ‘patients with brain tumours’ and the application of an a priori framework limits objectivity [33]. A qualitative review in this area would have been feasible, albeit on a smaller number of studies, which may have yielded information of greater depth or clarity than the quantitative review. However it is highly likely that such a review would have had significant overlap with Sterckx et al [27]. Conducting a systematic review of extant literature in such close proximity with my empirical paper could have also increased my exposure to contaminating preconceptions and assumptions, potentially hindering the construction of a grounded theory [34].

7.2.2. Searching the literature and extracting data

In conducting the systematic literature search, I adhered to the principles of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)
Statement[35]. These principles aim to promote transparency and consistency amongst systematic reviews. At this stage of the review, adherence to these principles provided a useful framework for identifying inclusion and exclusion criteria, defining search terms and constructing a data extraction template.

Conducting systematic reviews on topics of biomedical interest can be “tedious and time-consuming” due to the large number of citations indexed in major databases [36] where even the most stringent search protocols can produce a vast number of citations. Anticipating a large number of ‘false positives’, I was motivated to ensure that the inclusion and exclusion criteria were as specific as possible. Inclusion criteria were specified as to only include studies with adult patients exclusively, using at least one validated outcome measure and where there had been sufficient statistical information reported to comment on the significance of findings. Although I wanted to maintain a focus specifically on participants with PMBT, I became aware that the samples of a significant number of studies were comprised of a majority of participants with PMBT and a smaller number of patients with non-malignant brain tumours and did not wish to exclude data that may ultimately be of relevance (the virtue of this method of sampling is critiqued in the section on quality appraisal below). Following discussion with my supervisor, we decided that the 75% threshold criterion represented an appropriate balance of excluding studies where a substantial proportion of the sample contained non-PMBT patients and including studies where investigators had recruited small numbers in comparison to the PMBT majority

Papers were excluded if they were written in languages other than English. Exclusion of non-English language sources from systematic reviews of biomedical interest can lead to systematic bias [37], however the search protocol identified only a very small number of articles written in French or Chinese and professional translation

1 See appendix 3.
of sources was beyond the scope of this review. I elected to exclude unpublished literature such as PhD theses or conference proceedings, which may have enriched the synthesis [38]. The reasons for not publishing data are important and publication bias against non-significant findings is widely recognised across many fields [39-41]. In spite of these limitations I considered these criteria to be suitable for the purpose of the review question.

In specifying the search terms\(^{II}\), I made attempts to include all forms of PMBT. The World Health Organisation (WHO) defines PMBT as WHO grade III and IV tumours [42]. The majority of papers included in the review would have been identified by the search terms “glioblastoma” or “astrocytoma”, as these terms represent the most common variant and category of PMBT in adults. To ensure that patients with PMBT not accounted for by these terms were identified, such as those diagnosed with oligodendrogial tumours, it was necessary to become familiar with the WHO classification system. Studies of participants diagnosed with anaplastic ependymomas, a WHO grade III tumour, were excluded as these tumours are regarded as clinically and therapeutically distinct from other PMBT [43]. In defining the search terms to identify articles about HRQoL and psychological functioning, I first consulted the search terms in reviews conducted previously by Ownsworth et al [31], Ford et al [29] and Taphoorn et al [32] to facilitate comparison between my review and the extant literature. In addition to specifying terms associated with negative adjustment or poor HRQoL, I was keen to search for terms relating to positive psychological outcomes and posttraumatic growth.

7.2.3. **Appraising the quality of studies**

Quality assessments are a key component of systematic reviews and the use of structured assessment tools appropriate to the range of studies under review is

\(^{II}\) See appendix 2.
essential for maintaining systematic rigour [44]. As this was my first experience of conducting a formal quality assessment, I was anxious to choose the best measure. On searching through a wide number of published measures I realised that most were designed for reviews of randomised trials of interventions. In their review of the measures available to assess the quality of non-randomised studies, Sanderson et al concluded that there is no "single obvious candidate tool for assessing quality of observational epidemiological studies" [45].

Following discussion with my supervisors, and on the recommendations of Boland et al [46], I developed an idiosyncratic assessment tool closely based on the Newcastle-Ottawa Scale (NOS)[iii] [47], a widely-used measure for assessing non-randomised studies in meta-analysis. The NOS appears to have good face validity and is considered "easy to use [and] suitable for use in a systematic review" [48]. The NOS has however been criticised for poor inter-rater reliability, in part due to the "inherent greater difficulty with assessing the quality of observational studies compared with RCTs" [49], and for producing "arbitrary results" [50].

These criticisms notwithstanding, I elected to adapt the NOS to fit the requirements of my review, in keeping with the guidance on conducting systematic reviews published by the Centre for Reviews and Dissemination (CRD) at the University of York [51]. In place of the star rating system of the NOS, I applied a numerical scoring system to the criteria. This was initially a binary system representing whether a particular criterion had been met. Following a pilot of the assessment tool, this was changed to a 3-point scoring system to allow for differentiation between studies where a criterion had been fully met (2 points), partially met (1 point) or not met (0 points). Conditions for full and partial fulfilment were specified for each criterion. The quality

iliii See appendix 4.
assessment was conducted with the third iteration of the tooliv. I assessed all papers and two colleagues assessed a randomly-selected subset of ten papers. This yielded an intraclass correlation coefficient of 0.72 (95% CI 0.40-0.91)v, which suggests an adequate level of agreement between raters. Due to the distribution of quality scores, with no study scoring below 9 or above 14, I elected to retain all studies for review.

Although steps were taken to improve objectivity, quality assessment for some criteria felt open to subjective interpretation, such as determining whether the sampling method was described in adequate detail for replication. I had also not anticipated the level of effort required to conduct the quality assessment; as such, the ratings provided by myself and colleagues may have been sensitive to fluctuations in our levels of fatigue and concentration.

7.2.4. Developing the synthesis

Due to the nature of the review question and the level of data available from the studies included, meta-analysis was neither feasible nor appropriate. A narrative synthesis of the literature was conducted, following the guidance published by Popay et alvi [52], in order to “tell the story” of the findings in a systematic manner. The authors propose four main elements within their guidance:

1. Considering the role of theories of change or effect relevant to the review.
2. Developing a preliminary synthesis, through clustering, tabulating, describing and translating relevant data.
3. Exploring relationships within and between data.
4. Assessing the robustness of the synthesis product through critical reflection.

iv See appendix 5.
v See appendix 6.
vi See appendix 7.
Following data extraction, I was overwhelmed by the sheer amount of data available from the included studies. The main challenge was to identify salient data, understand the value of such data in relation to the quality and context of the work, and present a wide range of heterogeneous findings in a meaningful and cohesive way. Narrative methodologies are useful for managing heterogeneity while tentatively constructing theory [53], however are sensitive to authors being selective or placing undue emphasis on some findings over others [54]. This guidance provided a useful framework to maintain clarity and robustness when presenting such diverse findings, but did not completely abate my concern about bias and the validity of my subjective interpretation of the data. For instance, there were a number of occasions where I noticed my favourable bias towards evidence for relationships between HRQoL and mental health variables. It was therefore invaluable to discuss this risk of bias and unfair interpretation in supervision, and to maintain conscious awareness of this when proofing drafts. If unchecked, such bias may have led to biased interpretations that did not reflect the quality and robustness of the literature.

I elected to submit this review to a medical journal, reporting on the synthesis in a manner that would be of relevance and utility to clinicians working with this specific clinical population. As my previous research experiences had led me to publish work in psychologically-oriented journals, writing for a primarily medical audience was challenging and required some alteration to my writing style. In particular, some concepts of universal acceptance by practitioner psychologists had to be clarified for professionals unfamiliar with such modes of thinking. Conversely, in writing the review I had to ensure a greater level of familiarity with medical terminology than I would normally feel accustomed with using.
7.2.5. Conclusions

This narrative synthesis offered further understanding of factors relating to HRQoL and psychological outcomes in patients with high-grade brain tumours. This is an under-researched patient group and the review has identified a number of key areas in which clinical care and the research agenda can be advanced for patient benefit. Although the synthesis could be criticised for lack of robustness, I have endeavoured throughout the review to maintain clarity and rigour through adherence to published guidance and checklists. Regardless of conclusions drawn about factors that relate to HRQoL and psychological functioning, the review identifies methodological flaws within the literature, of which many could be easily surmounted to improve the quality of the evidence base.
7.3. Paper 2: Empirical Study

7.3.1. Rationale for the topic and developing the research question

Prior to gaining a place on the ClinPsyD programme, I worked as a research assistant on a project investigating the information and supportive needs of patients with breast, lung and prostate cancers. Beginning as a study of how patients received and used a recently-developed psychoeducational resource, the work quickly grew into an investigation of how patients’ support needs, psychological mindedness and construal of their illness developed throughout treatment [55, 56]. One particular theme that stuck with me from this research was how patients constructed multiple narratives of their experiences to address their relationships with their cancer. Regardless of their prognosis or ongoing struggles with illness, the function of these constructions appeared to provide space for patients and their families to reconcile present experiences with personal histories and wishes for the future.

The findings of this research bore similarity with the processes I observed throughout my experience as a support worker and assistant psychologist with people undergoing rehabilitation following acquired brain injury. For these individuals, their injury had left them with significant cognitive, behavioural and physical impairments that impacted on every aspect of their lives and relationships with others; yet despite being at their most vulnerable, they were required to start rebuilding and adjusting to their new worlds, many with remarkable success.

In the development of a research topic, I reflected on how Paul Broks described the neuroscience of the ‘self’ [57]:

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“We are all divided and discontinuous. The mental processes underlying our sense of self [...] are scattered through different zones of the brain [...] They come together in a work of fiction. A human being is a story-telling machine. The self is a story”

On the basis of my prior experiences and my interest in pursuing a career in neuropsychology, I wanted to explore how people adjusted to limitations on life imposed by a diagnosis of brain tumour, consider how these new experiences interacted with stories of ‘selfness’ and observe whether patterns in responses existed between individuals. I had some understanding of how patients re-wrote these stories following diagnosis of other cancers; brain tumours however represented something similar yet distinct, posing a “double threat, partly against the life itself and partly against the individual’s personality” [58]. Having observed this rewriting and readjustment process in participants I had previously interviewed and in members of my own family diagnosed with cancer, I was curious as to how these processes manifested in individuals whose cognitive abilities had been compromised by illness and treatment.

In my initial meetings with my field supervisor and my early reading on the topic, I was shocked to discover the lack of research into patients’ experiences of GBM. Despite accounting for the majority of brain tumour diagnoses and representing significant threat to life and function [42], there appeared to be very little understanding of how patients responded and adjusted to living with GBM. In talking with neurosurgeons and oncologists at the research sites it was clear that clinical priorities were, out of necessity, oriented towards the preservation of life and ‘fighting’ the illness for as long as possible. There was however recognition that their patients’ experiences were deserving of greater understanding and that this would translate into improved supportive care.
7.3.2. Theories of adjustment and relationship to other concepts

When discussing the concept of adjustment with my supervisors, I was repeatedly drawn to Brennan’s Social-Cognitive Transition model (SCT) [22], which aims to combine aspects of coping and social-cognitive theories to understand how patients respond to changes encountered during their experience of cancer. According to SCT, adjustment encompasses the range of dynamic processes that occur as people manage, learn from and integrate changes precipitated by altered life circumstances [59]. Individuals face cancer with internalised models of themselves, others and the world, which form the foundations of guiding assumptions and expectations of reality. With progression through the illness trajectory, such models are either reinforced by experiences confirming previously held assumptions, or challenged by disconfirmatory events. Rather than representing a pathological psychological experience, distress is an expected reaction as internal mental models and core assumptions are adjusted in response to incoming discontinuous information (see figure 7.1).

Although often conflated in the literature [60], adjustment is therefore not synonymous with coping. Coping can be understood as a collection of discrete “defences” that individuals deploy in response to specific, immediate stressors [61], or as the “thoughts and behaviours a person uses to regulate distress, manage the problem causing distress and maintain positive well-being” [62]. Coping styles common in patients with cancer include denial/avoidance, fighting spirit, helplessness/hopelessness, fatalism, and anxious preoccupation [25, 63], and the selection of particular styles appears to be influenced by personality factors [64]. Although the language of coping is central to patients’ talk [65], coping as a concept applied to adjustment to cancer is problematic. Firstly, coping implies relative consistency, whereas adjustment acknowledges patients’ responses to stressors vary according to the stage of disease and treatment [55]. Secondly, coping theory suggests that coping leads to a successful outcome where patients are free of distress, whereas
Figure 7.1. Social-Cognitive Transition model of adjustment.

Adapted from Brennan [59] and included with kind permission of the author (J. Brennan, personal communication, 31 May 2015.)
adjustment describes a cycle in which distress is a necessary part of the process. Lastly, coping does not account for the post-traumatic growth or benefit finding as observed in many patients with cancer [66-69]. Coping theory has been developed further in recent years to include state-dependent, goal-oriented responses, yet styles still remain closely related to individual disposition [70, 71]. The SCT model does not diminish the relevance of coping, but affirms that coping theory in isolation is insufficient in explaining how patients learn and develop through the illness trajectory [22].

7.3.3. Deciding on the methodology

The research sought to explore and understand the process of adjustment as experienced by individuals living with GBM. I was curious as to whether the unique effects of a neurological tumour and the associated treatments would lead to different experiences of adjustment compared to those of patients with others cancers [31, 58, 72, 73]. Using a qualitative design would allow the collection of data of greater richness than afforded by questionnaire-based designs, particularly as the preliminary development of my systematic review identified no clear precedent for conducting quantitative work for this purpose. Qualitative methodologies would allow a thorough exploration of patients’ experience of the mechanisms of adjustment.

As I aimed to gather data to support the development of theory, I elected to use a grounded theory methodology. Grounded theory has a substantial heritage in exploring and understanding life-limiting illness [74-79] and cancer [80], and is an effective qualitative methodology for developing theoretical frameworks in areas where there is little understanding [81, 82]. I had previous experience of using grounded theory approaches to build substantive theories within illness populations and was therefore confident that this methodology would be best suited to addressing the research questions under consideration. Alternative qualitative methodologies were
considered; interpretative phenomenological analysis may have provided a greater focus on participants’ lived experience and meaning-making processes [83-85] and has been effective in exploring experiences of identify change and distress in cancer patients [86-89]. As the aim of the research was to develop a theoretical understanding of the process of adjustment, rather than to capture “thick descriptions” of experience [90], I considered grounded theory most appropriate.

I conducted my research specifically within the constructivist approach advocated by Kathy Charmaz and other writers [91-95]. Grounded theorists have traditionally held positivist, objective perspectives towards knowledge, where researchers ‘discover’ data and context-free conceptualisations ‘emerge’ from analysis [96-98]. In contrast, constructivist approaches take a reflexive stance towards the process, embracing relativism and acknowledging that theory is an interpretation dependant on the researcher’s point of view. Within this approach, analysis serves to ‘construct’ categories to understand data; however constructions are embedded within pre-existing structures that “reflect the conditions of their production” [93]. Constructivist theorists must therefore use reflexive strategies to acknowledge their preconceptions, taken-for-granted assumptions and interpretations to establish their own ‘fit’ with products of their work [99, 100].

I am uncertain as to whether I chose to use this particular approach or whether I had a choice at all. The epistemology of constructivism corresponds with my own beliefs on how I as a researcher interact with participants and data. As a trainee clinical psychologist, my therapeutic experiences have lead towards an understanding that distress and disease are experienced within rich social contexts that can exacerbate or buffer present difficulties. As an individual, I find the concept of neurological damage terrifying but have seen how lives have been improved through evidence-based psychological practice, and believe that clinical psychology has much to offer patients
with brain tumours. I therefore approached this research with a belief that this methodology would be a good fit for the data [101] and would provide a suitable framework to construct a tentative theory of "real-life experiences and behaviours, in all their messy complexity" [102], while acknowledging my own position relative to the findings.

7.3.4. Recruiting participants and liaising with services

Patients were recruited from a large NHS cancer treatment centre with a wide catchment area covering Greater Manchester and Cheshire. As the expected treatment pathway for patients with GBM was to receive adjuvant therapy following resection, the majority of patients in this area would receive outpatient radiotherapy and/or chemotherapy at this centre or a satellite clinic. Recruiting from this centre therefore provided access to a broad range of patients, which would be beneficial to ensuring greater generalisability with the wider GBM population.

In accordance with the protocol approved by the NHS Research Ethics Committee, patients were introduced to the study by a clinician. In all cases, initial contact was via the sole clinical nurse specialist (CNS) responsible for patients at this point in treatment, who was experienced in the conduct of clinical research. The CNS was instructed about the inclusion and exclusion criteria for the study and was asked to mention the study during routine consultations with eligible patients. The CNS would then provide patients with a copy of the participant information sheet and obtain verbal consent to be contacted by me three days later. The CNS was requested to approach patients whom appeared to be coping well and those whom were experiencing distress.

Using a single pathway for recruitment was advantageous for maintaining consistency, reducing the level of co-ordination required and ensuring access to the study was equitable. The primary disadvantage of recruiting via this method was that
recruitment was very sensitive to fluctuations in the CNS’s workload. Although there were no significant service-level changes that would lead to a predictable increase in demand, there were times where the CNS apologised for being too busy to assist with recruitment. I endeavoured to maintain a good relationship with the CNS throughout the study and frequently sought their advice as to whether my requests for participants were putting undue strain on their clinical responsibilities. In addition, I could not recruit while they were on annual leave or training.

Recruitment was less successful than anticipated, with only 15 potential participants being referred to the study. In reference to the epidemiological data provided by the treatment centre (S. Gupta, personal communication, 6 August 2014), this represents 14.7% of the total number of adult patients diagnosed with GBM in the period August 2013-July 2014. I attempted to increase recruitment by contacting neuro-oncologists in the service to request that they mention the study to eligible patients on their caseloads; although all were enthusiastic about the need for the research, none referred any patients. Due to the regional nature of NHS cancer care, the only further option for increasing recruitment would have been to approach treatment centres in neighbouring regions, obtaining endorsement from clinicians with whom the research team had no prior relationships. On reflection, this contingency plan would have only been feasible if enacted prior to recruitment.

Although the specialist contribution of practitioner psychologists is recognised within clinical guidance [103], and psychosocial interventions have been demonstrated to be effective and economical [104, 105], I was curious about the perception of psychological research compared to large-scale clinical trials of cancer treatments. Despite the enthusiasm of the clinicians I spoke with about my work, I encountered some initial resistance from the research and development department whom questioned the relevance and cost-efficacy of the project, particularly as their
mandatory registration fee was significantly greater than my available budget. The scientific rigour of qualitative research and grounded theory can be misunderstood by those responsible for safeguarding research unfamiliar with their methodologies, particularly with vulnerable or medically unwell participants [106, 107], which can lead to unfair compromise or discrimination. It is important to recognise the burden that participation in research can place on patients with cancer [108]; however I wondered whether an institutional bias existed in viewing the demand of engaging in qualitative research as less worthwhile than the burden of participating in a clinical trial.

Of the 15 patients who provided verbal consent to be contacted about the study, 10 provided consent to be interviewed. Two patients deteriorated significantly before an interview could be arranged, and three had changed their mind. When contacting patients who had provided verbal consent to the CNS, I was particularly mindful that participation in research was likely at the bottom of their present priorities. While receiving adjuvant treatment, patients are often required to attend the treatment centre daily over several weeks, during which they may need to travel a significant distance and experience long waiting times for NHS transport schemes [109], which can lead to increased fatigue, distress and dissatisfaction [110]. At my initial telephone contact with patients, most patients requested I contact them at another time as they were currently travelling or waiting in the treatment centre. In some cases, I was required to make several attempts to contact potential participants as they were unable to answer their telephone. For the three patients who declined participation, none declined at the initial telephone call, all requesting that I contact them again the following day or week to discuss the study further; for these patients, at least two further telephone contacts were made before they declined the invitation to participate. I was particularly concerned about the balance between making all reasonable attempts to promote participation, ensuring patients were aware that their contribution would be valued, and inadvertently placing patients under pressure. Regrettably, I did not specify during
ethical review the number of times I would attempt to contact patients before I would assume they no longer wished to participate, and the research ethics committee did not stipulate that I had to provide detail on this in the recruitment protocol. My supervisors and I agreed that following three failed attempts to obtain either definite consent or definite refusal for participation, I would advise patients that they would no longer be contacted regarding the study and that they were free to contact me should they consider participation within the next four weeks. The complexity of the consent process is well recognised, and potential research participants can struggle with declining directly [111]. Personal benefit and altruism are common motivators for participation in health research [112-115]; social desirability therefore may have affected some patients’ ability to state directly their opinions regarding participation.

7.3.5. Conducting research interviews

Logistical considerations: All participants elected to be interviewed at their homes, rather than on NHS premises. The decision to offer participants a choice was one of practicality, however it has been recognised that the location of interview has significance for the data collected [115]. Providing participants with the option to be interviewed at an NHS site offers some convenience, as the interview could be held before a consultation at an outpatients clinic, and could allow participants space to talk away from their family; however being interviewed in a clinical setting may impress a medical dynamic that is not conducive to patients talking openly about their experiences. The socio-spatial construction of home interviews is markedly different and was preferable to my research question. Herzog observed that interviewing participants on their “home turf” alters the power dynamic implicit within the research relationship [116]:

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“The physical location in which the interview is conducted is one of the most concrete expressions of this process of boundary-crossing [...] A democratization takes place as both interviewer and participant become partners in structuring the event and, consequently, in consolidating the knowledge”

With participants extending the courtesy of inviting me into their homes, I was permitted to enter into their social words away from the environment of treatment. Home represents an area of safety and familiarity, and shares control of the interaction between researcher and participant [117]. In this space I was able to meet with them as a near-equal to discuss the processes of their adjustment to cancer. I believe was advantageous to data collection.

Interviewing at participants’ homes is however associated with additional difficulties compared to hosting interviews on NHS or university premises. Home environments can be associated with greater levels of disruption and distraction, particularly if other individuals are present in the environment [118]. One difficulty I encountered in a number of interviews was managing the expectations of family members present, informing them that they could not also participate. In these cases, it appeared that family members also had stories they wished to voice that they may not have had the opportunity to do so prior to my visit. In one case this lead to some difficulty, as the participant initially deferred many of my questions to his wife, whom insisted she be present throughout the interview to support her husband. I managed this situation by pausing the interview and reiterating the goals and procedure of the research as explained on the patient information sheetvii, emphasising that this work could only serve to document patients’ experiences, and having a brief conversation with the participant’s wife regarding local sources of support.

vii See appendix 12.
Conducting research ‘in the field’ is associated with a greater level of risk to the researcher as these settings lack the safeguards and security of clinical or academic environments [119]. This was of particular significance to my research, as individuals with brain tumours can often experience difficulties regulating their behaviour and arousal [120]. For each home visit, I adhered to the University of Manchester’s lone working policy. This involved notifying a colleague of the details of my visit, including pre-agreed start and finish times, a protocol should no contact be made at pre-agreed times and a code word to request immediate assistance in the event of an emergency. I did not consider myself in danger at any stage during this research.

Previous research has identified that participants experience research interviews as beneficial, valuing the opportunity to share their story with an empathic listener, particularly if interviews explored themes not discussed within their family or as part of routine clinical care [121-123]. Discussing sensitive topics within research interviews can cause distress, however such distress is no greater than that encountered by participants in their daily lives [124]. Nevertheless, qualitative researchers can find themselves in situations whereby participants experience strong emotional reactions and request support from the researcher. A distress protocol was developed to help guide my responses to participants’ distress. There were no incidents during this research where I was required to escalate my response beyond briefly pausing the recording. Following the interview, participants were given a debriefing sheet which listed telephone numbers for their CNS, local and national services whom they could contact for support or advice.

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viii See appendix 17.
ix See appendix 15.
x See appendix 16.
**Conduct of interviews:** Research interviews were conducted with reference to a semi-structured guide\(^\text{xi}\), revised throughout to meet the needs of the analysis and theory construction [93]. The guide began as a broad scope of questions, becoming more directional with each reiteration. Interview guides are beneficial in ensuring the researcher remains ‘grounded’ to the research question, particularly as interviews become more conversational in style [125]. My previous experience of conducting research interviews allayed some anxiety and allowed greater flexibility with the interview guide, however it still took some time for me to develop an effective style of questioning suitable for this project. An early revision to the interview guide saw the removal of initial questions where I asked participants for a brief overview of their experiences thus far. The first participants I met with spent a sizeable portion of the interview recounting their experience of admission, surgery and treatment in detail, as they might when meeting a new clinician; although this was of use in contextualising their experiences, it provided little data about adjustment processes. I also feared that beginning in this manner established a medical context for the remainder of the interview, which may have affected their ability to access a psychological appreciation of their experiences. In later interviews, I found it beneficial to inform participants directly that I would not be asking specific questions about their experiences of hospital or treatment. All appeared to respond well to this “frame and footing” [126], possibly as this reduced uncertainty about the forthcoming interaction and reinforced the stance of the interview as an activity different from clinical interaction.

I was curious as to how participants’ cognitive impairments would influence their ability to engage with the interview. In some cases, it was a challenge to maintain participants’ focus on the topic of questioning. A number told me that they were very talkative since diagnosis, which they attributed to a side-effect of their resection or corticosteroids. Others explained that they now struggle keeping pace in conversation

\(^\text{xi}\) See appendix 14.
or finding the right words. Throughout the interviews I found it useful to draw on the interaction techniques promoted in motivational interviewing, such as asking open-ended questions, providing affirmations, demonstrating reflective listening and summarising participants’ responses [127]. Although the objective was not to facilitate change, these techniques were useful in establishing rapport and encouraging participants to elaborate on their responses.

Interviews aim to create a space for an interpersonal interaction with a defined purpose. Although interviewers should approach each interaction with an open mind, it is impossible to meet with a participant and be a completely ‘blank slate’, devoid of assumptions or expectations [128]. I approached each interview both with a genuine curiosity about my participant’s experiences and a strong hope that the interview would yield suitable data. Participants also enter into the interview space with expectations about how the interaction will proceed [92]; although many hold positive expectations about being able to voice untold experiences and share their expertise to help others, some may fear the interview may be overly intrusive or threatening [124]. Consent to a dynamic experience, such as interview participation, is inherently more complex than consent to complete a questionnaire: it is the duty of the researcher to observe participants’ non-verbal cues and reaffirm consent during the discussion of sensitive issues [129]. Charmaz cautions that the comfort of the participant must remain at a higher priority than the acquisition of “juicy data” [93]. I was mindful of this advice while conducting these interviews, particularly as a common narrative of participants’ coping was to not engage actively with thoughts concerning some of the issues I wished to explore, such as prospects of deterioration and death. As such, developing a good rapport with participants was necessary to mitigate perceptions of power imbalance and facilitate openness. This required an awareness of participants’ social and cultural identities, a stance of courteous curiosity, sensitivity to nonverbal responses and an empathic, non-judgemental communication style. By taking time to establish and
maintain rapport throughout a research contact, the quality of data can be improved and research can be “rehumanised” [130].

During one interview, a participant shared with me his belief that he possessed a “healing energy” that had protected his body from harm and was of greater benefit than his chemotherapy. I considered this to be ‘juicy data’ about his construal of agency and responsibility, and began to probe further. I then noticed a change in his demeanour and wondered whether he had unintentionally disclosed more information than he was willing to share. I began to consider whether my questioning had been perceived as critical. This was certainly unintentional, but I could not deny that I may have unconsciously communicated that such beliefs were incongruent with my own. Wanting to manage this potential rift, I briefly stopped my questioning. I shared with the participant that I believed he had found a meaningful and personal way to make sense of the turbulent reality of having a brain tumour, that I would like his permission to gain a greater understanding and that I appreciate that it can be difficult talking about issues of such intimacy. The participant appeared pleased to hear this and the interview resumed, albeit on how his family had supported him throughout treatment. The interview continued for the full length yet he did not return to talk about his “healing energy.” In this situation, I believe I was successful in re-establishing rapport and allowing the participant to continue in trust, providing an opportunity for him to restate consent about areas he was willing to discuss.

7.3.6. Conducting the analysis

I transcribed the majority of the interviews personally. Although effortful and time-consuming, this process was beneficial in bringing me closer to the data. Listening to the recordings during transcription provided space for reflection away from the demands of conducting an interview. It can be argued that each exposure and re-
exposure to recorded data constitutes the formation of new data [131]. On a number of occasions, there were meaningful elements of participants’ responses I noticed only after listening to recordings multiple times. Such elements may have not been detected during the interview as I was focussed on a different line of questioning, or their salience may have only become apparent through subsequent re-exposure to the data. I likened this process as similar to a developing photograph; some elements of the image may be visible shortly after the initial exposure, whereas others may require further time to develop before they acquire form and meaning. Listening to interviews also provided an invaluable opportunity to reflect on and refine the interview guide and my interview technique. A small number of interviews were transcribed by a third party, which was beneficial in allowing me to produce transcripts at a faster rate than if I were transcribing alone. I found that these interviews however took longer to code than those I had transcribed personally, as I was less familiar with the data.

While reading transcripts and listening to recordings, I was mindful of how my emotional reactions to participants’ accounts emerged and evolved. With greater space to reflect on their responses than afforded during interviews, I observed that my reactions to some disclosures were more intense during re-exposure. In managing these reactions, I made attempts to ensure I dedicated specific time to engage with the recordings, listening to them during my allocated research days where I had space to connect with and reflect on the data rather than following a busy day on placement where my regulatory resources may have been depleted. In addition to discussing my emotional reactions during research supervision, it was useful to record these as ‘reaction memos’ in my reflective journal. At no point during my research did I consider such emotional reactions aberrant or excessive; rather I viewed them as a functional adjunct to analysis and used them to refine my empathic interviewing technique. Throughout the demanding process of conducting research, these reactions were invaluable in helping me to retain an appreciation of the human aspects of my data.
I analysed the interview data adhering to the framework described by Charmaz [93]. Transcripts of the first participants interviewed were coded line-by-line so that I could remain as close to the data as possible, identifying in vivo codes that appeared important. Memos were written shortly after this initial coding, incorporating field notes taken during the interview and a brief formulation of my understanding of participants’ accounts. As I became more accustomed to coding, I stopped coding line-by-line and commenced coding by gerunds to describe participants’ actions. The accuracy and suitability of these initial codes were reviewed in supervision. Once four interviews had been transcribed, I began to apply tentative focussed codes to the data, using memos to draw out comparisons and contrasts between individual cases. This process was used to adapt my interview topic guide to clarify particular questions or gaps in the data. As analysis advanced, codes of similar thematic content were clustered and conceptual maps were drafted to visualise patterns, relationships and movement within the data, providing a visual snapshot [132] of the foundations of the developing theory.

In collating data and organising my coding hierarchy, I elected to use NVivo 10 for Windows (QSR International, version 10.0.138.0). This was my first experience of using a CAQDAS (Computer-Assisted Qualitative Data Analysis Software) package. I found the software initially cumbersome compared to my previous experience of coding on printed transcripts and collating using word processing software. Once I had become familiar with the software, the benefits of CAQDAS packages became apparent. Using NVivo 10 allowed me to conduct Boolean queries across all transcripts and memos, have fast and portable access to current and previous versions of the coding hierarchy, and generate reports of coding distributions.

Researchers using a constructivist grounded theory methodology should aim to sample theoretically, continuing to recruit until a point of theoretical sufficiency, where
the collection of new data no longer generates new theoretical insight [133]. This is essential for advancing the credibility of the work [134]. The number of interviews required depends on the requirements of initial and emergent research questions [93]. The developing nature of grounded theory analyses therefore stands in contrast to the precision required when submitting a proposal for ethical review [107], where researchers must state a target sample size. It was decided that 14 participants would represent a balance between representativeness and theoretical sufficiency in analysis, and pragmatism in study design. I was unable to meet this target before my thesis submission date, despite my efforts to maximise recruitment. Following review of the results in research supervision, we agreed by consensus that the analysis approximated theoretical sufficiency and that the model was representative of experiences commonly reported by patients with GBM. I would have however liked to recruit a larger sample to add further credibility to the work and at times felt anxious that the analysis was insufficient to answer the research question. The constraints of conducting research as a trainee clinical psychologist frustrated me and I desperately wanted to dedicate more time to this project; at times I was motivated by a belief that more data would grant a deeper, comprehensive understanding of participants’ experience of adjusting to a life changed by GBM. At these uncertain points in analysis, I was grounded and reassured by the observation of Annemarie Mol and John Law [135]:

“The argument has been that the world is complex and that it shouldn’t be
tamed too much [...] that which is complex cannot be pinned down. To pin
it down is to lose it”

As part of the process of developing the theory beyond a preliminary model, researchers must make decisions about the direction of the developing analysis [93, 136] in order to “retain the parsimony of good grounded theory explanation” [137]. One significant decision that occurred during the analysis was whether to apply specific
focus to discourses of loss and grief. Diagnosis of a malignant cancer confronts one with prospects of a shortened lifespan, a "sudden amputation" of the future [138] and an undignified death [139]. Regardless of whether disease can be cured or not, patients with cancer often experience intense feelings of ‘existential threat’ [56, 140-142]. In the context of GBM, where the aim of treatment is rarely curative, themes of loss, grief and hopelessness are common amongst patients and families [143, 144]. Through discussion in supervision and personal reflection on the categories constructed during analysis, I elected to not actively develop these themes. As early interviews indicated agency in participants’ responses to illness and disability, I queried whether reflections on death and loss would be necessary in answering the research question. I was also mindful that participants were being recruited while they were still actively engaged in a standard treatment protocol rather than at a stage where all treatment options had been exhausted, where such existential themes may have greater resonance. As the theoretical model was developed, the understanding appeared sufficient without further exploration of categories concerning mortality and existential threat: where participants discussed loss and mortality, this was not independent of talk of being thankful for the lives they had led or their plans to accommodate anticipated change. I therefore considered my decision to retain focus on the active processes of adjustment beneficial to developing a useful explanatory model. In depth analysis of existential issues, although undoubtedly important for patients with GBM regardless of their stage in the treatment trajectory, would have necessitated additional theoretical sampling and a secondary topic guide in order to produce an understanding of sufficient fidelity. Pragmatically, this exploration would not have been feasible within the confines of this study.
7.3.7. Maintaining reflexivity and using supervision

Throughout analysis, research supervision provided an invaluable space to test hypotheses and interpretations of my data, and encouraged me to reflect on the degree to which such understanding was truly ‘grounded’ in the data. In approaching this data, my supervisors and I acknowledged we bore certain assumptions or expectations that may influence the products of analysis. With regards to my own bias, my previous clinical and research experiences provided me with lenses through which I viewed the data; although I strove to experience my interviews with participants afresh, I cannot deny that such preconceptions may have at times muted my ‘theoretical sensitivity’ [93]. The time constraints of completing the thesis made it impractical and infeasible to postpone completion of the literature review and systematic review until analysis had been completed. Within the purist Glaserian approach to grounded theory, this would be considered as contaminating or inhibiting the researcher’s capacity to derive an inductive understanding of their data [145, 146]. Modern grounded theorists however have argued that knowledge of extant literature is unavoidable, necessary and beneficial to research [95, 147]; through the effective use of supervision and by tracking one's preconceptions through the use of reflexive memos, it is possible to restore theoretical sensitivity [34] and approach data with “an open mind [...] not an empty head” [148]. A further threat to my ability to approach data with an ‘open mind’ was my need to complete this work as a requirement of my doctoral thesis. As much as I believed the findings of this work would translate to patient benefit by advancing clinicians’ understanding of adjustment (which in itself is a preconception), the ulterior motive for this research was to obtain my doctoral qualification. Research supervision offered a dedicated space to acknowledge the various drivers behind my work. I believe I conducted my interviews and analysis aware of these influences, rather than hindered by such expectations.
One recurrent theme of supervision was the differences between research and clinical interviews. On account of my experiences prior to clinical training, having had previous experience and receiving training in conducting interviews in complex health settings, the prospect of interviewing patients with brain tumours felt familiar. I felt some apprehension reconciling these experiences with the development of my clinical skills since commencing training. I was concerned that my interviews with participants would stray unwittingly into a therapeutic dialogue, particularly should participants express feelings of distress, and was curious to know whether I would be able to conduct the interview while inhibiting a drive to increase their awareness and facilitate change. On several occasions I was aware of the need to stop myself from interjecting or asking a particular question; whereas in a clinical setting I would be looking to test hypotheses or identify features of clients’ talk consistent with specific therapeutic models, research interviews required me to adopt a stance of non-intervention. I felt de-skilled during the initial interviews and it was useful to reflect on this experience in supervision. I was also wary of the influence of my knowledge of therapeutic models during analysis, and was concerned that I would try to fit my data into particular styles of formulation rather than remain atheoretical. Supervision acted to safeguard the developing theory by providing a forum in which my supervisors and I could acknowledge such preconceptions and ascertain our grounding within the data.

7.3.8. Limitations of the work

The principle limitation of the work was the sample size; although my supervisors and I considered that analysis had met a point of theoretical sufficiency. Recruitment of a larger sample may have yielded decisive data and enhanced the credibility of the study.
As all participants described themselves as White British, analysis may have been advanced by the recruitment of participants of other ethnicities and cultures. Previous work has established that psychosocial responses to cancer vary across cultures and are associated with variations in illness representations, access to support and spiritual beliefs [149-153]. Recruitment of ethnic minorities to clinical trials and health research is challenging due to beliefs about the nature of research in clinical settings and services’ limited attempts to make participation accessible to people of other cultures [154, 155]. As non-White ethnic origin is a significant risk factor for delayed presentation to oncology clinics for a number of cancers [156], with late diagnosis being associated with greater impairment and poorer survival [157], many patients of non-White ethnic groups may miss recruitment windows or be too ill for participation to be appropriate. With regards to brain tumours, age-standardised incidence rates are significantly greater in White males and females than for people of Black or Asian ethnicities [158], which may explain why no patients of non-White backgrounds were identified from clinics.

All participants were recruited by one CNS, increasing the risk of selection bias. In practice, the CNS assisting with my study was the sole neuro-oncology CNS for Greater Manchester: as the majority of patients diagnosed with GBM would receive radiotherapy, chemotherapy or concomitant treatment, the CNS would have contact with every patient eligible for participation. Although the Greater Manchester region is an area of significant ethnic and economic diversity [159, 160], additional recruitment pathways involving other regional NHS treatment centres or recruiting participants through charities may have provided access to a broader population and may have provided a larger sample of greater diversity.

In the United Kingdom, there is a history of significant regional differences in the provision of cancer treatments [161]. Care for patients with brain tumours has been
criticised for being “fragmented and uncoordinated” with access to specialist neuroscience services varying substantially between geographical areas [43]. Greater Manchester has traditionally been an area of neuroscience and oncology expertise, with close collaboration between specialist treatment services and research institutions; although care on a national level has been more consistent following service reconfiguration from 2006 onwards [7], Greater Manchester continues to attract funding to develop and implement novel and effective therapies [162, 163]. Many participants expressed feelings of pride and were thankful that they were receiving treatment from centres in this area. It is likely that this may have influenced their illness perceptions or buffered their emotional reactions due to a belief that they were receiving the best care available [164]. As such, the model presented may not sufficiently describe the adjustment of patients whom perceive they are receiving inadequate care, or whom do not hold their treatment centre or consultants in high regard. Recruiting patients from areas without the prestige of the Greater Manchester region may have enhanced the analysis.

Limiting recruitment of participants to 3-7 months post-diagnosis was based on pragmatism, as this coincided with a pause between treatments, and the findings of previous research [55], where patients in this timeframe were most able to reflect on their psychological responses to illness. It is possible that the model of adjustment presented in this paper does not account for patients’ experiences shortly after diagnosis or as they approach end-of-life. The study did not aim to develop a comprehensive model of adjustment across the whole illness trajectory, and would necessitate additional ethical considerations potentially beyond the scope of this work [165], but recruitment of participants at these stages may have provided additional depth to analysis. Conducting serial interviews with participants would have been of further benefit to analysis, providing temporal information on how adjustment evolves throughout the stages of treatment.
7.4. Overall reflections

7.4.1. What have I learnt from conducting this research?

Although I began the ClinPsyD programme with prior experience of conducting research within academic and clinical settings, this work was my first experience of doctoral level research and being involved with a project from beginning to end. My aims for this research were to conduct work beneficial to patients and clinical practice, to be of value to my own personal and professional development, and to be feasible within the time restrictions of a clinical doctorate. Although my enthusiasm and commitment to the project remained steady throughout, there were times when I struggled to engage with the work to the level I aspired. This was particularly noticeable when other aspects of the ClinPsyD programme demanded my attention, such as in response to busy periods during placements or assessment deadlines. As these demands were typically acute in nature, this increased my fatigue and necessitated a reduction in the priority of my research. I also experienced initial difficulty reconciling the natural ebb and flow of the workflow and complexity of research with the time constraints of the ClinPsyD programme. Whereas previous posts had afforded me greater flexibility in my role to respond to the fluctuating demands of various projects, as a trainee I often found that my research activity rarely fell within working hours during allocated research days. I believe this challenge has been of benefit and has required further development of my time management skills and self-discipline. As I aim to continue my engagement with research post-qualification, the need to appreciate and enforce boundaries within my working hours and appreciate what level of involvement is feasible, will continue to be a feature of my career trajectory.

Paper 1 was my first experience of conducting a systematic review. Although I was familiar with using systematic reviews within clinical practice and research, I had limited appreciation for the process of completing one. Conducting the review was
significantly more taxing than anticipated and I found it difficult to estimate with accuracy the length of time required to complete each section. I was surprised at the significant effort required to complete what I viewed initially as relatively uncomplicated tasks, such as screening abstracts or extracting data. This left me feeling frustrated and concerned that I had misunderstood something fundamental to the process. Through discussion with my supervisor and colleagues, I was relieved to discover that this appeared to be a common experience when conducting systematic reviews. As such I believe I will be able to conduct future reviews with a greater appreciation of the engagement required. The guidance by Popay et al [52] provided an invaluable framework for approaching the synthesis and granted me a working understanding of theory and process, which I believe I will be able to draw on in producing or critiquing similar reviews in the future. I had no prior experience of systematically appraising the quality of studies using an assessment framework and found I enjoyed this aspect of the review. It was interesting to see how methodological flaws were systemic throughout the field, even within published work that appeared superficially to possess high methodological rigour. This experience granted me greater appreciation for good experimental design and how seemingly minor methodological decisions at the design stage can have significant impact on the overall credibility of studies.

Although I had prior experience working on studies employing a grounded theory methodology, Paper 2 represents my first experience of leading the analysis. This required greater awareness of the development and philosophy of the constructivist approach than I had held previously. While requiring a significant amount of background reading, having a greater understanding of the methodology was beneficial to navigating the challenges of analysis.
7.4.2. What are the implications for my professional development?

Completing this work has provided experience of the reality of conducting research while in a clinical post. On commencing the doctoral programme, my objective was to study towards a career that provides equitable responsibility for clinical practice and producing research. This model underpinned the foundation of graduate education in clinical psychology [166, 167] and continues to be of relevance for current training programmes [168, 169]. The research output of qualified clinical psychologists however remains low [170] and my experiences on placement have illustrated that services struggle to release staff from clinical obligations to allow time for research activity. Although the priority of research is identified within the NHS Constitution [171] and the current Research and Development Strategy [172], I am concerned that the flexibility and protection of time allocated to research afforded to trainees will not be sustained as I progress to a career in the NHS. Conducting this work has affirmed to me that clinical psychologists should continue to promote the important and unique contributions they offer to advancing evidence-based, person-centred care in medical settings.

Interviewing patients about their experiences of GBM has relevance to my current clinical work and my anticipated future career in neuropsychology. Many themes described by participants have resembled difficulties recounted by clients I have worked with on placement with other neurological diagnoses. Conducting a grounded theory analysis of my interviews with participants has also served to enhance my development as a clinician, providing insight in how meaning is constructed and reconstructed through a therapeutic relationship. Listening to recordings of interviews and embracing the reflective stance of a grounded theorist has provided an appreciation of the interactions and use of language that occur within dialogue, perhaps to a greater degree than prior to engaging in this research.
7.4.3. Overall conclusions

The empirical paper and the systematic review both attest to the multifaceted nature of patients’ experiences of GBM and PMBT. Although clinicians are likely aware of a wide range of influences on patients’ reactions, attention to such complexity may be lost in busy clinical settings where the main priority is sustaining life. These findings add to the small body of work attempting to clarify the relationship between patient, illness and context.

Paper 1 highlighted that mental health factors appear to play a key role in how patients’ respond to the challenges of PMBT and should be considered within routine clinical practice. The review also identified systemic flaws in the available evidence base that must be addressed to improve the quality of future research and optimise the provision of supportive care.

Paper 2 provided a tentative conceptual model of adjustment processes encountered by patients with GBM, which advocates the targeted provision of supportive intervention and the need to adopt a multifaceted understanding of patient need and distress. Further work of this nature is necessary to maximise patient HRQoL and psychological wellbeing, regardless of prognosis.
7.5. References


6. Burnet NG, Jefferies SJ, Benson RJ, et al. Years of life lost (YLL) from cancer is an important measure of population burden and should be considered when allocating research funds. *Br J Cancer* 2005; **92**: 241-245.


55. Baker P, Beasley H, Dinwoodie R, et al. 'You're putting thoughts into my head': a qualitative study of the readiness of patients with breast, lung or prostate cancer to address emotional needs through the first 18 months after diagnosis. *Psycho-Oncol* 2013; **22**: 1402-1410.


102. Kaptein AA. Pick up the pieces and go home–on the demise of health psychology. *Health Psychol Rev* 2011; **5**: 39-47.


111. Huntington I and Robinson W. The many ways of saying yes and no: Reflections on the research coordinator’s role in recruiting research participants and obtaining informed consent. *IRB Ethics Hum Res* 2007: 6-10.


126. Garton S and Copland F. 'I like this interview; I get cakes and cats!': the effect of prior relationships on interview talk. *Qual Res* 2010; **10**: 533-551.


144. Ownsworth T, Goadby E, and Chambers SK. Support after brain tumor means different things: family caregivers’ experiences of support and relationship changes. *Front Oncol* 2015; **5**.


8. Appendices
Appendix 1: Neuro-Oncology author guidelines

MANUSCRIPT SUBMISSION

Submittal of a manuscript to *Neuro-Oncology* implies that the authors of the paper understand and fully accept the policies of the journal as detailed in these Instructions to Authors. Please read these instructions carefully and follow them strictly to ensure that the review and publication of your paper is as efficient and quick as possible. The editors reserve the right to return manuscripts that are not in accordance with these instructions.

All manuscripts submitted for possible publication, including text, tables, graphics, and supplementary materials, should be submitted online via the journal’s online submission system at [www.editorialmanager.com/n-o/](http://www.editorialmanager.com/n-o/). Once you have prepared your manuscript according to the instructions below, please read our instructions on how to submit your manuscript online [here](http://www.editorialmanager.com/n-o/). If you have any problems with the submission process or any questions about the guidelines in these instructions, please contact the *Neuro-Oncology* editorial office by e-mail ([neuonc.editorialoffice@oup.com](mailto:neuonc.editorialoffice@oup.com)).

If your manuscript is thought more appropriate for our sister journal *Neuro-Oncology Practice* (either before or after peer-review) we may pass it to the editor-in-chief of that Journal for consideration. Authors will be informed in advance if this is the case and may, of course, opt out.

REVIEW OF MANUSCRIPTS

All articles and features, whether invited or not, will undergo peer-review. Papers will normally be reviewed within 3–4 weeks of submission. Authors may suggest appropriate reviewers to whom the manuscript could be assigned or stipulate those reviewers who may have a bias or conflicting interest. Full names and e-mail addresses of suggested reviewers should be provided. Final assignments, however, are at the discretion of the Editor-in-Chief. Manuscripts and illustrations are not returned to the author unless the author requests them. Journal policy dictates that the identity or information leading to the identity of any reviewer is not to be revealed.

TYPES OF ARTICLES PUBLISHED

The following types of unsolicited articles are published in *Neuro-Oncology*:

- *Basic and Translational Investigations* or *Clinical Investigations* that report original experimental, translational, clinical, epidemiological, quality-of-life, or other studies relating to neuro-oncology and that are well documented, novel, and significant; included in this group are Phase 1–4 clinical trials reports.
- *Reviews* and *Editorials* that cover subjects of timely interest and importance to cancer researchers. (These are written by invitation of the Editor in Chief. Authors wishing to write a review or an editorial should send a letter
to the Editor in Chief outlining the proposed article. All reviews, whether
invited or not, will be subjected to full peer review.)

- *Letters to the Editor* offering considered opinions on manuscripts published
in the journal within the last 6 months (correspondence concerning articles
that have not been published in *Neuro-Oncology* will not be considered).
Letters containing brief results or technical notes of interest to the neuro-
ology community may also be considered for publication.
- *Case Studies* are only rarely published in *Neuro-Oncology*, and authors are
discouraged from submitting them except when the case is of extraordinary
importance.

The following types of articles typically are solicited by the Editor-in-Chief:

- *Symposia* on subjects selected by the Editor-in-Chief
- *Invited Meeting Reports* selected and invited by the Editor-in-Chief
- *Book Reviews* by invitation of the Editor-in-Chief (if you are interested in
reviewing books for *Neuro-Oncology*, please contact the Editorial Office)

Please note that *Neuro-Oncology* has suspended the category *Rapid Reports* as a
submission option. The journal editors may, however, elect to accelerate review and
publication of articles dealing with particularly important, timely, or urgent information
on a case-by-case basis.

*Announcements* of scientific meetings and courses of interest to *Neuro-Oncology* readers
should be submitted to Dr. Nicholas Butowski.

**MANUSCRIPT FORMAT**

No manuscript will be sent out for review until all items are received. The preferred
software for text is Microsoft Word, although manuscripts generated in other word
processing programs are acceptable if saved in Rich Text Format. Papers prepared using
desktop publishing software are not acceptable. The preferred software for illustrations is
described in the Figures & Illustrations section.

The manuscript text (title page, abstract, article text, acknowledgments, reference list,
and figure captions), figures, and tables (in .doc or .rtf format) should be submitted as
separate files. This applies to the original version of the manuscript and any revised
versions.

Please use short, simple filenames when saving all your documents and avoid special
characters, punctuation marks, symbols (such as &,), and spaces. Macintosh users must
also type the extension at the end of the file name (.doc, .rtf, .jpg, .gif, .tif, .xls, .pdf, .eps,
.ppt, .mov, or .qt).

Other helpful hints are: (i) use the TAB key once for paragraph indents; (ii) where
possible, use Times New Roman for the text font and Symbol for any Greek and special
characters; (iii) use word processing formatting features to indicate Bold, Italic, Greek,
Math, superscript, and subscript characters; (iv) please avoid using underline: for cases,
use italic; for emphasis, use bold; (v) clearly identify unusual symbols and Greek letters;
and (vi) differentiate between the letter O and zero and among capital I, lowercase L, and the number 1.

Footnotes should not be used in the text.

At the time of submission, please also include the files for any supplementary material that should accompany your manuscript.

Double-space the entire manuscript (including references, tables, figure captions, and supplementary materials) on U.S. letter-sized paper, leaving at least 1-inch (2.54-cm) margins all around and set to print on one side of the paper only. Manuscripts should conform strictly to journal style. Those not in Neuro-Oncology style (described below) or not written in good idiomatic U.S. English may be returned to the author without review. Terminology and abbreviations not consistent with internationally accepted guidelines should be avoided (see Abbreviations & Acronyms below), as should laboratory jargon.

It is recommended that authors spell-check (with the language set to U.S. English) all files before submission. Particularly if English is not your first language, before submitting your manuscript, you may wish to have it edited for language. This may help to ensure that the academic content of your paper is fully understood by journal editors and reviewers. Language editing does not guarantee that your manuscript will be accepted for publication. A list of such services is provided here. Other specialist language editing companies offer similar services. Authors are liable for all costs associated with such services.

Style guides that may be helpful in writing the manuscript are the current editions of the American Medical Association Manual of Style and The ACS Style Guide. Essentials of Writing Biomedical Research Papers, 2nd ed. (M. Zeiger, ed., McGraw Hill, 2000), which addresses the content and format of scientific articles. Authors are urged to proofread and edit their manuscripts carefully before submission. Alterations at the proof stage delay publication and are expensive. Excessive changes at the proof stage not due to printer’s errors will be charged to the authors.

Arrange the sections of text in the following order, and number all pages, beginning with the title page:

- Title page
- Abstract and keywords
- Text
- Acknowledgments
- References
- Captions for all illustrations
- Tables (these must be submitted as separate files)

Basic format for Basic and Translational Investigations and Clinical Investigations articles
The basic format for basic and translational investigations and clinical investigations, including reports of clinical trials is described here. (Articles with unique formatting requirements (editorials, review articles, and invited meeting reports) are covered below).

Basic and translational investigations and clinical investigations should adhere to the following guidelines:

- 250-word abstract (maximum)
- 6000-word limit of text and references combined (i.e. all text in manuscript file)
- 6 display items (figures and/or tables)
- 50 references (maximum)

**Title page**

- Title
- Authors' full names; given name(s) followed by surname
- Affiliation of each author at the time of the study, including complete addresses with zip codes. If authors are from more than one department or institution, each author's initials should be placed in parentheses after the applicable address.
- Running title, not to exceed 50 characters and spaces
- Name and contact information for the corresponding author, including telephone, fax, and e-mail address
- Footnotes regarding change of address or affiliation, co-first authorship, or new sequence accession numbers
- Statement (titled "Funding") detailing any funding that supported the research
- Statement (titled "Conflict of Interest") detailing any conflicts of interest for all authors
- List of any unpublished papers cited (see Unpublished Material under References)
- If applicable, a statement that the paper being submitted is one of a series
- Mention of total manuscript word count, including words in references, figure legends, etc.

Any deletions or additions to the author list after acceptance of the paper must be submitted in writing or by email, signed by all authors (including those added or deleted), to the *Neuro-Oncology* editorial office. Publication of manuscripts will be withheld until all such written approvals are received. *Neuro-Oncology* accepts no responsibility for such changes.

Similarly, all conflicts of interest (or relationships that would be suspected of constituting conflicts) should be declared and explained at the time of submission and reflect not only current conflicts but those in place at the time the research was conducted. Any changes made to the list of conflicts after the paper is accepted must be submitted in writing, signed by the appropriate authors (that is, the corresponding author and the author for whom the conflict exists), to the *Neuro-Oncology* editorial office. Publication of
manuscripts will be withheld until all such written approvals are received. *Neuro-Oncology* accepts no responsibility for such changes.

**Authorship**

All authors listed on the manuscript should have contributed significantly to the experimental design, its implementation, or analysis and interpretation of the data. All authors should have been involved in the writing of the manuscript at draft and any revision stages, and have read and approved the final version. Any other individuals who contributed to the experiment or the writing of the manuscript should be listed in the Acknowledgment section.

*Authorship Requirements.* For guidelines on authorship, please refer to the Uniform Requirements for Manuscripts Submitted to Biomedical Journals, formulated by the International Committee of Medical Journal Editors. The cover letter should state that all authors have seen and approved the manuscript.

**Abstract**

The abstract should not exceed 250 words. All abstracts, except those accompanying review articles, should be written in structured format:

- **Background:** State the clinical (or other) importance of the work. Include a hypothesis or purpose statement (e.g., “To determine whether…. we…”).
- **Methods:** Give the materials (or patients) and methods used to answer the research question.
- **Results:** State the study’s findings. Make sure the results match the methods.
- **Conclusions:** In a sentence or two, explain how the findings address the purpose of the study. The conclusions should be supported by the results given.

Because abstracts often appear apart from the text of a paper (e.g., in PubMed or Medline), they should not cite references. Keep nonstandard abbreviations and acronyms to a minimum (no more than five in the abstract), defining them in parentheses at first mention. It is essential that the Abstract clearly states the biological importance of the work described in the paper.

**Keywords**

Below the abstract, list up to five keywords that may be used for indexing.

**Text**

*Introduction.* This section should state the problem or question being addressed and summarize relevant background information to provide context for the research question.

*Materials and Methods.* The explanation of the experimental methods should be brief but adequate for repetition by qualified investigators. Procedures that have been published previously should merely be cited in appropriate references. Only new and significant modifications of previously published procedures need complete exposition. The sources
and manufacturers of special chemicals or preparations used should be named. Some of
the method details (buffer composition, PCR primers, incubation conditions, etc.) may be
placed in a Methods supplement but each method must be mentioned in the main
manuscript with enough information so that a reader does not have to consult the
supplement to understand the procedures. Reference to the supplement should be made in
the main manuscript text where appropriate. NOTE: Your ethics statement(s) must
remain in the main manuscript.

For experimental investigations of human or animal subjects, state in the Methods section
of the manuscript that an appropriate institutional review board approved the project.
Investigators who do not have formal ethics review committees should follow the
principles outlined in "World Medical Association Declaration of Helsinki: Research
involving human subjects". For investigations of human subjects, state in the Methods
section the manner in which informed consent was obtained from the subjects. Statistical
methods should also be clearly and completely described in the Methods section.

If cell lines are used, please include a statement that addresses:
• Where and when the cell line was obtained,
• Whether the cell lines have previously been tested and authenticated (e.g., by a cell
  bank),
• The method by which the cell lines were tested, and
• How and when the cell lines were tested.

Results. This section should include a concise summary of the data presented in the tables
and illustrations. Excessive elaboration of those data should be avoided. The Results and
Discussion sections may be combined if doing so saves space or improves the logical
sequence of the material.

Discussion. The data should be interpreted concisely, without repeating material already
presented in the Results section. Speculation is permissible, but it must be well founded
and clearly identified as speculation.

Funding. Details of all funding sources for the work in question should be given in a
separate section entitled "Funding". This should appear before the "Acknowledgments"
section. The following rules should be followed: the full official funding agency name
should be given (that is, "National Institutes of Health", not "NIH"); grant numbers
should be given in brackets; multiple grant numbers should be separated by a comma;
agencies should be separated by a semi-colon; no extra wording such as "Funding for this
work was provided by ..." should be used; where individuals need to be specified for
certain sources of funding, explanatory text should be added after the relevant agency or
grant number "to [author initials]" (e.g., "National Institutes of Health (CB5453961 to
C.S., DB645473 to M.I.); Funding Agency (hfygr67789)."

Acknowledgments (optional). An Acknowledgments section (not footnotes) should be
included, if appropriate, to recognize the following:

• Special assistance or contributions by non-authors (e.g., supply of materials
  or editorial support)
• Financial support for the research or a researcher (specifying grant numbers and recipients) other than that described in the Funding statement (see Title Page, above)
• Previous presentation of the material at a meeting, workshop, or other event

Personal acknowledgments should precede those of institutions or agencies. Please note that acknowledgment of funding bodies and declarations regarding conflict of interest should be given in separate Funding and Conflict of Interest sections on the title page (see above).

References. See "References" for specific instructions.

Figure Captions and Tables. Figures should be numbered sequentially with Arabic numerals. Figures may have subparts (A, B, C, etc.); each subpart should be described in the caption. See recent issues of the journal for examples of acceptable styles.

Captions are required for all figures and should be typed, double-spaced, after the list of references. Captions should briefly describe the data shown and should not repeat details given in the text. Include the type of staining, magnification, and similar information required for accurate interpretation where applicable. Each caption should adequately identify all symbols (where not defined on the figure itself) and abbreviations used in the figure. Captions and symbols should make the figure interpretable without reference to the text. Figure numbers or captions should not be included on the face of an illustration.

Number tables with Arabic numerals. Tabular material should not simply duplicate data presented in the text or figures. Large groups of individual values should be avoided; instead, these should be averaged and an appropriate designation of the dispersion, such as standard deviation or standard error, included.

Tables should be typed in the manuscript file format with double spacing, but minimizing redundant space; tables must be submitted as separate files and include a descriptive title. Note that each column, including the first column, must carry an appropriate heading, and if numerical measurements are given, these units should be added to the column heading. Identify footnotes with superscript lowercase italic letters (a, b, c, etc.). Tables should not have subparts.

Special requirements for other articles

Clinical Trial Reports are formatted like clinical investigations. However, before submitting a clinical trial report, authors should consult the GNOSIS guidelines (published in the October 2005 issue of Neuro-Oncology [Vol. 7, Issue 4] [PDF]) and, to ensure completeness, crosscheck their manuscript against these guidelines. For negative studies, highest priority will be given to manuscripts that are written concisely.

Randomized controlled trials should conform to the Consolidated Standards of Reporting Trials (CONSORT) guidelines.
**Review Articles** should provide timely updates of advances in an area of neuro-oncology. Authors of unsolicited reviews should contact the Editor-in-Chief Patrick Wen, M.D. (patrick_wen@dfci.harvard.edu) first to determine if the review is appropriate for *Neuro-Oncology*.

Because of the nature of review articles, which may cover a broad scope of topics related to the subject at hand, authors should use short headings to identify major manuscript sections. Though potentially broad in scope, reviews should be as concise as possible and should focus on seminal findings and important developments contributing to understanding of (or controversy about) the subject at hand.

Reviews should include maximally:

- 200-word abstract
- 7000 words of text and references combined
- 7 tables and/or figures
- 100 references

**Advances-in-Brief** should provide brief updates of advances in a focused area of neuro-oncology. These are shorter than Reviews and provide either a brief review of important advances in the understanding of an aspect of biology pertinent to neuro-oncology, enhancing the understanding of articles published in *Neuro-Oncology*, or a thoughtful discussion of new paradigms important to the field. Advances-In-Brief will normally be solicited by the Editor-In-Chief; however, authors who wish to submit this type of article should contact the Editor-In-Chief, Patrick Wen, M.D. (patrick_wen@dfci.harvard.edu), first to determine if the article is appropriate for *Neuro-Oncology*.

Advances-in-Brief should include maximally:

- 200-word abstract
- 3500 words of text and references combined
- 5 tables and/or figures
- 50 references

**Invited Meeting Reports** should typically have a total length—including the title page, text, references, and tables or figures—of five printed pages (or about 15 typed pages).

**REFERENCES**

If you use EndNote and Reference Manager to facilitate referencing citations (not required for submission), this journal's style is available for use.

*Neuro-Oncology* uses a numbered reference list, with references presented in order of citation in the text; superscript Arabic numbers are used to cite references in the text.

Within the reference list at the end of the paper, please follow the format shown in the samples below. Note that the author’s surname and initials (without commas or periods) are used. In accordance with the current edition of the *AMA Manual of Style*, for works
with more than six authors, list the first three authors and then “et al.”: Rose PR, Walker BK, Matthews CP Jr, et al.

Sample reference entries:

- **Journal Article**

- **Correction**

- **Supplement**

- **Chapter in Book**

- **Book**

- **Web References**


- **Abstract**

- **Unpublished Material**
  Cite unpublished articles (including those in review or preparation), data, and observations parenthetically in the text as either "unpublished data" or "unpublished manuscript," along with the name of the investigator responsible for those data (e.g., the lead author of a paper in preparation). No manuscript title or presumed year of publication is needed. In the case of "personal communications," give the name of the original speaker/correspondent and, if possible, the date of the communication; note that the Editorial Office requires a signed statement from the speaker/correspondent giving the author permission to quote him or her in the manuscript. (Example: Nonetheless, it appears that peptides become associated in some fashion with chaperones prior to or upon extraction from cells (M.W. Graner, unpublished data), and the effects of exogenous chaperones on the innate immune cells are certainly not denied.)
ABBREVIATIONS AND ACRONYMS

*Genes:* All gene names should be in italic type, while their corresponding proteins should appear in roman type. For human gene names, the Human Genome Organisation’s database style (all caps, no hyphens) and name (not alias) are used. Visit the OMIM database for human protein terminology.

*Other:* Nonstandard abbreviations should be kept to a minimum. They should be defined at the first occurrence and introduced only when the abbreviation will be used several times.

The term “nonstandard” refers to abbreviations that are not a part of the Système International d’Unités (International System of Units, known as SI units) and those that are not widely known. Some standard abbreviations not needing expansion at first use are listed in the current edition of the *AMA Manual of Style.* A list of standard abbreviations is also included at the end of these instructions. Nonstandard abbreviations used in a manuscript should be established in parentheses when they are first mentioned in the text (e.g., “The study population was drawn from the institution’s neonatal intensive care unit (NICU) . . .”).

**Abbreviations list.** Authors may use, without definition, the following abbreviations:
- ADP adenosine diphosphate
- ATP adenosine triphosphate
- cDNA complementary DNA
- CNS central nervous system
- CoA, acyl-CoA coenzyme A and its acyl derivatives (e.g., acetyl)
- CT computed tomography
- DNA deoxyribonucleic acid
- DNase deoxyribonuclease
- EDTA ethylenediaminetetraacetate
- ELISA enzyme-linked immunosorbent assay
- FDA Food and Drug Administration (U.S.)
- IR infrared
- KPS Karnofsky performance status
- MR magnetic resonance
- MRI magnetic resonance imaging
- mRNA messenger RNA
- NAD+, NADH nicotinamide adenine dinucleotide and its reduced form
- NADP+, NADPH nicotinamide adenine dinucleotide phosphate and its reduced form
- NCI National Cancer Institute (U.S.)
- NIH National Institutes of Health (U.S.)
- nRNA nuclear RNA
- PCR polymerase chain reaction
- PET positron emission tomography
- RBC red blood cell
- RNA ribonucleic acid
- RNase ribonuclease
- rRNA ribosomal RNA
- tRNA transfer RNA
- Tris tris(hydroxymethyl)methyamine
- UV ultraviolet
WBC white blood cell
WHO World Health Organization

Units of Concentration:
Gy gray
M (not used for moles) molar (moles/liter)
mM (preferred to 10-3 M) millimolar (millimoles/liter)
µM (preferred to 10-6 M) micromolar (micromoles/liter)
nM (not µM) nanomolar
pM (not nM) picomolar
g/ml, g/100 ml, g per liter, etc. avoid using mg%

Units of Length, Area, Volume, Mass, Time:
The abbreviations below are correct for both singular and plural forms of each term.
cm centimeter
g gram
h hour
kg kilogram
m meter
min minute
µm micrometer (not micron)
mm millimeter
ml milliliter
µl microliter
µg microgram
mg milligram
nm nanometer
pm picometer
s second

Physical and Chemical Units:
°C degree Celsius (centigrade)
°F degree Fahrenheit
g acceleration of gravity (closed with number [e.g., 200g])
K Kelvin

Others:
Ci Curie
cpm counts per minute
Da dalton
dpm disintegrations per minute
eq equivalent log logarithm (Briggsian)
ln logarithm (natural)
mol mole
Mr molecular weight
P probability
R roentgen
rpm revolutions per minute
S Svedberg unit
SD standard deviation
SEM standard error of the mean
V volt

In chemical compounds:
o- ortho
m- meta
p- para
sec- secondary
tert- tertiary

Routes of administration:
 i.c. intracranial
 i.m. intramuscular
 i.p. intraperitoneal
 i.v. intravenous
 p.o. oral
 s.c. subcutaneous

Tables

All tables should be on separate pages and accompanied by a title and footnotes where necessary. The tables should be numbered consecutively using Arabic numerals. Units in which results are expressed should be given in parentheses at the top of each column and not repeated in each line of the table. Ditto signs are not used. Avoid overcrowding tables and using excessive text. The format of tables should be in keeping with that normally used by the journal; in particular, vertical lines, colored text, and shading should not be used. Please be certain that the data given in tables are correct.

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Appendix 2: Search terms used to identify articles for inclusion in the review

1. “brain tumo*r*” or “brain neoplasm*” or “glioblastoma” or “GBM” or “astrocytoma” or “oligodendrogliaoma” or “oligoastrocytoma” or “high-grade glioma” or “high grade glioma” or “primary malignant brain tumo*r*”

2. “adjustment” or “adaptation” or “acceptance” or “satisfaction” or “happiness” or “happy” or “adaptation” or “optimism” or “optimistic” or “well-being” or “quality of life” or “QoL” or “anxiety” or “depression” or “stress disorder*” or “stress, psychological” or “mood” or “affect”

3. 1 and 2

4. “child*” or “p?ediatric” or “adolescen*”

5. 3 not 4
Appendix 3: PRISMA checklist

<table>
<thead>
<tr>
<th>Section/topic</th>
<th>#</th>
<th>Checklist item</th>
<th>Reported on page #</th>
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</thead>
<tbody>
<tr>
<td><strong>TITLE</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Title</td>
<td>1</td>
<td>Identify the report as a systematic review, meta-analysis, or both.</td>
<td>1</td>
</tr>
<tr>
<td><strong>ABSTRACT</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Structured summary</td>
<td>2</td>
<td>Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.</td>
<td>2</td>
</tr>
<tr>
<td><strong>INTRODUCTION</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rationale</td>
<td>3</td>
<td>Describe the rationale for the review in the context of what is already known.</td>
<td>3-4</td>
</tr>
<tr>
<td>Objectives</td>
<td>4</td>
<td>Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).</td>
<td>4</td>
</tr>
<tr>
<td><strong>METHODS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protocol and registration</td>
<td>5</td>
<td>Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.</td>
<td>-</td>
</tr>
<tr>
<td>Eligibility criteria</td>
<td>6</td>
<td>Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.</td>
<td>5</td>
</tr>
<tr>
<td>Information sources</td>
<td>7</td>
<td>Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.</td>
<td>5</td>
</tr>
<tr>
<td>Search</td>
<td>8</td>
<td>Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.</td>
<td>Appendix 2</td>
</tr>
<tr>
<td>Study selection</td>
<td>9</td>
<td>State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).</td>
<td>5</td>
</tr>
<tr>
<td>Data collection process</td>
<td>10</td>
<td>Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.</td>
<td>5</td>
</tr>
<tr>
<td>Data items</td>
<td>11</td>
<td>List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.</td>
<td>8</td>
</tr>
<tr>
<td>Section/topic</td>
<td>#</td>
<td>Checklist item</td>
<td>Reported on page #</td>
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</tr>
<tr>
<td>Risk of bias in individual studies</td>
<td>12</td>
<td>Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.</td>
<td>-</td>
</tr>
<tr>
<td>Summary measures</td>
<td>13</td>
<td>State the principal summary measures (e.g., risk ratio, difference in means).</td>
<td>-</td>
</tr>
<tr>
<td>Synthesis of results</td>
<td>14</td>
<td>Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis.</td>
<td>6</td>
</tr>
<tr>
<td>Risk of bias across studies</td>
<td>15</td>
<td>Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).</td>
<td>-</td>
</tr>
<tr>
<td>Additional analyses</td>
<td>16</td>
<td>Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.</td>
<td>6</td>
</tr>
<tr>
<td>RESULTS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study selection</td>
<td>17</td>
<td>Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.</td>
<td>5</td>
</tr>
<tr>
<td>Study characteristics</td>
<td>18</td>
<td>For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.</td>
<td>7</td>
</tr>
<tr>
<td>Risk of bias within studies</td>
<td>19</td>
<td>Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).</td>
<td>-</td>
</tr>
<tr>
<td>Results of individual studies</td>
<td>20</td>
<td>For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.</td>
<td>Table 1</td>
</tr>
<tr>
<td>Synthesis of results</td>
<td>21</td>
<td>Present results of each meta-analysis done, including confidence intervals and measures of consistency.</td>
<td>8-15</td>
</tr>
<tr>
<td>Risk of bias across studies</td>
<td>22</td>
<td>Present results of any assessment of risk of bias across studies (see item 15).</td>
<td>-</td>
</tr>
<tr>
<td>Additional analysis</td>
<td>23</td>
<td>Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).</td>
<td>7-8, Table 1, Appendix 4</td>
</tr>
<tr>
<td>DISCUSSION</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Summary of evidence</td>
<td>24</td>
<td>Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).</td>
<td>16-18</td>
</tr>
<tr>
<td>Limitations</td>
<td>25</td>
<td>Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).</td>
<td>21</td>
</tr>
<tr>
<td>Section/topic</td>
<td>#</td>
<td>Checklist item</td>
<td>Reported on page #</td>
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<tr>
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</tr>
<tr>
<td>Conclusions</td>
<td>26</td>
<td>Provide a general interpretation of the results in the context of other evidence, and implications for future research.</td>
<td>19-22</td>
</tr>
<tr>
<td>FUNDING</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Funding</td>
<td>27</td>
<td>Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.</td>
<td>-</td>
</tr>
</tbody>
</table>

**Additional information**

<table>
<thead>
<tr>
<th>Item</th>
<th>Comment</th>
</tr>
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<tbody>
<tr>
<td>12</td>
<td>Risk of bias was not explicitly assessed as the review did not aim to assess evidence for interventions. Studies included in the review were subject to critical appraisal (see pages 6-8, table 1, appendix 4) to identify flaws that may bias reported findings.</td>
</tr>
<tr>
<td>19</td>
<td>Risk of bias was not explicitly assessed as the review did not aim to assess evidence for interventions. Studies included in the review were subject to critical appraisal (see pages 6-8, table 1, appendix 4) to identify flaws that may bias reported findings.</td>
</tr>
<tr>
<td>27</td>
<td>This review was conducted as part of a doctoral thesis with no funding.</td>
</tr>
</tbody>
</table>
Appendix 4: Newcastle-Ottawa Scale (Wells et al, 2012)

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE
CASE CONTROL STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

Selection

1) Is the case definition adequate?
   a) yes, with independent validation
   b) yes, eg record linkage or based on self reports
   c) no description

2) Representativeness of the cases
   a) consecutive or obviously representative series of cases
   b) potential for selection biases or not stated

3) Selection of Controls
   a) community controls
   b) hospital controls
   c) no description

4) Definition of Controls
   a) no history of disease (endpoint)
   b) no description of source

Comparability

1) Comparability of cases and controls on the basis of the design or analysis
   a) study controls for ___________________________ (Select the most important factor.)
   b) study controls for any additional factor (This criteria could be modified to indicate specific control for a second important factor.)

Exposure

1) Ascertaintment of exposure
   a) secure record (eg surgical records)
   b) structured interview where blind to case/control status
   c) interview not blinded to case/control status
   d) written self report or medical record only
   e) no description

2) Same method of ascertainment for cases and controls
   a) yes
   b) no

3) Non-Response rate
   a) same rate for both groups
   b) non respondents described
   c) rate different and no designation
NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE
COHORT STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

Selection
1) Representativeness of the exposed cohort
   a) truly representative of the average __________________ (describe) in the community ✭
   b) somewhat representative of the average __________________ in the community ✭
   c) selected group of users eg nurses, volunteers
   d) no description of the derivation of the cohort

2) Selection of the non exposed cohort
   a) drawn from the same community as the exposed cohort ✭
   b) drawn from a different source
   c) no description of the derivation of the non exposed cohort

3) Ascertainment of exposure
   a) secure record (eg surgical records) ✭
   b) structured interview ✭
   c) written self report
   d) no description

4) Demonstration that outcome of interest was not present at start of study
   a) yes ✭
   b) no

Comparability
1) Comparability of cohorts on the basis of the design or analysis
   a) study controls for __________________ (select the most important factor) ✭
   b) study controls for any additional factor ✭ (This criteria could be modified to indicate specific control for a second important factor.)

Outcome
1) Assessment of outcome
   a) independent blind assessment ✭
   b) record linkage ✭
   c) self report
   d) no description

2) Was follow-up long enough for outcomes to occur
   a) yes (select an adequate follow up period for outcome of interest) ✭
   b) no

3) Adequacy of follow up of cohorts
   a) complete follow up - all subjects accounted for ✭
   b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____% (select an adequate %) follow up, or description provided of those lost ✭
   c) follow up rate < ____% (select an adequate %) and no description of those lost
   d) no statement
<table>
<thead>
<tr>
<th>Question</th>
<th>Criteria</th>
<th>Yes (2 points)</th>
<th>Partial (1 point)</th>
<th>No (0 points)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Research aim</td>
<td>The research aim is clearly specified; the authors have hypothesized potential findings.</td>
<td>Research aim clearly specified, no hypotheses stated.</td>
<td>Research aim is not clearly specified</td>
</tr>
<tr>
<td>2</td>
<td>Validity of measures</td>
<td>All assessment tools used in the study have been previously validated for use in health populations.</td>
<td>The study uses a combination of validated and non-validated assessment tools.</td>
<td>The study only uses non-validated measures.</td>
</tr>
<tr>
<td>3</td>
<td>Sampling method</td>
<td>Sampling method is described and is adequate for replication.</td>
<td>Sampling method described, would require further information to replicate (such as referring to a previously published paper)</td>
<td>Sampling method is not described.</td>
</tr>
<tr>
<td>4</td>
<td>Exclusivity of diagnosis</td>
<td>Every participant in the brain tumor group has a diagnosis of high-grade brain tumor.</td>
<td>At least 90% of the brain tumor group has a diagnosis of high-grade brain tumor.</td>
<td>Less than 90% of the brain tumor group has a diagnosis of high-grade brain tumor.</td>
</tr>
<tr>
<td>5</td>
<td>Specificity of diagnosis</td>
<td>Participants have been differentiated in terms of WHO grade and/or tumor type.</td>
<td>Participants have been differentiated in terms of high-grade/low-grade. There is no information on tumor type.</td>
<td>There is no differentiation in terms of tumor grade.</td>
</tr>
<tr>
<td>6</td>
<td>Representativeness of the sample</td>
<td>The sample is generally representative of the average in the target population AND this is clearly demonstrated.</td>
<td>The sample is likely representative of the average in the target population.</td>
<td>The sample is not representative OR there is no description of the representativeness of the sample.</td>
</tr>
<tr>
<td>7</td>
<td>Sample size</td>
<td>The study describes an a priori power calculation or other justification.</td>
<td>The study describes a post-hoc justification.</td>
<td>Not justification for sample size.</td>
</tr>
<tr>
<td>8</td>
<td>Statistical test(s)</td>
<td>The statistical test(s) used to analyze the data is clearly described and appropriate, and the measurement of the association is presented, including the probability level.</td>
<td>The statistical test(s) is appropriate. Certain details are missing but there is sufficient information to report.</td>
<td>The statistical test(s) is not appropriate or not described in adequate detail.</td>
</tr>
</tbody>
</table>

* As the majority of studies included in the review recruited participants from the United States (n=11), this criterion was met if the sample roughly matched the median age at diagnosis and sex ratio for incidence as specified by the CBTRUS Statistical Report: Primary Brain and Central Nervous System Tumors Diagnosed in the United States in 2007-2011.
Appendix 6: Intraclass correlation output from SPSS for inter-rater reliability check for quality assessment measure
Appendix 7: Summary of guidance on the conduct of narrative synthesis in systematic reviews (Popay et al, 2006)

The following summary has been included with permission of the author (J. Popay, personal communication, 11 May 2015)

Do domestic smoke alarms save lives? Can young offenders be ‘scared straight’ through tough penal measures? What factors should be considered when designing and implementing a multi-sectoral injury prevention programme in a local area? Making sense of large bodies of evidence drawn from research using a range of methods is a challenge. Ensuring that the product of this synthesis process can be trusted is important for policy makers, for practitioners and for the people research is intended to benefit.

There are a number of ways in which research evidence can be brought together to give an overall picture of current knowledge that can be used to inform policy and practice decisions. However, the trustworthiness of some of these methods remains problematic. This guidance, produced with a grant from the UK Economic and Social Research Council’s Methods Programme funding, focuses on a particular approach - narrative synthesis. Variants of this approach are widely used in work on evidence synthesis, including Cochrane reviews, but there is currently no consensus on the constituent elements of narrative synthesis and the conditions for establishing trustworthiness – notably a systematic and transparent approach to the synthesis process with safeguards in place to avoid bias resulting from the undue emphasis on one study relative to another – are frequently absent. This guidance therefore aims to contribute to improving the quality of narrative approaches to evidence synthesis.
Narrative synthesis (NS) as used in the guidance, refers to an approach to the systematic review and synthesis of findings from multiple studies that relies primarily on the use of words and text to summarise and explain the findings of the synthesis. Whilst it can involve the manipulation of statistical data, the defining characteristic is that it adopts a textual approach to the process of synthesis to ‘tell the story’ of the findings from the included studies. NS can be used to synthesise evidence focusing on a wide range of questions, not only those relating to the effectiveness of a particular intervention. It is part of a larger review process that includes a systematic approach to searching for and quality appraising research based evidence as well as the synthesis of this evidence but the guidance does not provide advice on these other elements of a systematic review.

The guidance provides an over-arching framework to guide the conduct of a narrative synthesis and describes specific tools and techniques that can be used in this process. For practical reasons, the guidance is focused on the conduct of the two types of systematic review which have particular salience for those who want their work to inform policy and practice: reviews addressing questions concerned with the effects of interventions and those concerned with the implementation of interventions shown to be effective in experimental settings. Two demonstration syntheses are also included to illustrate how the guidance can be used to inform decisions about which specific tools and techniques to use in the context of a particular review. the guidance also includes an extensive methodological bibliography.

The guidance is intended to be accessible to a range of people involved in systematic reviewing. However, whilst users of the guidance will not need to be systematic review experts, they will need a reasonable level of research literacy and users without experience of systematic review work should collaborate with more experienced colleagues.

For more information and to obtain the full guidance document go to:

http://www.lancs.ac.uk/shm/research/nssr/research/dissemination/publications.php
Appendix 8: Psycho-Oncology author guidelines

Manuscript Submission

All papers must be submitted via the online system.

Psycho-Oncology operates an online submission and peer review system that allows authors to submit articles online and track their progress via a web interface.

Please read the remainder of these instructions to authors and then click http://mc.manuscriptcentral.com/pon to navigate to the Psycho-Oncology online submission site, ScholarOne Manuscripts (formerly known as Manuscript Central).

IMPORTANT: Please check whether you already have an account in the system before trying to create a new one. If you have reviewed or authored for the journal in the past year it is likely that you will have had an account created.

File types. Preferred formats for the text and tables of your manuscript are .doc, .rtf, .ppt, .xls. LaTeX files may be submitted provided that an .eps or .pdf file is provided in addition to the source files. Figures may be provided in .tiff or .eps format.

Please note: This journal does not accept Microsoft Word 2007 documents at this time. Please use Word's "Save As" option to save your document as a .doc file type. If you try to upload a Word 2007 document in ScholarOne Manuscripts you will be prompted to save .docx files as .doc files.

Initial Submission

Non-LaTeX Users: Upload your manuscript files. At this stage, further source files do not need to be uploaded.

LaTeX Users: For reviewing purposes you should upload a single .pdf that you have generated from your source files. You must use the File Designation "Main Document" from the dropdown box.

Revision Submission

Non-LaTeX Users: Editable source files must be uploaded at this stage. Tables must be on separate pages after the reference list, and not be incorporated into the main text. Figures should be uploaded as separate figure files.

LaTeX Users: When submitting your revision you must still upload a single .pdf that you have generated from your now revised source files. You must use the File Designation "Main Document" from the dropdown box. In addition you must upload your TeX source files. For all your source files you must use the File Designation "Supplemental Material not for review". Previous versions of uploaded documents
must be deleted. If your manuscript is accepted for publication we will use the files you upload to typeset your article within a totally digital workflow.

Copyright and Permissions

If your paper is accepted, the author identified as the formal corresponding author for the paper will receive an email prompting them to login into Author Services; where via the Wiley Author Licensing Service (WALS) they will be able to complete the license agreement on behalf of all authors on the paper.

For authors signing the copyright transfer agreement

If the OnlineOpen option is not selected the corresponding author will be presented with the copyright transfer agreement (CTA) to sign. The terms and conditions of the CTA can be previewed in the samples associated with the Copyright FAQs below:

CTA Terms and Conditions

For authors choosing OnlineOpen

If the OnlineOpen option is selected the corresponding author will have a choice of the following Creative Commons License Open Access Agreements (OAA):

- Creative Commons Attribution License OAA
- Creative Commons Attribution Non-Commercial License OAA
- Creative Commons Attribution Non-Commercial -NoDerivs OAA

To preview the terms and conditions of these open access agreements please visit the Copyright FAQs hosted on Wiley Author Services and visit http://www.wileycoppenaccess.com/details/content/12f25db4c87/Copyright--License.html.

If you select the OnlineOpen option and your research is funded by The Wellcome Trust and members of the Research Councils UK (RCUK) you will be given the opportunity to publish your article under a CC-BY license supporting you in complying with Wellcome Trust and Research Councils UK requirements. For more information on this policy and the Journal’s compliant self-archiving policy please visit: http://www.wiley.com/go/funderstatement.

Submission of a manuscript will be held to imply that it contains original unpublished work and is not being submitted for publication elsewhere at the same time. Submitted material will not be returned to the author, unless specifically requested.

Manuscript style. The language of the journal is English. 12-point type in one of the standard fonts: Times, Helvetica, or Courier is preferred. It is not necessary to
double-line spacing your manuscript. There should be a separate title page with full information and another page for an abstract, prior to the Introduction. Tables must be on separate pages after the reference list, and not be incorporated into the main text. Figures should be uploaded as separate figure files.

- During the submission process you must enter the full title, short title of up to 70 characters and names and affiliations of all authors. Give the full address, including email, telephone and fax, of the author who is to check the proofs.
- Include the name(s) of any sponsor(s) of the research contained in the paper, along with grant number(s).
- Enter an abstract of up to 250 words for all articles. An abstract is a concise summary of the whole paper, not just the conclusions, and is understandable without reference to the rest of the paper. It should contain no citation to other published work. You must submit your abstract according to these headings: objective; methods; results; conclusions.
- Include up to six keywords which must contain the words cancer and oncology that describe your paper for indexing purposes.
- Research Articles should not exceed 4000 words (including no more than four figures and/or tables) plus up to 40 references. Review papers of up to 6000 words will be considered, with 80 references - authors should contact the Editors for advice. All papers should use the following headings: Background, Methods (including statistical methods), Results, Conclusions. Word counts should include the title page, abstract, main manuscript, tables and figures, but exclude the references.
- Qualitative manuscript submissions should usually be based on a minimum of 20 respondents. Authors may contact the Editors if they require further details.
- When submitting a randomised trial, please complete and supply the CONSORT checklist and include diagram. For systematic reviews or meta-analyses please complete the PRISMA checklist and include flowchart. Please complete and supply AMSTAR for systematic reviews which are narrative reviews not meta-analyses.
- When you upload your files on the ScholarOne Manuscripts site, please use the file designation 'Supplementary File for Review' for any files which need to be seen by reviewers but should not be included in the final published version of your paper (if accepted for publication). This may include CONSORT checklists, PRISMA flowcharts, or tables and figures which are referred to in the text but which can appear online only as Supporting Information.

*Psycho-Oncology* publishes Clinical Correspondence. This replaces the previous Brief Reports section. Items submitted as Clinical Correspondence may include:

1. Feasibility studies
2. Case studies
3. Phase I/II clinical trials
4. Questionnaire development studies
5. Service Development
6. Commentary
7. Novel clinical techniques

The following requirements apply to this section:

1. Five succinct key points (and no abstract)
2. Text 1500 words maximum, including the title page, abstract, figures and tables, but excluding the references.
3. Two figures/tables maximum
4. Ten references maximum

- Letters to the Editor should not exceed 400 words including a maximum of one reference. No figures or tables. Please note that if Letters to the Editor include a comment on a previously published paper the authors of said paper should be allowed 4 weeks in which to respond. If no response after 4 weeks the Letter will simply be accepted with an Editor's Footnote "The authors of [Title of Paper previously published] offered no comments".

All abbreviations except for SI symbols should be written in full the first time they appear. Generic or clinical names should be used for all compounds: materials and products should be identified. The species of any animals used should be stated precisely. Sources of unusual materials and chemicals, and the manufacturer and model of equipment should be indicated. materials and products should be identified in the text followed by the trade name in brackets.

**Reference style.** References should be cited in the text by number within square brackets and listed at the end of the paper in the order in which they appear in the text. All references must be complete and accurate. If necessary, cite unpublished or personal work in the text but do not include it in the reference list. Where possible the DOI for the reference should be included at the end of the reference. Online citations should include date of access. References should be listed in the following style:


**Illustrations.** Upload each figure as a separate file in either .tiff or .eps format, with the figure number and the top of the figure indicated. Compound figures e.g. 1a, b, c should be uploaded as one figure. Tints are not acceptable. Lettering must be of a reasonable size that would still be clearly legible upon reduction, and consistent within each figure and set of figures. Where a key to symbols is required, please
include this in the artwork itself, not in the figure legend. All illustrations must be supplied at the correct resolution:

Black and white and colour photos - 300 dpi

Graphs, drawings, etc - 800 dpi preferred; 600 dpi minimum

Combinations of photos and drawings (black and white and colour) - 500 dpi

Tables should be part of the the main document and should be placed after the references. If the table is created in excel the file should be uploaded separately.

Colour Policy. Where colour is necessary to the understanding of the figures, colour illustrations will be reproduced in the journal without charge to the author, at the Editor's discretion.

Ethics. Authors of research papers should provide information about funding, a Conflict of Interest statement, details of ethical committee review, and (if the paper is a clinical trial) details of trial registration. All of these declarations should be in the research paper itself, not a covering letter. If authors include named individuals in the Acknowledgements they must confirm that they have approval from those individuals in their covering letter

Post Acceptance

Further Information. For accepted manuscripts the publisher will supply proofs to the submitting author prior to publication. This stage is to be used only to correct errors that may have been introduced during the production process. Prompt return of the corrected proofs, preferably within two days of receipt, will minimise the risk of the paper being held over to a later issue. Free access to the final PDF offprint of your article will be available via Author Services only. Please therefore sign up for Author Services if you would like to access your article PDF offprint and enjoy the many benefits the service offers.

Authors Resources: Manuscript now accepted for publication?

If so, check out our suite of tools and services for authors and sign up for:

Article Tracking

E-mail Publication Alerts

Personalization Tools

Cite EarlyView Articles
To link to an article from the author’s homepage, take the DOI (digital object identifier) and append it to "http://dx.doi.org/" as per following example: DOI 10.1002/hep.20941, becomes http://dx.doi.org/10.1002/hep.20941.

To include the DOI in a citation to an article, simply append it to the reference as in the following example:

Prior to acceptance there is no requirement to inform an Editorial Office that you intend to publish your paper OnlineOpen if you do not wish to. All OnlineOpen articles are treated in the same way as any other article. They go through the journal's standard peer-review process and will be accepted or rejected based on their own merit.

**Note to NIH Grantees**

Persuant to NIH mandate, Wiley-Blackwell will post accepted version of contributions authored by NIH grant-holders to PubMed Central upon acceptance. This accepted version will be made publicly available 12 months after publication. For further information, see www.wiley.com/go/nihmandate
Appendix 9: Approval letter from National Research Ethics Service Committee North West – Greater Manchester East

Health Research Authority
National Research Ethics Service
NRES Committee North West - Greater Manchester East
3rd Floor, Barlow House
4 Minshull Street
Manchester
M1 3DZ
Telephone: 0161 625 7831
Facsimile: 0161 625 7299

14 March 2014

Mr PD Baker
Trainee Clinical Psychologist
Manchester Mental Health and Social Care Trust
Doctorate in Clinical Psychology Programme
University of Manchester
Zochonis Building
Brunswick Street
Manchester
M13 9PL

Dear Mr Baker

Study title: Psychological processes of adjustment to glioblastoma multiforme in adults: An exploratory qualitative study
REC reference: 14/NW/0081
IRAS project ID: 143080

Thank you for your emails of 12th and 14th March 2014. I can confirm the REC has received the documents listed below and that these comply with the approval conditions detailed in our letter dated 20 February 2014.

Documents received
The documents received were as follows:

<table>
<thead>
<tr>
<th>Document</th>
<th>Version</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participant Consent Form</td>
<td>2.0</td>
<td>12 March 2014</td>
</tr>
<tr>
<td>Participant Information Sheet</td>
<td>2.0</td>
<td>12 March 2014</td>
</tr>
</tbody>
</table>

Approved documents
The final list of approved documentation for the study is therefore as follows:

<table>
<thead>
<tr>
<th>Document</th>
<th>Version</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Covering Letter</td>
<td></td>
<td>29 January 2014</td>
</tr>
<tr>
<td>Evidence of insurance or indemnity</td>
<td></td>
<td>23 January 2014</td>
</tr>
<tr>
<td>Interview Schedules/Topic Guides</td>
<td>1.0</td>
<td>23 January 2014</td>
</tr>
</tbody>
</table>

A Research Ethics Committee established by the Health Research Authority
You should ensure that the sponsor has a copy of the final documentation for the study. It is the sponsor’s responsibility to ensure that the documentation is made available to R&D offices at all participating sites.

14/NW/0081  Please quote this number on all correspondence

Yours sincerely

Signed on behalf of
Elaine Hutchings
REC Manager

E-mail: nrescommittee.northwest-nmeast@nhs.net

Copy to: Ms L Macrae - University of Manchester
R&D Department - The Christie NHS Foundation Trust
Appendix 10: Approval letter from R&D at Salford Royal NHS Foundation Trust

---

Dear Mr Baker,

**Study Title:** Psychological Adjustment to Glioblastoma Multiforme in Adults: An Exploratory Qualitative Study  
**REC Reference:** 14/NW/0081  
**EuDraCT Reference:** N/A  
**CSP Reference:** N/A  
**R&D Reference:** 2014/009N4URO

Thank you for providing all the study documentation for the above mentioned study.

I am pleased to inform you that the above study has been given R & D approval and you may begin this study at Salford Royal NHS Foundation Trust.

This study is subject to external Performance Management of recruitment on time and to target. You are responsible for ensuring that recruitment targets are met. The Trust expects the first patient to be recruited with 30 days of receipt of R & D approval. When the first patient is consented to enter this study please notify R&D Governance Team.

Permission is granted in accordance to the Research Governance Framework (2005), Medicines for Human Use (Clinical Trials) Regulations 2004, and Salford Royal NHS Foundation Trusts local policies.

Whilst you are conducting this study at Salford Royal NHS Foundation Trust the conditions of this approval is that you are compliant with local Trust Policies and Mandatory Training. It is also conditional that research passports and letters of access are in place before you come on site at Salford Royal NHS Foundation Trust to conduct this research.

---

Research & Development Dept.  
Summerfield House  
554 Eccles New Road, Salford, M5 5AP
On completion of the study you are required to submit a ‘Declaration of End of Study’ form to the main REC, which should also be copied and forwarded to the R&D office at the address shown above.

Good Luck with recruitment

Yours sincerely,

Maureen Daniels
Associate R&D Manager

c.c. Dr J Bamborough
Sponsor – University of Manchester
Appendix 11: Recruitment process flowchart

Patient diagnosed with GBEH

CNS meets with patient at routine consultation

Is patient 3-7 months post diagnosis and aged ≥ 18 years?

Does patient meet any exclusion criteria at consultation?

CNS introduces study, provides PIS

Does patient provide verbal consent for researcher to contact by telephone?

CNS sends details to researcher via secure email

Researcher contacts patient to introduce study, answer questions

Does patient provide verbal consent to participate?

Researcher and patient arrange interview date, time and location

Participant provides written consent, completes DT, DASS-21 and interview

Exit from study

Exclude from participation
Appendix 12: Participant information sheet

Participant Information Sheet (12/03/2014, v2.0)

Psychological adjustment to glioblastoma multiforme in adults

Interview

You are being invited to take part in a research study. Before deciding if you would like to take part or not, it is important for you to understand why the research is being done and what it will involve. Please take time to read this information sheet carefully and discuss it with others if you wish. Please ask if anything is unclear or if you would like more information.

What is the study about and why is it being conducted?
In this study, we want to look at the important issues in the lives of patients who have been diagnosed with grade 4 brain tumours (glioblastoma multiforme). In particular, we are interested in how people think about and ‘make sense’ of this new situation. Taking part will involve one interview. The findings will add to our understanding of how best to support people who are diagnosed with high-grade brain tumours in the future.

Who is being asked to take part?
Patients who are over 18 years old, who have been diagnosed with a grade 4 brain tumour in the past three or four months and who are receiving treatment at The Christie.

Who is conducting this study?
The study is being conducted by Paul Baker, a trainee Clinical Psychologist at the University of Manchester; Dr John Fox, a Lecturer in Clinical Psychology from the University of Manchester; and Dr Jacki Bambrough, who is a Consultant Neuropsychologist at Salford Royal NHS Foundation Trust. The study has been organised by the University of Manchester.

Do I have to take part?
It is up to you to decide if you would like to take part in this study. If you are interested in taking part, you will be given a copy of this information sheet to keep and a consent form. You will be asked to sign this consent form when you meet with the researcher.

If you decide you do not want to participate then this will not affect the clinical care that you receive in any way. If you decide to take part but then change your mind, you are free to withdraw from the study at any time without giving a reason and without your clinical care being affected.

What does taking part involve?
1. With your consent, your clinical nurse specialist at The Christie will pass on your name and telephone number to the researcher (Paul Baker), who will telephone you three days from now to answer any questions. If you would still like to take part, the researcher will arrange an appointment to interview you.

2. You can choose to be interviewed either at home or at Salford Royal hospital, where you may have received your surgical treatment and where we have facilities to see you away from treatment clinics.
3. The researcher will telephone you on the morning of the interview appointment to confirm that you are still interested in participating and that the appointment time is convenient for you.

4. When the researcher meets you, they will ask you to sign a consent form to say you agree to take part in the study. You will also be asked to complete two short questionnaires which asks questions about how you have been feeling over the past week.

5. You will then be interviewed about your experience of having a brain tumour and how you have ‘made sense’ of this new experience. The interview will last between 60 and 90 minutes. We will ask for your permission to audio-record your interview.

6. The interview will then be transcribed (typed up) by the researcher or another member of staff at the University of Manchester. All information which identifies you will be removed and replaced by a code. No personal information will be included in the research.

7. If you agree to take part, we will ask for your permission to look at your medical notes to check details of your illness and treatment.

8. We will then write up this study in reports for publication so that other people can learn from it. If you would like a summary of our findings, we will send one to you when the study is complete.

Will my answers be kept confidential?
Your interview will be completely confidential, but if you say something that makes us think you or someone else was at risk and not safe, we may have to tell someone. Any information which identifies you or others will be removed from transcripts. You will be identified by a code number only. All data collected for this study will be kept safely and securely in password-protected computer files for up to 10 years after the study finishes. When we write up this research, we might include brief statements that people have made. However, we will ensure that these do not give any information that might identify the person who made them.

To ensure the study is being carried out properly, data collected for this study (including interview recordings and transcripts) may be accessed by authorised individuals from the University of Manchester, regulatory authorities, Salford Royal NHS Foundation Trust or The Christie NHS Foundation Trust, with your consent. These individuals will have a duty of confidentiality to participants and their data.

Are there any possible risks from taking part?
People generally find taking part in interview studies to be a positive experience; however cancer is a very emotional issue for many people and the interviews will involve discussing sensitive issues that may be upsetting. If you become upset during the interview and feel you would like a short break, the researcher will offer to pause the recording. The researcher will spend some time talking with you at the end of the interview to see if you require support with any particular issues that may have been raised. If necessary, the researcher may offer to contact your clinical nurse specialist for further advice on your behalf. Additional support is also available from the psychology service at Salford Royal as required.

Will I benefit from taking part?
We will use the findings of this study to help us improve the support we provide for patients in the future. Although there are no direct benefits from taking part in the study, we know that patients who have previously taken part in similar research have found the interview to be a positive experience.

Will I be reimbursed for taking part in this study?
If you choose to be interviewed at Salford Royal, we will be able to reimburse you for parking or travel costs up to a value of £12.00.
What if there is a problem?

If you have a concern about any aspect of this study, please contact the researcher, Paul Baker, on 07507 217 477 (work mobile). If they are unable to resolve your concern or you wish to make a complaint regarding the study, please contact a University Research Practice and Governance Co-ordinator on 0161 275 7583 or 0161 275 8093 or by email to research.complaints@manchester.ac.uk. Alternatively, you can call the Patient Advice and Liaison Service at The Christie on 0161 446 3000.

Who has reviewed this study?

This study was reviewed by the NRES Committee North West – Greater Manchester East on 18 February 2014.

I still have some questions...

Please feel free to contact Paul Baker on 07507 217 477 (work mobile). If there is no answer, please leave a message and Paul will call you back as soon as possible.

Thank you for your time.

Paul Baker
Trainee Clinical Psychologist
University of Manchester

Jacki Bamforth
Consultant Neuropsychologist
Salford Royal NHS Foundation Trust

John Fox
Lecturer in Clinical Psychology
University of Manchester

Cathie McBain
Consultant Clinical Oncologist
The Christie NHS Foundation Trust
Appendix 13: Participant consent form

Participant Consent Form (12/03/2014, v2.0)

Psychological adjustment to glioblastoma multiforme in adults

Interview

1. I have read the information sheet (dated 12/03/2014, v2.0) for the above study. I have had the opportunity to think about the information, ask questions and have these answered satisfactorily.

2. I understand that my participation is my decision. I understand that I am free to withdraw from the study at any time, without giving any reason and without my medical care or legal rights being affected.

3. I understand that my interview will be audio recorded.

4. I understand that quotations from my interview may be included in study reports word for word. These quotations will not mention my name or disclose my identity.

5. I understand that sections of my medical notes may be looked at by the researcher from the University of Manchester, where relevant to the study. I give permission for these individuals to have access to my records.

6. I agree to an anonymised transcript (a written record) of my interview being held on password-protected computers at the University of Manchester for up to 10 years after the end of this study.

7. I understand that relevant sections of the data collected during the study may be looked at by individuals from the University of Manchester, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.

8. I agree to take part in the study.

If you would like to have a summary of our findings once the study has ended, please tick this box [ ]

Once you are happy with this form, please print, sign and date below:

_________________________  ____________________________  ___________________________
Your name                   Your signature               Today’s date

_________________________  ____________________________  ___________________________
Researcher’s name           Researcher’s signature       Today’s date
Appendix 14: Interview schedules

**Interview schedule (23/01/2014, v1.0)**

Review impact of diagnosis on physical, cognitive and emotional functioning.
   a. What were the first symptoms you noticed/others noticed?
   b. How have things changed since diagnosis?

Review social impact on diagnosis.
   c. Who has been most affected? And how has that affected you?
   d. Who has been least affected? Has this surprised you?
   e. Who have you shared your experiences with?
   f. Who have you not? Have avoided since diagnosis?
   g. What roles have changed? What have you still been able to do?

1. **What do you understand by the term ‘adjustment’?**
   a. Provide ‘our’ definition of adjustment, contrast with ‘acceptance’?
   b. What can adjustment look like? How long can it take?
   c. Do you think you have begun to adjust to this new experience? What do you want to be like? What would you have been like if you didn’t do x, y and z?
   d. Do patients need to adjust to this? Or do they experience something else? (Have we got this all wrong?)

2. **What [external] things have been useful/helpful in helping you adjust/accept/’put up with’/’get used to’ this?**
   a. Who have you spoken to? Who has helped? What have they done?
   b. What hasn’t been helpful?

3. **And what [internal] things have been useful/helpful? How have you approached this in your mind?**
   a. How do you think about your current situation? Has this changed since the beginning?
   b. Have you managed better/worse than you ever thought you would? If you met yourself 6 months/2 years ago, what would that conversation be like?
   c. What are your helpful/unhelpful thoughts?

4. **What could have been asked differently in this interview? Have any important details been missed out? Are there any points that you think other patients might be interested in talking about?**
**Interview schedule (19/08/2014, v2.0)**

**Introduce study**
Emphasise non-medical nature of research, interested in the challenges and changes the participant has encountered between their diagnosis and today.

1. **What has been your greatest difficulty so far? What have been the biggest changes to your life so far?**
   a. Focus on each in turn, maintain participant’s focus on particular challenge/change.
   b. Redirect participants who begin to give a step-by-step guide to their medical experience post-diagnosis.

2. **What have you done to try and make sense of X/how have you managed to cope with X?**
   a. Identify social/psychological/spiritual/practical/other resources that participant has used to facilitate adjustment, or that have acted as barriers against adjustment.
      - **What has been the most important thing that has helped you with this/that has helped you through this time? How has that been useful?**
      - **What has made this more difficult? What has got in the way of you getting on with this?**
   b. When talking about social resources, try to identify positive or negative role changes in self or others, and difficulties balancing the needs of others with their own needs.
      - **Has anyone surprised you in how they’ve responded? What’s changed about their relationship with you now? How did you think they were going to act?**

3. **Discuss adjustment as a broader concept**
   a. When talking about social resources and changes they have seen in others, some participants have spontaneously discussed how their identity has changed/stayed the same.
      - **Did you expect you’d be like this? What’s different? How has it changed? Does the way you are make this easier or more difficult?**
b. Discuss future adjustment.
   - *Is there anything else you need to do? Do you think you’ll ever get to a point where you’ll be happy/content/accepting of this? What would that look like?*

c. Discuss ‘fit’ of illness with life immediately before diagnosis.
   - *What would it have been like if you’d been diagnosed ten years earlier/later? What about if you were still working/had retired?*

d. If participant describes feeling positive or fully acceptant, explore what could affect this attitude.
   - *If you didn’t have X or Y, what would life be like now? What would be the worst thing to happen that would make it a struggle to be positive?*
Appendix 15: Distress protocol

Distress protocol (23/01/2014, v1.0)

Psychological adjustment to glioblastoma multiforme in adults

Interview

i. If the participant becomes distressed during the interview, they will be asked if they would like to pause the interview. The participant will be asked to indicate if they feel ready to resume the interview or if they would like to end the interview. Their decision to end the interview will be respected.

ii. If the participant wishes to continue, the researcher will monitor their distress throughout the remainder of the interview. The researcher will revisit their distress explicitly at the end of the interview.

iii. As a trainee clinical psychologist, the researcher will make an assessment of the participant’s distress and use clinical judgement as appropriate.

iv. The participant will be provided with a debriefing sheet at the end of the interview, which lists local and national sources of support.

v. The participant will be encouraged to contact their CNS, the Cancer Information Centre at The Christie or their GP should they feel distressed and/or in need of support. The decision regarding whether or not they wish to access support remains their own.

vi. If the participant showed a level of distress which the researcher assessed as a sign of risk to themselves or others, the researcher would assess further at the interview. The participant’s CNS would be made aware of any level of risk identified.

vii. If the risk is considered immediate, the researcher will contact the participant’s CNS or GP at the interview session for further advice. The researcher will facilitate access to further assessment/attendance at A&E if necessary.
Appendix 16: Participant debriefing sheet

Participant Debriefing Sheet (23/01/2014, v1.0)

Psychological adjustment to glioblastoma multiforme in adults

Interview

Many thanks for taking part in this study. If you have any concerns or questions and would like to talk about these with someone, the following telephone numbers and websites may be useful.

Local services

Elizabeth Molloy, Clinical Nurse Specialist at The Christie  0161 446 8441
Sarah Benson. Clinical Nurse Specialist at Salford Royal  0161 206 0613
Cancer Information Centre at The Christie  0161 446 8100
Counselling Service at The Christie  0161 446 8038
Patient Advice and Liaison Service (PALS) at The Christie  0161 446 8217

National services

The Brain Tumour Charity (www.thebraintumourcharity.org)  0800 800 0004
Brain and Spinal Injury Charity (BASIC)  0870 750 000
Macmillan Cancer Support (www.macmillan.org.uk)  0808 808 0000
Epilepsy Action (www.epilepsy.org.uk)  0808 800 5050
CancerHelp UK (www.cancerresearchuk.org/cancer-help/)  0808 800 4040
NHS Direct  111

Alternatively, you may find it useful to contact your GP surgery.

Thank you for your time.
Appendix 17: University of Manchester lone working policy

Safety Services Guidance

Guidance on lone working

Key word(s) : Lone working, remote working, working without supervision

Target audience : Anyone working beyond earshot of another person, or otherwise unable to summon assistance; managers responsible for preparing risk assessments for lone workers.

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Management cycle | Useful paragraphs
--- | ---
Plan | 1-7
Do | 8-20
Monitor | Review 21-22
Introduction

1. This Guidance should be read in conjunction with the University Arrangements Chapter 10 on Lone Working. This chapter defines lone working as: “A person working without close or direct supervision and without contact from others. It can take place both out of hours and during the normal working day.” The key point is that the lone worker may not be able to summon assistance quickly in the event of an emergency.

2. This definition covers those workers who could be working in a university building or similar environment, in a community or research setting.

3. This guidance should be used to develop or revise local arrangements and systems to protect lone workers, reflecting the local needs of staff and the environments within which they work.

4. Line managers and staff who supervise students have a duty of care and responsibility to ensure that risk assessments and local procedures are developed, implemented, monitored and adhered to. Lone workers also have a responsibility to follow the procedures for their own safety.

5. In order that lone workers feel safe and secure, and perform their duties in a relatively safe environment they must be confident that there is organisational commitment and support, backed up by strong management procedures.

6. Incidents involving lone workers are very rare; however, it is important that lone workers are encouraged to report all incidents of physical and non-physical assault, using the University’s incident report form. This will also ensure that any lessons learned can be fed back into risk management processes and further preventive measures can be developed. Some incidents may need to be reported to the enforcing authorities via the University Safety Office.

Objectives

7. This guidance is designed to provide lone workers and their line managers with practical advice to assist in preparing for a lone worker situation and meet legislative responsibilities under the Health and Safety at Work Act 1974 and the Management of Health and Safety at Work Regulations 1999. In particular, it can be used to:

• raise staff awareness of safety issues relating to lone working
• ensure that lone working is risk-assessed in an appropriate way and that safe systems and methods of work are put in place to reduce the risk, so far as is reasonably practicable
• help staff recognise risks and provide practical advice on safety when working alone, including, where appropriate, how to use technological solutions
• identify the organisational structures, communication links, and those with responsibilities to support lone workers if they need assistance
• encourage full reporting and recording of any adverse incidents relating to lone working.

Managing risk

8. The University is required to implement measures to manage, control and mitigate risks to lone workers. Once an incident occurs, the level of follow-up action should be proportionate to the risk. As a minimum, the risk assessment should be reviewed. Other measures might include removing weaknesses or failures that have allowed an incident to take place (procedural, systematic or technological), and identifying further training needs of staff and students in relation to the prevention and management of verbal or physical assault, or other training such as correctly identifying and operating the relevant technology.

Risk assessment

9. Schools and Directorates should use their existing risk assessment arrangements to manage risks in relation to lone workers: to identify risks in relation to lone working to:

• assess the risks to lone workers
• implement measures to reduce the risks to lone workers, including appropriate information, instruction, training and supervision to minimise these risks
• evaluate the control measures and ensure that risks to lone workers are appropriately managed.

10. A suitable and sufficient risk assessment for lone working should be based on the University’s Lone Working Chapter 10, and consider the following factors, together with any specific risks associated with the work being undertaken:

• Who is going to be working alone?
• Where will they be working?
• Are they competent to carry out the work?
• Does the workplace present a special risk to the lone worker in addition to risks associated with the work itself?
• Is there a safe means of access and egress from the work location?
• Can all plant, substances and materials involved in the work be safely handled by one person? (Consider whether the work involves lifting objects too large or awkward for one person or whether more than one person is needed to operate essential controls for the safe running of equipment).
• Are some individuals more at risk than others when working alone?
• Are young persons especially at risk if they work alone?
• Is the person medically fit and suitable to work alone?
• Are the fire precautions for the building fully operational and understood by the lone worker?
• Are all fire precautions available if the work takes place out-of-hours?
• Is the lone worker fully familiar with how to respond in an emergency? E.g. do they know how to activate the fire alarm, phone numbers to call, who to contact?
• Are there effective communication links in the area they will be working at the time they are working?
• Is the level of supervision at other times sufficient to ensure that any problems are identified and dealt with?
• Is there a risk of accidental release of material which could cause acute injury or require extensive decontamination? E.g. gas release, explosion, spillage (Work such as this should not take place unaccompanied)
• Are any other precautions necessary?

Example risk assessments

11. To assist with the production of risk assessments, the following lone worker example risk assessments and checklists have been produced:

• Community based lone worker risk assessment
• Community based lone worker checklist
• On-campus lone worker in an office setting risk assessment
• On-campus lone worker in an office setting checklist

The above documents can be accessed at
http://www.healthandsafety.manchester.ac.uk/toolkits/lone_working/example_ras/
Dynamic risk assessment

12. There may be a requirement for risk assessments to be carried out by the lone worker on a dynamic basis, e.g. in response to frequent changes in circumstances. A generic risk assessment will need to explain the circumstances under which dynamic risk assessments take place, and address the competency and training needs of the individuals carrying them out.

13. See Guidance on generic and dynamic risk assessment

Lone worker movements

14. The specific controls necessary must be proportionate to the risk and will be informed by the risk assessment process but could include:

- details of location and anticipated time of return left with a manager or colleague
- details of vehicles used by lone workers left with a manager or colleague, for example, registration number, make, model and colour
- regular contact with a manager or relevant colleague, particularly if they are delayed or have to cancel an appointment
- panic buttons in isolated offices or consultation rooms
- mobile phone solutions with text, panic, GPS, ‘man down’ and smartphone solutions.

15. Where there is genuine concern, for example, as a result of a lone worker failing to attend a visit or an arranged meeting within an agreed time, or to make contact as agreed, the manager should use the information provided in a log or Outlook diary to locate them and ascertain whether they turned up for previous appointments that day. Depending on the circumstances and whether contact through normal means (mobile phone) can be made, the manager or colleague should involve University Security if necessary (see escalation process para 22).

16. If it is thought that the lone worker may be at risk, it is important that matters are dealt with quickly, after considering all the available facts. Security will advise if police involvement is needed, and will need full access to information held and personnel who may hold it, if that information might help trace the lone worker and provide a fuller assessment of any risks they may be facing.

17. It is important that contact arrangements, once in place, are adhered to. Many such procedures fail simply because staff forget to make the necessary call when
they finish their shift. The result is unnecessary escalation and expense, which undermines the integrity of the process.

The buddy system

18. It is essential that lone workers keep in contact with colleagues and ensure that they make another colleague aware of their movements. This can be done by implementing management procedures such as the ‘buddy system’.

19. To operate the buddy system, managers must ensure that a lone worker nominates a buddy. This is a person who is their nominated contact for the period in which they will be working alone. The nominated buddy will:
   - be fully aware of the movements of the lone worker
   - have all necessary contact details for the lone worker
   - attempt to contact the lone worker if they do not contact the buddy as agreed
   - follow the agreed local escalation procedures for alerting their senior manager and Security if the lone worker cannot be contacted or if they fail to contact their buddy within agreed and reasonable timescales.

20. The buddy must understand their role and what the procedures and requirements are. Contingency arrangements should be in place for someone else to take over the role of the buddy in case the nominated person is unavailable, for example if the lone working situation extends past the end of the nominated person’s normal working day or shift, if the shift varies, or if the nominated person is away on annual leave or off sick.

Escalation process

21. It is important for School and Directorates to have a risk-based escalation process, outlining who should be notified if a lone worker cannot be contacted or if they fail to contact the relevant individual within agreed or reasonable timescales. The escalation process should provide identification of contact points at appropriate stages which may include, line manager, senior manager, security and, ultimately, the police. Any individual nominated in an escalation process should be fully aware of their role and responsibilities.

Researcher safety

22. Researcher safety is well documented by the Social Research Association (SRA), in their code of practice.
23. The University of Manchester has issued Guidance on conducting interviews and research in fieldwork. Safety Services Lone Working toolkit contains useful checklists.

Further sources of guidance

Suzy Lamplugh Trust

For information on lone worker alarms and alerting devices:

For safety apps
http://www.suzylamplugh.org/personal-safety-tips/app-directory/

For advice on safe travelling alone
http://www.suzylamplugh.org/personal-safety-tips/free-personal-safety-tips/travelling-for-work/ and

HSE Publication on Lone Working

Royal College of Nursing Guide to Lone Working

British Sociological Society Statement of Ethical Practice, March 2002 contains some guidance on conducting interviews.
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<td>Head of Safety Services, Dr Melanie Taylor</td>
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Appendix 18: Transcription extract with line-by-line coding

[Table]

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32 again- the other hard thing was that everyone who saw me and knew what
33 had happened, all said “Oh you’re looking very well!” and I did look well. I
34 looked well, I was working perfectly well and once I came home I was doing
35 the cooking and the washing and that’s the hardest thing. You’re looking like-
36 you look in the mirror, you’re looking perfectly normal, but you’re not. And
37 that is really very difficult to cope with. It’s just- how can this be right? Have
38 they made a mistake? You know they haven’t but that’s what you’re sort of
39 hoping. So then, course we had to go up to [GENERAL HOSPITAL], you
40 know, go through and see the neurosurgeon and he said “there’s definitely a
41 tumour there but I’m not even sure when I do the biopsy that I can actually
42 get to the tumour” so you think to yourself well in that case it’s got to be pretty
43 deep seated, you know, which makes it worse. But maybe that’s why I had
44 no symptoms at all because it wasn’t affecting the bit of the brain that I
45 needed most of the time. So they say they do the biopsy and again that was
46 a bit stressful obviously. But again the biggest relief is when you wake up
47 from the actual operation is Oh I’m still in one piece. I can still talk I can still
48 walk and that again gives you sort of a boost.

[04:20] Had you been worrying about that before?

[04:21] Well yes I said to him, and my daughter and son were both there
when we had the meeting, you see. And to be honest my biggest fear is
being a vegetable. I don’t want to end my life as a vegetable. In a bed.
Because I’ve seen too much of it. And just not being able to get out or
walking I would find very very difficult to cope with because I’ve always been
an incredibly active person all my life. Err anyway waking up from the
operation and finding I’d still got mental faculties and I could still walk was a
huge relief. So again I was sent home from [GENERAL HOSPITAL] and got
back to normal here and built my strength up. And of course I had to go to
[CANCER TREATMENT CENTRE], and going to [CANCER TREATMENT
CENTRE] is a very positive experience because the staff are so positive and
they’re trying to make you be positive all the time. But I must say the
radiotherapy does wipe you out, it really does. I mean they warn you about it
they say even when its finished in two weeks you will feel incredibly lethargic
Appendix 19: Transcription extract with selected NVivo codes