QUALITY OF LIFE IN PAEDIATRIC BRAIN CANCER

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OVERVIEW

This thesis is comprised of three parts. Part I is a literature review that examines the literature pertaining to quality of life (QOL) in paediatric brain cancer survivors. The concept of QOL is initially considered, followed by a review of the relevant evidence regarding incidence and predictors of QOL in this population. Part I concludes with a discussion regarding the implications of the literature and possible areas for future research. Part II presents an empirical paper describing the quantitative study that was conducted for this thesis. This paper explores the impact of tumour recurrence, neurological status, and attentional coping style on the QOL of survivors of paediatric brain tumours. In Part III of the thesis, the process of conducting the empirical study is reflected upon, and particular attention is paid to the different agendas that arose during the research process and the impact of the research on the researcher.

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PART I: LITERATURE REVIEW

A Systematic Review of Quality of Life in Survivors of Paediatric Brain Cancer

1. ABSTRACT

This paper reviews the recent literature on quality of life (QOL) in survivors of paediatric brain tumours. QOL is defined as comprising three domains (physical, emotional and social), and studies investigating single or multiple domains are included. A psychological perspective is taken on QOL whereby it is the degree to which circumstances relating to these domains are distressing or problematic for the individual that is considered key, rather than the circumstances themselves. A total of 23 studies are reviewed and findings are presented in terms of overall QOL, physical QOL, emotional QOL and social QOL. Overall, paediatric brain-tumour survivors appear to be at risk of reduced QOL both when compared to population norms and to other paediatric cancer-populations. Possible risk factors are discussed but further research is needed before definitive conclusions can be reached. Methodological limitations observed in the literature are considered and directions for future research are proposed. In particular, the need for more theory-driven studies is highlighted.

2. INTRODUCTION

Over the last fifty years, dramatic improvements in treatment and care for children with cancer have resulted in steadily increasing survival rates. Whereas at one time life-expectancy was measured in months rather than years, today over 70% of children diagnosed with cancer are alive and disease-free ten years post diagnosis (Dolgin, Somer, Buchvald & Zaizov, 1999; Fuemmeler, Elkin & Mullins, 2002; Langeveld, Stam, Grootenhuis & Last, 2002; Stiller, Bunch & Lewis, 2000; UK Childhood Cancer Research Group, 2004).

However, survival comes at a cost. The damage done by the cancer itself, together with lengthy and frequently aversive diagnostic, treatment and follow-up procedures can result in a wide range of physiological and psychological sequelae (Armstrong & Horn, 1995; Langeveld et al., 2002). This is particularly true for cancers of the brain. The presence of a brain tumour and the treatments directed at it can have a profound effect on physical, neurocognitive and psychosocial outcomes (Fuemmeler et al., 2002; Moore, 2005; Mulhern, Hancock, Fairclough & Kun, 1992; Patenaude & Kupst 2005).

Such cancer-related sequelae have an impact on the quality of life (QOL) of survivors and in recent years this has become the focus of an increasing amount of research. QOL is important as it tells us about the subjective experiences of survivors and can be used as a basis for the development and optimization of treatments (Calaminus & Kiebert, 1999). In particular, if specific risk-factors related to poor QOL can be identified, then resources aimed at improving QOL can be effectively directed towards those most at risk. Review articles published in the last ten years

have looked at QOL in survivors of adult-onset brain tumours (Heimans & Taphoorn, 2002; Huang, Wartellea, Kreutzer, Broaddus & Lyckholm, 2001; Weitzner & Meyers, 1997), QOL in survivors of childhood cancer (Calaminus & Kiebert, 1999; Langeveld et al., 2002), and psychosocial adjustment following paediatric brain tumour (Fuemmeler et al., 2002). However, there is no comprehensive review of up-to-date research investigating QOL in survivors of paediatric brain tumours and this review aims to go some way towards filling the gap in the literature.

This review begins by presenting background information regarding diagnoses and treatment of brain tumours in children, and this is followed by a discussion regarding the definition of QOL in this population. A review of the literature is then presented followed by a discussion about the implications of the findings and ideas for future research.

3. PAEDIATRIC BRAIN TUMOURS

3.1 Incidence and classification

In the UK, the current risk of developing cancer during the first 15 years of life is 1 in 500 and cancer accounts for around 20% of all deaths in children aged 1 to 14 years old. Central Nervous System (CNS) cancers are the second most common type of paediatric cancer (after leukaemia) accounting for approximately one quarter of all childhood cancers. Five-year survival rates for such cancers have increased from less than 40% in 1966 to nearly 70% in 1996 (Stiller, Quinn & Rowan, 2004).

Cancer is essentially a disease of cell division and is characterised by uncontrolled cell growth which can damage and destroy surrounding healthy tissue. CNS tumours can be classified by location, histology (i.e. tissue type), and malignancy (i.e. rate of cell growth).

CNS tumours can be located anywhere in the brain or spinal cord although spinal cord tumours are rare. Those originating in the lower part of the brain (e.g. in the cerebellum and brainstem) are called infratentorial tumours, and this is the most common location in which paediatric CNS tumours originate. Those originating in the upper part of the brain (including those in the diencephalon, cerebral hemispheres and suprasellar, pineal, intraventricular or leptomeningeal regions) are called supratentorial tumours (Siffert, Greenleaf, Mannis & Allen, 1999). Paediatric CNS tumours vary in histologic type with the most common types being astrocytoma, medulloblastoma and ependymoma (Ullrich & Pomeroy, 2003). The degree of malignancy of a tumour is classified by "grading" the tumour in terms of its aggressiveness. Tumours are assigned grades from I to IV with Grade I representing tumours that are slow growing, and Grade IV representing the fastest growing and most aggressive tumours.

3.2 Diagnostic procedures and treatments for childhood CNS tumours

Neuro-imaging and biopsy are the most common methods used in diagnosing brain tumours although in some cases lumbar puncture is also required. Such procedures are able to determine the size, location, histology and malignancy of tumour. Treatment options for CNS tumours include surgical resection, radiotherapy and chemotherapy. Surgical resection aims to remove as much of the cancerous tissue as

possible, as tumours will recur if any cancer-cells remain. However, the risk of surgery-induced damage to surrounding brain structures has to be balanced with the benefits of tumour removal, and therefore resection is not always possible and even when it is, may only be partial.

Radiotherapy uses beams of high energy waves or particle streams to kill off cancerous-cells and is usually recommended after surgery or when the tumour is inoperable. Radiotherapy is painless and affects only the site of the tumour and the surrounding areas. It does not distinguish between healthy and cancerous cells so normal tissue is also affected, which can cause side-effects such as mouth soreness, ulcers and skin damage in the short-term and cognitive decline, vasculopathy (blood vessel damage) and endocrinopathy (e.g. growth impairment and precocious puberty) in the long-term (Bruce, 2006; Ullrich & Pomeroy, 2003). Dosage and frequency of administration can vary, but typically radiotherapy is given on a daily basis, five days a week, for five to eight weeks and children are hospitalised for this period (Bruce, 2006; Stiegelis, Ranchor & Sanderman, 2004).

Chemotherapy aims to destroy cancerous cells using chemical agents that are usually taken either orally or intravenously. Unlike surgery and radiotherapy, chemotherapy has a direct impact throughout the body resulting in a wide range of side-effects that can include nausea, hair loss, headaches, and lethargy. The length of chemotherapy treatment ranges from three to twelve months (Bruce, 2006).

Such diagnostic and treatment procedures are beneficial in terms of survival but can be lengthy, frightening and painful for the child and can have significant and

sometimes extensive short- and long-term side-effects (Bruce, 2006) which are likely to have a considerable impact on the child's QOL.

4. DEFINING QUALITY OF LIFE IN PAEDIATRIC BRAIN CANCER

The concept of health related quality of life (QOL) with respect to cancer survivors is a complicated one. There is no universally accepted definition and researchers have used an array of measures, focusing on a variety of dimensions in an attempt to investigate this concept (Langeveld et al., 2002).

The World Health Organisation (WHO) define QOL as "individuals' perceptions of their position in life in the context of the culture and value system in which they live and in relation to their goals, standards and concerns" (WHO, 1993).

An important element of this definition is the weight it places on the individual's *subjective* experience of their situation. In the past, some studies have used solely objective measures to determine QOL (Jenkin, Danjoux, & Greenberg, 1998; Skowronska-Gardas, Pedziwatr & Chojnacka, 2004). Whilst variables such as type of school attended, medical status, and intellectual functioning are highly valuable in terms of determining an objective measure of the circumstances that survivors of cancer face, such indicators represent the situation as perceived by the researcher, rather than the individual's subjective perception and experience of the situation, and as such it is arguable whether they truly represent QOL. Indeed, whilst objective and subjective indicators may be correlated in some circumstances, this should not be presumed. As Schipper, Clinch & Olweny (1996) point out, "individuals with the

same objective status may report very different quality of life" and this statement has been supported by several empirical studies (Dolgin et al., 1999; Schmidinger, Linzmayer, Becherer et al., 2003)

Subjective measures of QOL may be divided into two types: those eliciting the person's *subjective description* of the situation and those that elicit the *subjective psychological impact* (SPI) that the situation has on the individual. To illustrate the difference between these concepts consider the following example. A child who has undergone surgery for a brain tumour may be observed to have been left with scarring (the objective description of the situation). The child's awareness of the scarring (the subjective description) may depend on a variety of factors such as the age of the child. The subjective description could be elicited by asking questions such as "did you have scarring following the surgery?" and "how big were the scars that you were left with following surgery?" Whilst such questions provide us with important information, they do not tell us how the child *feels* about the scarring (i.e. how distressed the child is about the scarring, how problematic the scarring is for the child or how satisfied they are with their physical appearance). As implied by the WHO definition, the SPI will be determined by the individual's own personal goals, standards and concerns, as well as the cultural environment within which they live. So for a child whose culture places a heavy emphasis on physical "perfection" and whose ambition it is to become a fashion model, having post-surgery scarring may be far more problematic and distressing than for a child growing up in a different environment.

If it is the psychological impact of the cancer that is of interest, another useful indicator to use (in addition to measures that capture SPI) would be the presence of distressing psychological disorders or symptoms such as depression or anxiety. Whilst strictly speaking clinician-determined diagnoses may be counted as objective measures, the presence of such disorders or psychological problems does indicate a level of subjective distress on the part of the patient.

However, matters are somewhat complicated when trying to measure QOL in children. Younger children or children who have been left cognitively impaired following brain tumour diagnosis and treatment may not be able to answer questions about their experiences, and therefore whilst not strictly subjective, it may be necessary to use parent or teacher proxy-reports to try to determine the impact that particular experiences are having on the child (Calaminus & Kiebert, 1999). In terms of psychological disorders or difficulties, distress in children can manifest in many different ways and so behavioural, emotional, and somatisation problems need to be considered when measuring psychological aspects of QOL. In a population of paediatric brain tumour survivors, the identification of somatisation problems can be particularly difficult as many somatic symptoms overlap with those that occur as a result of the tumour and treatment. Therefore it is important to try to distinguish between the physical symptoms that arise as a result of the tumour and treatment, the distress that such physical symptoms cause (physical QOL), and distress (related to any aspect of the cancer experience) that manifests as somatic symptoms (somatisation).

A further dilemma faced by investigators of QOL in survivors of childhood brain tumours is which domains to identify as being relevant to the concept of QOL. WHO specify six QOL domains; physical health, psychological state, levels of independence, social relationships, environmental features and spiritual concerns. Some studies focus on a single domain and others use multi-dimensional measures of QOL that incorporate several of these domains to get a total QOL score and individual domain-specific scores. In their review of QOL in young adult survivors of childhood cancer, Langeveld et al. (2002) state that the key domains relevant to their population were the physical, emotional and social dimensions. Dolgin et al. (1999) also emphasize the importance of these particular domains in survivors of cancer quoting Schipper & Levitt (1985) who state that "quality of life should be conceptualized as a composite of multidimensional factors measuring the patient's physical, psychological, and social functioning".

With these matters in mind, the present review aims to evaluate the QOL of survivors of paediatric brain tumours focusing on social, physical and/or psychological domains. The WHO definition of QOL is adopted such that studies are included if they utilise a) measures eliciting the subjective psychological impact (self- or parent-proxy) of illness-related experiences, or b) objective measures of psychological disorders or difficulties. Particular attention is paid to findings that identify potential risk-factors for poor QOL, and the implications such findings have for future interventions.

It is acknowledged that by focusing on just 3 domains, and only looking at SPI (and not objective and subjective descriptions) for the physical and social domains, such a

definition of QOL is narrower than may traditionally have been adopted. However, it would be beyond the scope of this review to broaden the definition further and, by restricting the definition, a better understanding of the distress related to the experience of childhood brain cancer can be reached.

Fuemmeler et al. (2002) reviewed the literature relating to the emotional, behavioural and social functioning of paediatric brain tumour survivors that was written prior to the turn of the century. In order to avoid duplication, the present review does not re-review the studies included by Fuemmeler et al. (and therefore focuses primarily on studies that have been conducted from 2000 onwards). However, where relevant, more recent findings reviewed here will be compared to those summarised by Fuemmeler et al. in order to establish as comprehensive a picture of this area as possible.

5. LITERATURE SEARCH

A literature search for studies published up until the start of 2006 was conducted using the PSYCHINFO and PUBMED databases. Synonyms of "brain tumour", "childhood" and "quality of life" together with words specific to psychological, social and physical domains of QOL were entered. Studies that were not published in English were excluded from this review, as were single-case studies, and dissertation abstracts that were not published in recognised journals. Results were cross-referenced with other literature reviews and pertinent papers (Bruce, 2006; Calaminus & Kiebert, 1999; Foley, Barakat, Herman-Liu, Radcliffe & Molloy, 2000; Fuemmeler et al., 2002; Langeveld et al., 2002; Siffert et al., 1999; Ullrich &

Pomeroy, 2003). Studies were included if they had paediatric brain-tumour survivors as their primary focus or if they separately presented data specific to this population. The term "paediatric" was defined as children diagnosed before the age of 18. As recognised by Langeveld et al. (2001), there is no consensus in the paediatric oncology literature with regards to the definition of "survivor". This review incorporated studies that evaluated QOL domains at any stage of the illness post-diagnosis, so "survivor" refers to a person who has been diagnosed before the age of 18 and is alive at the time of assessment. Comparisons are made to other cancer populations (for example acute lymphoblastic leukaemia (ALL)), so type of cancer will be specified.

For the psychological domain, studies that investigated psychological problems via questionnaire, interview, diagnoses, or psychiatric hospitalisations were reviewed. For the overall, social and physical domains, only studies that used measures evaluating SPI were included. It is beyond the scope of this review to provide detailed descriptions of all the measures utilised and the reader should refer to the original research papers for this information. However, as SPI is a new concept, a brief description of the measures and diagnostic techniques that were considered to measure this aspect of QOL is provided in Figure 1 for the readers' assistance.

Figure 1: Measures used that elicit subjective psychological impact (SPI)

Ferrans and Powers Quality of Life Index (QLI; Ferrans & Powers, 1992)
The QLI is a 66-item self-report questionnaire that asks how satisfied the individual is with particular areas of their life and how important each area is to them. Individuals rate themselves using 6-point Likert scales, ranging from "very dissatisfied" to "very satisfied", and "very unimportant" to "very important". Five scores are calculated from the individual's responses: total quality of life, health and functioning subscale, social and economic subscale, psychological/spiritual subscale and family subscale.

The Paediatric Quality of Life Inventory (PedsQL; Varni, Katz, Seid et al., 1998; Varni, Seid & Kurtin, 2001)
The PedsQL aims to measure QOL in a paediatric population of children aged 2 to 18. There are four different versions of the PedsQL corresponding to four different age-groups (2-4, 5-7, 8-12, and 13-18). Each age-group has self-report and equivalent parent proxy-report questionnaires (apart from for the 2-4 year olds, where there is only a parent-report form). Whilst the exact phrasing of the items and the response scales provided are slightly different dependent on the age of the child, all versions of the questionnaires include the same items and scales.

The PedsQL consists of a generic core scale, and several disease specific scales. The modules of relevance to this review are the generic core scale (PedsQL-G), the cancer-specific scale (PedsQL-C) and the multidimensional fatigue scale (PedsQL-F).

The PedsQL-G is a 23-item questionnaire that produces five scores: total QOL, physical functioning, emotional functioning, social functioning and school functioning. The PedsQL-C is a 26-item questionnaire producing eight scores: total cancer-QOL, pain and hurt, nausea, procedural anxiety, treatment anxiety, worry, cognitive problems, perceived physical appearance and communication. The PedsQL-F is an 18-item questionnaire that produces four scores: total fatigue, general fatigue, sleep/rest fatigue and cognitive fatigue.

All items on the PedsQL are worded "In the past one month, how much of a **problem** have you/has your child had with..." Responses are made using a five-point Likert scale ranging from "never" to "almost always" (apart from for the child self-report questionnaires for the 5-7 year olds, who use a simpler 3-point Likert scale).

The emphasis placed on the word "problem" suggests distress or difficulty and therefore it could be argued that it elicits SPI. However, given the "frequency" nature of the response scales, it is possible that the response could be more subjective description. For example, on the PedsQL-G physical functioning scale, the item "how much of a problem have you had with feeling very tired" combined with response options that are frequencies ("never" to "almost always") could mean the question is misinterpreted as "how often have you been very tired?". The PedsQL is included here as a measure of SPI but this potential problem with the scale is acknowledged.

Semi-Structured Interviews
Poretti, Grotzer, Ribi, Schonle, & Boltshauser (2004) used a semi-structured interview whereby survivors were asked whether they were affected by specific characteristics associated with survivorship (i.e. subjective description) and for those who were affected, whether it limited the quality of their lives (i.e. subjective psychological impact). 25 characteristics were asked about including those in the physical domain (e.g. short stature, impaired vision, frequent headaches), psychological domain (e.g. mood swings), and social domain (e.g. difficulties making friends, rejection by other children).

Ribi, Relly, Landolt et al. (2005) used a different semi-structured interview and part of this asked about satisfaction with physical appearance. This item from the interview has been included as a SPI measure of physical QOL.

6. REVIEW OF THE LITERATURE

A total of 23 studies met the criteria for inclusion in this review (see Table 1), the results of which are presented below. General findings for each domain of QOL are considered first, followed by a section discussing predictors. A variety of instruments were used to assess various aspects of the different QOL domains and Table 2 outlines those used by different studies.

6.1 Overall QOL.

Eight studies investigated measures of "overall QOL" from an SPI perspective. In general, the evidence suggests that brain tumour (BT) survivors had significantly worse QOL than population norms or healthy control groups, both when rated by patient self-report (Bhat, Goodwin, Buwinkle et al. 2005; Eiser, Vance, Glaser et al., 2005) and parent-proxy report (Bhat et al., 2005; Poretti, Grotzer, Ribi, Schonle, & Botlshauser., 2005). Only one study failed to find a significant difference (Maddrey, Bergeron, Lombardo et al., 2005). BT survivors also had worse overall QOL in comparison to survivors of acute lymphoblastic leukaemia (ALL; Eiser, Eiser & Greco, 2004; Eiser et al., 2005; Eiser, Vance, Horne, Glaser & Galvin, 2003; Meeske, Katz, Palmer, Burwinkle, & Varni, 2004) with one study reporting that 63% of the BT sample versus 37% of the ALL sample had scores more than 1 standard deviation below the normative value on the PedsQL-G scale. However, the BT and ALL groups appeared to be comparable on the PedsQL-C, a cancer-specific measure of QOL (Meeske et al., 2004). These findings make sense when the content of the two PedsQL scales are considered. The PedsQL-G evaluates overall outcome which, due to the critical location of the tumour in brain cancer survivors, might be expected

Table 1: Summary of studies investigating QOL in survivors of paediatric brain tumours.

#	*Study (country)*	*Design*	*Sample*	*Time-related factors (in years).*	*Assessment methods used*	*Results/outcome*
1	Aarsen et al., 2004 (Holland)	Cross-sectional Interview with parent & child.	N=23 survivors of paediatric cerebellar pilocytic astrocytoma who'd received surgery only.	C_{AGE}=9.17 (range 3.92-17.5) A_{AGE}=12.75 (range 6.58-22.92)	DSM-IV diagnosis (from semi-structured interview with parent & survivor)	30% of sample had diagnosable DSM-IV disorders, & a further 35% had identifiable emotional/behavioural problems but did not meet criteria for a diagnosis.
2	Barr et al., 1999 (Canada)	Cross-sectional Interview with child & Questionnaire	N=41 survivors of paediatric CNS tumours (mixed type). Mixed treatment	D_{AGE}=6.2 (range 0.1-14.2) A_{AGE}=9.5 (range 1.7-17.9) t_{D-A}=3.3 (range 0.2-8.6) t_{C-A} = 2.6 (range < 0.1-8.6)	Emotion items from HUI2 & HUI3 (parent & survivor report)	2% of sample reported being somewhat unhappy, often fretful, angry, irritable, anxious or depressed. The rest were either generally happy & worry free, or somewhat happy with only occasional fretfulness, anger, irritability, anxiety or depression.
3	Beebe et al., 2005 (US)	Cross-sectional Questionnaire	N=103 survivors of paediatric cerebellar astrocytomas (brainstem tumours excluded) who'd received surgery only. Assessed within 1 yr of surgery.	A_{AGE} = 8.5 (range 3-18, SD 4.1) t_{C-A} =108 days (SD 78 days)	CBCL (parent report)	Survivors were more impaired than population norms on measures of internalising problems but not on externalising problems.
4	Bhat et al., 2005 (US)	Cross-sectional Questionnaire	N=134 survivors of paediatric brain tumour (mixed type).Mixed treatment. N= 730 healthy controls	D_{AGE}=7.56 (SD 5.03) A_{AGE}=11.8 (SD 5.4) t_{D-A}=4.26 (SD 4.41)	PedsQL-G (survivor & parent report) PedsQL-C (survivor & parent report)	Survivors had lower overall, physical, emotional & social QOL than control group. Older children had less procedural anxiety but worse social QOL & more worry about illness. Presence of shunt indicated lower QOL.
5	Carey et al., 2001 (US)	Cross-sectional Questionnaire	N=15 survivors of paediatric malignant brain tumours (mixed type, brainstem tumours excluded). Mixed treatment.	D_{AGE}=5.33 (SD 3.14, range 0.34-10.18) A_{AGE}=10.31 (SD1.63) t_{C-A}=3.65 (SD 2.35, range 0.76-10.16)	CBCL (parent report) YSR (survivor report)	Non-significant trend for more internalising problems in survivor group in comparison to population norms.

6	Copeland et al., 1999 (US)	Cross-sectional Questionnaire	N=27 survivors of posterior fossa tumours diagnosed at less than 3 years old. Mixed treatment	D_{AGE}=1.83 (range 0.58-2.92) A_{AGE}= 9.23 t_{D-A}=6.97	CBCL (parent report)	Mean scores on overall, internalising & externalising problem scales were all within normal limits.
7	Eiser et al., 2004 (UK)	Cross-sectional Questionnaire	N=24 survivors of paediatric CNS tumour (mixed type) N=40 survivors of paediatric ALL (control group)	D_{AGE}=7.55 (SD 3.05) A_{AGE}=14.46 (SD2.6, range 8-19)	PedsQL-G (survivor & parent report)	CNS-tumour survivors reported significantly lower overall QOL than survivors of ALL. Parenting style was evaluated & results found that compromised QOL in survivors was associated with prevention-focused rather than promotion-focused parenting style.
8	Eiser et al., 2005 (UK)	Cross-sectional Questionnaire	N=26 survivors of paediatric CNS tumour (astrocytoma & medulloblastoma). 16 had received GHT (GHT+), 10 had not. (GHT-) N=51 survivors of paediatric ALL (control group). 9 had received GHT, 42 had not	<u>CNS GHT+ group:</u> D_{AGE}=5.96 (SD 3.13) A_{AGE} =13.50 (SD 3.56) t_{D-A}=7.75 (SD2.61) <u>CNS GHT- group:</u> D_{AGE}=8.75 (SD 2.45) A_{AGE} =13.90 (SD 1.97) t_{D-A}=5.58 (SD 1.49)	PedsQL-G (survivor & parent report)	Survivors of CNS tumours had significantly worse QOL than population norms, & than survivors of ALL. No effect of radiation therapy or age-effect on QOL.
9	Eiser et al., 2003 (UK)	Cross-sectional Questionnaire	N=23 survivors of paediatric CNS tumour (mixed type) N=45 survivors of paediatric ALL (control group).	D_{AGE}=6.96 (SD 2.49) A_{AGE}=13.74 (SD 3.06) t_{D-A}=7.23 (SD 2.42)	PedsQL-G (survivor & parent report)	Significantly worse overall, physical & psychosocial QOL in survivors of paediatric CNS-cancer than in the ALL control group.
10	Holmquist & Scott, 2002 (US)	Cross-sectional	N=54 survivors of paediatric CNS tumour (astrocytoma & medulloblastoma). N=24 survivors of paediatric ALL.	D_{AGE}=6.4 (SD 3.22) A_{AGE}=10.45 (SD 2.84) t_{D-A}=3.93 (SD 2.73)	CBCL (parent report) CPRS-R (parent report)	No difference between CNS-tumour survivors & either population norms, or ALL survivors. Radiation did not correlate with levels of internalising or externalising problems.

11	Levisohn et al., 2000 (US)	Cross-sectional Questionnaire & interview with parent	N=19 survivors of paediatric cerebellar tumour (medulloblastoma, astrocytoma, ependymoma) Excluded those who'd received radiation or chemotherapy using methotrexate prior to assessment.	D_{AGE}= not given. Surgery occurred within 2 weeks of diagnosis, mean age at surgery =8.17 (range=3.25-14.83) A_{AGE}=8.39 t_{D-A}= not given. Mean time between surgery & assessment =5.1 (SD 0.53)	CBCL (parent report) Rutter Behaviour Rating Scale (parent report) Semi-structure interview with parent	6 out of 19 were rated as having deficits in affect regulation. Those who had affect deficits also had extensive vermis damage & cognitive impairment.
12	Maddrey et al., 2005, (US)	Cross-sectional Questionnaire	N=16 ten-year-survivors of paediatric medulloblastoma. Mixed treatment	D_{AGE}=7.3 (SD 4.5) A_{AGE}= 21.9 (SD 3.6) t_{D-A}=14.6 (SD 3.5)	QLI (survivor report) SCL-90-R (survivor report)	Self-reported QOL was not decreased in comparison to population norms, despite objective factors indicating a significant impairment.
13	Martinez-Climent et al., 1994 (Spain)	Cross-sectional Interview	N=39 survivors of paediatric posterior fossa tumours. Mixed treatment.	D_{AGE}=not given. Median age at diagnosis=5 yrs (range 1-10) A_{AGE}=not given. Median age at assessment=14 yrs (range 4-23) t_{D-A}=not given. Median time between diagnosis & assessment=9 yrs (range 3-20)	Used a QOL scale developed for this study. This identified via interview with survivor & parent whether or not the child met diagnostic criteria for a mental disorder.	18% of sample had identifiable mental disorder.
14	Meeske et al., 2004 (US)	Cross-sectional Questionnaire	N=86 BT survivors (mixed types) (n = 36 in treatment, n=26 no treatment for <1yr, n=24 no treatment for >1yr.) N=170 ALL survivors (controls)	D_{AGE}=5 (SD 3.7) A_{AGE}=9.7 (SD 4.4)	PedsQL-G (parent report) PedsQL-C (parent report) PedsQL-F (parent report)	BT survivors reported worse physical & social QOL, more fatigue but less illness-related worry than survivors of BT.

15	Meyer & Kieran, 2002 (US)	Cross-sectional Interview	N=34 survivors of paediatric brain tumours (mixed types). Treatment by surgery only.	D_{AGE}=not given. But mean age of first surgery = 9.6 A_{AGE} =Not given (assessments were between 2 weeks & 5 years post surgery).	Semi-structured interview with parent & survivor re. child's mood & behaviour. Concerns were followed up with DSM-IV diagnostic questions.	56% had significantly higher rates of psychological problems than in the general population). 34% warranted two or more diagnoses. 69% of those who'd terminated treatment less than a year ago had emotional problems, compared to 47% of those whose treatment was completed 1-5 years previously.
16	Poggi et al., 2005a (Italy)	Cross-sectional Questionnaire	N=76 survivors of paediatric brain tumours (mixed types) divided into three groups: Group 1 (n=20) ages 0-6yrs, Group 2 (n=35) ages 7-13 yrs, Group 3 (n=21) ages 14-18 yrs. Mixed treatment.	Overall group: D_{AGE}=7.4 (SD 4.4) A_{AGE}=11.9 (SD 1.9) t_{D-A}=4.5 (SD 5.2) Group 1: D_{AGE}=2.9 (SD 1.9) A_{AGE} = 4.1 (SD 1.8) t_{D-A}=1.2 (SD 1.1) Group2: D_{AGE}=7.7 (SD 2.8) A_{AGE}=10.6 (SD 1.9) t_{D-A}=2.9 (SD 2.7) Group 3: D_{AGE}=11.2 (SD 4.5) A_{AGE}= 21.3 (SD 6.2) t_{D-A}= 10.1 (SD 6.4)	CBCL (parent report)	35% of overall sample rated with pathological levels of emotional problems. Internalising problems were the most common across all three age groups. In general, levels of problems tended to be increased in the older age groups.
17	Poggi et al,. 2005b (Italy)	Cross-sectional Questionnaire	N=22 survivors of paediatric brain tumours (mixed types) Mixed treatment. N=24 survivors of traumatic brain injury (control group)	D_{AGE}= 8.7 (SD 2.3) A_{AGE} = 10.9 (SD 2.1)	CBCL (parent report)	No difference between groups on internalising, withdrawal, or social problems. A trend towards better functioning in the BT group on measures of externalising problems, anxiety/depression, & attention/hyperactivity problems. Brain tumour survivors exhibited significantly better functioning than survivors of traumatic brain injury on measures of delinquent & aggressive behaviour.

18	Pompili et al., 2002 (Italy)	Cross-sectional Questionnaire	N=20 adult survivors of paediatric cerebellar pilocytic astrocytoma All had received surgery & none had undergone cranial irradiation.	D_{AGE}=not given. Mean age at time of surgery = 8 yrs (range 2-16). A_{AGE}=27 (range18-40)	Mackworth et al's QOL questionnaire (modified version; Mackworth, Fobair & Prados, 1992). (survivor report)	Significantly worse functioning on all domains of QOL for BT survivors when compared to population norms.
19	Poretti et al., 2004 (Switzerland)	Cross-sectional Questionnaire & Interview	N=21 survivors of paediatric craniopharyngioma (al having undergone surgery).	D_{AGE}=9.17 (SD 4.25) A_{AGE}=20.58 (SD 7.33) t_{C-A}=11.25 (SD 7.58)	Semi-structured interview with parent & child. CBCL (parent report) YSR (survivor report) PedsQL-G & PedsQL-C (parent & survivor report)	Lower overall QOL in BT survivors than population norms. Survivors were asked whether the presence of certain physical & emotional symptoms impacted on their QOL & results were mixed. Overall, QOL did not correlate with a measure of objective functional outcome.
20	Ribi et al., 2005 (Switzerland)	Cross-sectional Questionnaire	N=18 survivors of paediatric medulloblastoma. Mixed treatment.	D_{AGE}=6.8 (range 1.1-14.7) A_{AGE}=18.9 (range 8.5-31.9) T_{D-A}=12.2 (range 3.0-24.0)	Semi-structured interview with parent & child CBCL (parent report) YSR (survivor report) PedsQL-G & PedsQL-C (parent & survivor report)	42% of the sample were rated by their parents as having behavioural/emotional disturbances, versus 17% when rated by survivors themselves.
21	Ross et al., 2003 (Denmark)	Case-note information over time.	N=973 survivors of paediatric CNS tumour.	Not available.	Retrospective information from DCR & DPCR	In this population cohort study, there was a significantly increased risk of psychiatric hospitalisation for survivors of paediatric CNS tumours than for survivors of other paediatric cancers, or population norms.
22	Sands et al., 2005 (US, Canada, Italy, Argentina, Brazil, Australia)	Cross-sectional Questionnaire	N=19 survivors of paediatric CNS germ-cell tumours. Mixed treatment.	D_{AGE}=8.95 (SD 3.2) A_{AGE}=14.9 (SD 3.2) T_{D-A}=6.01 (SD 0.97)	CHQ-PF50 (parent report)	Mean scores on psychosocial functioning were in the low-average range.

23	Weissenberger et al., 2001 (US)	Cross-sectional Interview & Questionnaire	N=12 survivors of paediatric hypothalamic harmatoma with gelastic seizures. N=12 healthy siblings (control)	D_{AGE}=not given. Mean age of onset of gelastic seizures =6 wks A_{AGE}=7.7	VAS (survivor report) DICA-R-P (interview with parent & survivor)	83% of sample met criteria for at least one psychiatric diagnosis, versus only 25% of the control group. Survivors were significantly more likely to present with affective aggression than their siblings.

A_{AGE} = mean age at assessment; ALL = Acute Lymphoblastic Leukaemia; BT = brain tumour; C_{AGE} = mean age at completion of treatment; CBCL = Child Behaviour Checklist (parent-report version of YSR); CHQ-PF50 = Child Health Questionnaire - Parent Form 50; CPRS-R = Conner's Parent Rating Scale – Revised version; D_{AGE} = mean age at diagnosis; DCR = Danish Cancer Registry; DICA-R-P = Diagnostic Interview for Children & Adolescents – revised parent version; DPCR = Danish Psychiatric Central Register; DSM-IV = Diagnostic & Statistical Manual of Mental Disorders – 4th edition; GHT = Growth Hormone Treatment; HUI2 = Health Utilities Index Mark 2; HUI3 = Health Utilities Index Mark 3; PedsQL-G = Paediatric Quality of Life Inventory, Generic scale; PedsQL-C = Paediatric Quality of Life Inventory, Cancer module; PedsQL-F = Paediatric Quality of Life, Multidimensional Fatigue Module; QLI = Ferrans & Powers Quality of Life Index; SCL-90-R = Symptom Checklist 90 – Revised version; SD = standard deviation; t_{C-A} = mean time between completion of treatment & assessment; t_{D-A}= mean time between diagnosis & assessment; VAS = Vitiello Aggression Scale; YSR = Youth Self-Report (child-report version of CBCL); # = study number. This is used so that individual studies can be referred to easily in Tables 3 and 4 (see section 6.5 which considers predictors of QOL).

Table 2: Methods used to evaluate different domains of QOL.

Method	*Studies using that method*
Overall QOL:	
PedsQL-G total score	Bhat et al., 2005*^; Eiser et al., 2004*^; Eiser et al ., 2005*^; Eiser et al., 2003*^; Meeske et al., 2004^; Poretti et al., 2004*^; Ribi et al., 2004*^.
PedsQL-C total score	Meeske et al., 2004^
QLI total score	Maddrey et al., 2005*
Physical Functioning:	
PedsQL-G physical subscale score	Bhat et al., 2005*^; Eiser et al., 2005*^; Eiser et al., 2003*^; Meeske et al., 2004^; Poretti et al,. 2004*^;
PedsQL-C pain subscale score	Bhat et al., 2005*^; Meeske et al., 2004^
PedsQL-C nausea subscale score	Bhat et al., 2005*^; Meeske et al., 2004^
PedsQL-C perceived physical appearance subscale score	Bhat et al., 2005*^; Meeske et al., 2004^
PedsQL-F total score	Meeske et al., 2004^
PedsQL-F general fatigue subscale score	Meeske et al., 2004^
PedsQL-F cognitive fatigue subscale score	Meeske et al., 2004^
PedsQL-F sleep-rest fatigue subscale score	Meeske et al., 2004^
QLI health and functioning subscale	Maddrey et al., 2005*
SSI (reports of whether various physical symptoms impacted on QOL)	Poretti et al., 2004*
SSI (question re satisfaction with physical appearance)	Ribi et al., 2005*
Psychological Functioning:	
Overall emotional functioning	
DCR & DPCR	Ross et al., 2003
PedsQL-G emotional subscale score	Bhat et al., 2005*^; Eiser et al., 2005*^; Meeske et al., 2004^; Poretti et al., 2004*^; Ribi et al., 2005*^
CBCL total score	Beebe et al., 2005^; Copeland et al., 1999^; Levisohn et al., 2000^; Poggi et al., 2005a^, Poggi et al,. 2005b^; Poretti et al., 2004^; Ribi et al., 2005^
YSR total score	Carey et al., 2001*; Poretti et al., 2004*; Ribi et al., 2005*
HUI2 & HUI3 – emotion items	Barr et al., 1999*^
QLI – psychological/spiritual subscale score	Maddrey et al., 2005*
Diagnoses of psychiatric disorders	
– via interview	Aarsen et al., 2004*^; Martinez-Climent et al., 1994*^; Meyer & Kieran, 2002*^
– via DICA-R-P	Weissenberger et al., 2001^
Own QOL questionnaire – wellbeing subscale score	Pompili et al., 2002*
CHQPF-50 psychosocial subscale score	Sands et al., 2005^
Internalising problems	
Measure of overall internalising problems	
CBCL internalising subscale score	Beebe et al., 2005^; Carey et al., 2001^; Copeland et al., 1999^; Holmquist & Scott, 2002^; Poggi et al., 2005a^, Poggi et al., 2005b^; Poretti et al., 2004^; Ribi et al., 2005^
YSR internalising subscale score	Carey et al., 2001*; Poretti et al., 2004*; Ribi et al,. 2005*
Measures of anxiety & depression	
CBCL anxious-depressed subscale score	Holmquist & Scott, 2002^; Poggi et al., 2005a^; Poggi et al., 2005b^; Poretti et al., 2004^; Ribi et al., 2005^
YSR anxious-depressed subscale score	Poretti et al., 2004*; Ribi et al., 2005*
CHQPF-50 anxious-depression subscale score	Sands et al., 2005^;
PedsQL-C procedural anxiety subscale score	Bhat et al., 2005*^; Meeske et al., 2004^
PedsQL-C treatment anxiety subscale score	Bhat et al., 2005*^; Meeske et al., 2004^
PedsQL-C worry subscale score	Bhat et al., 2005*^; Meeske et al., 2004^

QOL questionnaire depression subscale score	Pompili et al., 2002*
CHQPF-50 self-esteem score	Sands et al., 2005^
DSM-IV diagnoses of anxiety/depression disorders	
– via interview	Aarsen et al., 2004*^; Martinez-Climent et al., 1994*^; Meyer & Kieran, 2002*^
– via DICA-R-P	Weissenberger et al., 2001^
Measures of withdrawal	
CBCL withdrawn subscale score	Holmquist & Scott, 2002^; Poggi et al., 2005a^; Poggi et al., 2005b^; Poretti et al., 2004^; Ribi et al., 2005^
YSR withdrawn subscale score	Poretti et al., 2004*; Ribi et al., 2005*
Measures of somatisation	
CBCL somatisation subscale score	Holmquist & Scott, 2002^; Poggi et al,. 2005a^; Poggi et al., 2005b^; Poretti et al., 2004^; Ribi et al., 2005^
YSR somatisation subscale score	Poretti et al., 2004*; Ribi et al., 2005*
Externalising problems	
Measures of overall externalising problems:	
CBCL externalising subscale score	Beebe et al., 2005^; Carey et al., 2001^; Copeland et al., 1999^; Holmquist & Scott, 2002^; Poggi et al., 2005a^, Poggi et al., 2005b^; Poretti et al., 2004^; Ribi et al., 2005^
YSR externalising subscale score	Carey et al., 2001*; Poretti et al., 2004*; Ribi et al., 2005*
DSM-IV diagnoses of behavioural disorders via interview	Meyer & Kieran, 2002*^
Attention problems/Hyperactivity:	
CBCL attention & hyperactivity subscale score	Holmquist & Scott, 2002^; Poggi et al., 2005a^; Poggi et al., 2005b^; Poretti et al., 2004^;
YSR attention & hyperactivity subscale score	Poretti et al., 2004*
CPRS-R total score	Holmquist & Scott, 2002^
DSM-IV diagnoses for ADHD	
– via interview	Aarsen et al., 2004*^;
– via DICA-R-P	Weissenberger et al., 2001^
Aggression:	
CBCL aggression subscale score	Holmquist & Scott, 2002^; Poggi et al., 2005a^; Poggi et al,. 2005b^; Poretti et al., 2004^; Ribi et al., 2005^
YSR aggression subscale score	Poretti et al., 2004*; Ribi et al., 2005*
VAS (Affective aggression and predatory aggression subscales)	Weissenberger et al., 2001^
DSM-IV diagnoses for ODD via DICA-R-P	Weissenberger et al., 2001^
Delinquent behaviour:	
CBCL delinquent behaviour subscale	Holmquist & Scott, 2002^; Poggi et al,. 2005a^; Poggi et al., 2005b^; Poretti et al., 2004^; Ribi et al., 2005^
YSR delinquent behaviour subscale	Poretti et al., 2004*; Ribi et al., 2005*
DSM-IV diagnoses for CD via DICA-R-P	Weissenberger et al., 2001^
Social Functioning:	
PedsQL-G social subscale	Bhat et al., 2005*^; Meeske et al., 2004^; Poretti et al., 2004*^; Ribi et al., 2005*^
PedsQL-C communication	Bhat et al., 2005*^
QLI	Maddrey et al., 2004*
SSI self-(reports of whether various social problems impacted on QOL)	Poretti et al., 2004*

* self report version, ^ parent-proxy report version

to be worse in the BT population. However, the PedsQL-C focuses to a large extent on specific treatment-related experiences (for example, anxiety associated with injections, and nausea following treatments). Whilst ALL survivors do not have to endure the distressing experience of brain surgery, they have to undergo more frequent aversive medical procedures such as lumbar punctures and bone marrow aspirations at every clinic visit. When this is taken into consideration it is perhaps unsurprising that the ALL and BT survivors are comparable on what is largely a treatment-focused scale.

6.2 Physical QOL

Only 7 papers were identified that looked at physical QOL from an SPI perspective (see Table 2). In general, these studies showed that BT survivors rated worse than healthy controls or other cancer populations on several measures of physical QOL, although not on all. Ribi, Relly, Landolt et al. (2005) found that half of their participants were dissatisfied with their physical appearance. In comparison to population norms, 2 studies found that BT survivors reported higher levels of dissatisfaction related to overall physical health difficulties (Eiser et al., 2005; Poretti, Grotzer, Ribi et al., 2004), but Maddrey et al. (2005) failed to find a difference. Meeske et al. (2004) found that BT survivors scored much higher (i.e. worse) on measures of problems with fatigue than population norms.

When compared to ALL survivors, results suggested that BT survivors fared worse on measures of problems related to overall physical health (Eiser et al., 2003; Meeske et al., 2004), cognitive fatigue, general fatigue and total fatigue (Meeske et

al., 2004). No difference was found between the two groups on problems resulting from pain, nausea and sleep-rest fatigue or on perceived physical appearance.

6.3 Psychological QOL

Twenty of the 23 studies investigated psychological functioning in BT survivors. The prevalence of diagnosable psychiatric disorders ranged from 18% to 83% (Aarsen, Van Dongen, Paquier, Van Mourik, & Catsman-Berrevoets, 2004; Martinez-Climent, Sanchez, Menor, Miralles & Tortajada, 1994; Meyer & Kieran, 2002; Weissenberger, Dell, Liow et al., 2001) and Meyer & Kieran (2002) found that 34% of their sample warranted multiple diagnoses. A wide range of psychological problems were investigated and findings are separated into three sections looking at overall emotional QOL, internalising problems and externalising problems. Rates of problems are reported, and where possible, comparisons are made between BT survivors and normative or other control populations.

6.3.1. Overall Emotional QOL

In agreement with what was found in Fuemmeler et al.'s earlier review (Fuemmeler et al., 2002), rates of psychological diagnoses and difficulties varied widely. In Aarsen et al.'s (2004) sample, 65% experienced significant psychological difficulties. Rates of clinically elevated emotional problems were reported to be 17% for self-report data (Ribi et al., 2005) and 35-42% for parent-proxy report (Poggi, Liscio, Galbiati et al., 2005a; Ribi et al., 2005). Barr, Simpson, Whitton et al. (1999) found that 73% of their sample were generally happy, with only 2% reporting being somewhat unhappy, or frequently feeling fretful, angry, irritable, anxious, or depressed. Sands, Kellie, Davidow et al. (2005) reported that the mean score

obtained by BT survivors on a measure of overall psychosocial functioning was in the low-average range.

When comparing the overall emotional QOL of BT survivors to other groups, the findings were mixed. Poretti et al. (2004) found that emotional functioning of BT survivors was worse than for population norms, with 42% of patient self-reports and 67% of parent-proxy reports displaying clinically elevated scores on the total problems scales of the YSR and CBCL respectively. Furthermore, when compared to a healthy sibling control group, Weissenberger et al. (2001) found that significantly more BT survivors met diagnostic criteria for a psychiatric disorder (83% versus 25%). Pompili, Caperle, Ramazzotti et al. (2002) found that BT survivors scored significantly worse on a wellbeing dimension than healthy controls. However all of these studies utilised small samples and other studies, including those with larger numbers of participants, found no significant difference between BT survivors and population norms, both when rated by parent-proxy report (Beebe, Ris, Armstrong et al., 2005; Copeland, deMoor, Moore & Ater, 1999; Meeske et al., 2004) and by patient self-report (Carey, Barakat, Foley, Gyato, & Phillips, 2001; Maddrey et al., 2005).

Perhaps the most persuasive finding however, comes from Ross, Johansen, Dalton et al. (2003). In a nationwide, population-based retrospective cohort study, they used the Danish Cancer Registry and the Danish National Psychiatric Central Register to follow-up 973 children diagnosed with brain-tumours to establish the frequency of subsequent psychiatric hospitalisations. They found that when compared to rates in the general population, paediatric BT survivors were 1.8 times more likely to be

admitted to a psychiatric hospital in adulthood (95% confidence interval 1.5-2.2), and 5.2 times more likely during childhood (95% confidence interval 1.4-13.2). Rates of psychiatric hospitalisations following other types of childhood cancer were not significantly different from what was observed in the general population suggesting that the increased risk of psychiatric difficulties was specific to survivors of brain tumours.

6.3.2. Internalising problems

a) Overall internalising problems: Studies looked both at levels of overall internalising problems, and also at levels of specific internalising problems such as depression, anxiety disorders and somatisation.

In terms of proportion of samples with clinically elevated scores on measures of overall internalising problems, rates ranged from 25%-50% when measured using patient self-report (Ribi et al., 2005; Poretti et al., 2004), and 48%-58% for parent-proxy reports (Ribi et al., 2005; Poretti et al., 2004; Poggi et al., 2005a). This variation was even more pronounced in Fuemmeler et al.'s review who reported rates of elevated levels of internalising problems ranging between 15-78% of samples.

Two studies found that BT survivors were significantly more impaired than population norms on measures of overall internalising problems (Beebe et al., 2005; Carey et al., 2001), but Copeland et al. (1999) and Holmquist & Scott (2002) both found that scores were within normal limits. It is difficult to determine the reason for this discrepancy: all four studies used parent-proxy reports and referred to samples of survivors with similar mean ages at time of assessment. However, there was

considerable variation, both within and between studies with regards to the ages of survivors, and lengths of time since treatment completion. It might be anticipated that both of these factors could impact on the levels of internalising difficulties experienced (see later section on predictors of QOL) and the utilisation of such heterogeneous samples may obscure meaningful results. Only one study compared patient self-reports of overall internalising scores to population norms and it found that they were not significantly different (Carey et al., 2001). Poggi, Liscio, Adduci et al. (2005b) compared survivors of paediatric brain tumours to a sample of children who had experienced traumatic brain injury. They found no significant difference between the groups.

b) Anxiety & Depression disorders: Five studies used the Child Behaviour Checklist (CBCL) or Youth Self-Report (YSR) anxiety-depression subscale scores to give an indication of combined anxiety and depression levels. The proportions of participants with clinically elevated scores on these subscales were approximately 8% for parent-proxy reports (Poretti et al., 2004; Ribi et al., 2005; Poggi et al., 2005a) and ranged from 0% - 25% for patient self-reports (Poretti et al., 2004; Ribi et al., 2005). Poggi et al. (2005b) compared BT survivors to survivors of traumatic brain injury and found that there was a non-significant trend towards worse anxiety-depression scores for the latter group, whereas there was no difference between ALL and BT survivors (Holmquist & Scott, 2002). The Child Health Questionnaire – Parent Form 50 (CHQPF-50) also provides a combined anxiety-depression score and Sands et al. (2005) found that the average score for their sample of BT survivors on this subscale was within the average range for population norms.

Four studies provided information relating to the prevalence of specific anxiety disorders in their samples. Weissenberger et al. (2001) found of their sample of 12 survivors of hypothalamic hamartoma, 2 met criteria for PTSD (17%), 2 for specific phobias (17%), 3 for OCD (35%) and 2 for GAD (17%). These appeared to be higher rates than were observed in the sibling control group (where only 2 siblings met criteria for GAD) but sample sizes were too small to be able to detect reliably a significant difference. Aarsen et al. (2004) found that in a sample of 23 BT survivors, 4 (18%) met diagnostic criteria for an anxiety disorder. Lower rates were reported by Martinez-Climent et al. (1994) and Meyer & Kieran (2002) who found that 3 out of 39 (8%) and 3 out of 34 (9%) had anxiety disorders. Unfortunately, none of these studies incorporated a control group, and only Meyer & Kieran made a comparison with rates of anxiety disorders in the normal population (which they reported to be similar to those found in the BT sample). Meeske et al. (2004) compared BT survivors to ALL survivors and found that there were no differences between the groups on ratings of procedural anxiety or treatment anxiety but that BT survivors rated having less worry than ALL survivors.

Only 2 studies calculated rates of depression in their samples. Martinez-Climent et al. (1994) found that out of 39 survivors of paediatric posterior fossa tumours, only 2 (5%) met diagnostic criteria for depression. This was a low rate in comparison to the findings of Meyer & Kieran (2002) where 35% (12 out of 34) of their sample met criteria for a diagnosis of major depression or dysthymia (a substantially higher rate than the 6.2% found in the normal population). This finding is supported by Pompili et al. (2002) who found that survivors of brain tumours had statistically worse outcomes than population norms when measured on the depression dimension of

their QOL questionnaire, although this measure has not been standardised for use as a diagnostic tool. Sands et al. (2005) did not investigate depression per se, but looked specifically at self-esteem of survivors and found that the average score was in the borderline range.

The variation in these findings may result from differing methods utilised to identify depression in the samples. Martinez-Climent et al. (1994) relied on researchers who were assessing other aspects of psychological functioning (such as cognitive skills) to be alert for any signs of depression or other emotional difficulties. If these were noticed, the child was referred to a paediatric psychologist who would then complete a diagnostic assessment. The detection of depression therefore, was largely dependent on the aptitude of the researchers to identify signs of illness without the use of any specific standardised assessment measures. As such, it is perhaps unsurprising that rates in this sample were so low, particularly as the age range (and therefore expected ways in which depression would present) varied enormously within the sample. In contrast, all participants in Meyer & Kieran's study were assessed by a psychologist who asked specific probe questions related to depression and followed these up with questions based on the relevant DSM-IV diagnostic criteria as appropriate. Although, as in the study by Martinez-Climent et al., this study did not administer a standardised assessment tool, the fact that all participants were fully assessed by a psychologist makes it less likely that true cases of depression would go undetected. Only Sands et al. (2001) employed a standardised measure but this looked at one specific symptom associated with depression, rather than depression as a whole.

c) Withdrawal: Prevalence of clinically elevated levels of withdrawal symptoms ranged from 22.6-42% on parent-proxy reports (Poggi et al., 2005a; Poretti et al., 2004; Ribi et al., 2005) and 0-17% on patient self-reports (Poretti et al., 2004; Ribi et al., 2005). Studies comparing BT survivors to survivors of ALL (Holmquist & Scott, 2002) and survivors of traumatic brain injury (Poggi et al., 2005b) found that there was no significant difference between groups on withdrawal symptoms.

d) Somatisation: Prevalence of clinically elevated scores on somatisation scales were investigated by two studies, both using the CBCL and YSR questionnaires. Poretti et al., (2004) found that 6 out of 12 (50%) of their sample were rated by their parents as having elevated somatisation symptoms although only 2 out of 12 (16%) rated themselves with somatisation symptoms. Ribi et al., (2005) found lower levels with only 2 out of 12 parents reporting elevated symptoms in their child, and 0 out of 12 of the children themselves reporting such symptoms. With such small sample sizes, it is impossible to draw definitive conclusions from these studies.

When compared to control groups, there was no difference between BT and ALL survivors on numbers displaying elevated somatic symptoms (Holmquist and Scott 2002), but a trend towards higher levels of problems reported by those who had experienced traumatic brain injury (Poggi et al., 2005b).

Overall, it is difficult to interpret these results with any certainty as the number of studies that have investigated levels of internalising problems in BT survivors is small. Furthermore, the majority of those that have done so utilised relatively small

samples. In general there was little evidence of a difference between BT survivors and ALL survivors or survivors of traumatic brain injury. When compared to population norms, findings were mixed with some evidence suggesting a worse outcome for survivors of BT, but other studies finding no difference. Possible explanations accounting for these discrepancies are discussed in the methodological limitations section of this review.

6.3.3 Externalising problems

a) ***Overall externalising problems:*** Several studies looked at the rates of clinically elevated scores on measures of overall externalising problems. Studies using the CBCL parent-proxy reports found that 8-42% of their samples had externalising problems (Poggi et al., 2005a; Poretti et al., 2004; Ribi et al., 2005). Those using the patient self-report scores on the YSR found that between 0% and 17% reported externalising problems (Poretti et al., 2004; Ribi et al., 2005). Four studies compared BT survivors to population norms on scores obtained on the CBCL externalising scale and all found no significant difference (Beebe et al., 2005; Carey et al., 2001; Copeland et al., 1999; Holmquist & Scott, 2002). This was also the case for patient self-reports of externalising problems (Carey et al., 2001). However, Meyer & Kieran (2002) investigated rates of disruptive behaviour disorders such as Attention-deficit hyperactivity disorder (ADHD), Oppositional Defiant Disorder (ODD), and Conduct Disorder (CD). They found that 35% (12 out of 34) of their BT survivor sample met diagnostic criteria for a disruptive behaviour disorder which was higher than rates of 10% observed in the general population.

b) Attention problems/hyperactivity: 2 studies looked specifically at diagnoses of ADHD. Aarsen et al. (2004) found that only one of the 23 BT survivors in their sample met diagnostic criteria for ADHD. This finding contrasted with that of Weissenberger et al. (2001) who found that nine out of twelve (75%) of their BT sample met diagnostic criteria (significantly more than the 17% in the sibling control group). Poretti et al. (2004) found that 17% of child self-reports, and 25% of parent-reports indicated a clinically significant attention problem. Although small sample sizes may have accounted for some of the discrepancy between these findings, a considerable proportion of the inconsistency may be accounted for by the substantial differences between the samples utilised in the studies. In comparison to the survivors in the Aarsen et al. (2004) and Poretti et al. (2004) studies, Weissenberger et al. (2001) looked at a very restricted sample of tumour survivors, and included only those who had survived a hypothalamic hamartoma[1] and suffered from associated gelastic seizures[2]. Typically these children were experiencing daily seizures (up to 10 per day), receiving anticonvulsant treatment and two thirds of the participants were also receiving medication for the treatment of psychiatric symptoms. Any of these factors may have impacted on levels of ADHD but anticonvulsant medication in particular has been linked to increased levels of irritability, hyperactivity and aggression, and has been found to interfere with several aspects of cognitive function, including attention and concentration, and therefore it is unsurprising that this sample had elevated levels of ADHD (Brent, Crumrine, Varma et al., 1987; Lee, Steingard, Cesena et al., 1996; Mattes, 1990; Reynolds,

[1] These are benign tumours that encroach upon the hypothalamus and typically straddle the optic nerve making removal difficult (Faulkner & Christy, 2006).
[2] Gelastic seizures are recurrent episodes of inappropriate smiling, giggling, or laughter, accompanied by electroencephalographic changes, and are unrelated to external social or interpersonal stimulation (Go, 1999).

1985; Tallian, Nahata, Lo & Tsoa, 1996; Voorhies, Behar, Hunt, Stoff & Ricciuti, 1988; Wolf, Shinnar, Kang et al., 1996; all cited in Weissenberger et al., 2001).

When comparing BT and ALL survivors, Holmquist & Scott (2002) found no significant difference between groups on attention problems as identified by the Conner's Parents Rating Scale (CPRS-R) or the CBCL attention problems subscale. When compared to survivors of traumatic brain-injury, Poggi et al., 2005b found that there was a trend towards less attention problems in BT survivors.

c) ***Aggression:*** Both Poretti et al. (2004) and Ribi et al. (2005) reported very low levels of aggression in survivors, with no survivors in either study reporting clinically elevated levels of aggression, and only one parent-proxy report in the former study identifying a significant level of aggression. In contrast, Weissenberger et al. (2001) found that 83% of survivors met DSM criteria for diagnosis of ODD (significantly more than in the sibling control group). They also evaluated survivors on the Vitiello Aggression Scale (VAS) and found that these survivors were significantly more likely to present with affective aggression than their siblings (with eight out of the eleven survivors displaying at least 4 out of 8 affective aggression characteristics). As highlighted earlier, Weissenberger et al. (2001) looked at a very specific sample of BT survivors who were all on anticonvulsant medication which has been linked to increased levels of aggression. Additionally, the authors reflect that animal studies have shown that hypothalamic dysfunction is associated with increased levels of aggressive behaviour, and so the specific location of the tumours in this sample may also explain the high levels of aggression.

Holmquist & Scott (2002) compared survivors of BT to survivors of ALL and found no significant difference between groups in terms of levels of aggression as measured by the CBCL. Poggi et al. (2005b) found higher levels of aggression in paediatric survivors of traumatic brain injury than in BT survivors.

d) Delinquent behaviour: As with the results for aggression, Poretti et al. (2004) and Ribi et al. (2005) reported relatively low frequencies of clinically elevated scores on the CBCL and YSR delinquent behaviour scales (on average 8% of samples). This was again in contrast to higher ratings of delinquent behaviour identified by Weissenberger et al. (2001) where they found that 33% of their sample met diagnostic criteria for conduct disorder (which was a significantly higher rate than found in their sibling control group). There were no significant differences in terms of delinquent behaviour between BT survivors and survivors of ALL (Holmquist & Scott, 2002), but compared to traumatic brain-injury survivors, BT survivors displayed a lower prevalence of delinquent behaviour.

Overall, the majority of studies showed little evidence of an increased level of externalising problems in BT survivors when compared to population norms or ALL survivors, and they appeared to have lower levels of externalising difficulties than survivors of traumatic brain injury. The main exception to these findings was the Weissenberger et al. (2001) study, where BT survivors showed highly elevated levels of aggression, ADHD, and delinquent behaviours in comparison to a healthy control group. This discrepancy may be a result of factors including specific differences in sample characteristics and small sample sizes.

6.4 Social QOL

Very few studies investigated the social functioning domain of QOL from an SPI perspective. The majority of the studies used measures that provided the researchers with a subjective description of the situation (e.g. "I am not liked by other kids"), but they did not look at the extent to which that situation caused distress to, or was a problem for, the child.

One study that clearly distinguished between subjective description and SPI was that of Poretti et al. (2004). They asked questions that elicited subjective descriptions (for example about difficulties making friends or being rejected by others) and then asked participants whether that situation affected their quality of life. The results were interesting. Of 11 survivors who said they had experienced difficulties making friends, 9 (82%) said it affected their QOL. Of the 7 survivors who had experienced rejection by others, all 7 (100%) said it affected their QOL. Survivors over the age of 18 were asked whether they had any partnership experience and of the 5 who had not, 2 (40%) said it affected their QOL. The over-18s were also asked whether they had any sexual experience. Of the 7 that reported that they had not, 5 (71%) said that this affected their QOL. The survivors over the age of 20 were asked about having a family and children of their own. Of the 9 survivors that had no family (i.e. a partner, children) of their own, only 1 rated this as affecting their QOL. None of the survivors over 20 had children and 3 (out of 11, 27%) said this affected their QOL.

It is difficult to draw conclusions from the results of Poretti et al. (2004). The sample size was very small and there was no control group, making it hard to say whether these social difficulties were specifically associated with the experience of having a

brain tumour. Nevertheless, it is interesting that whilst there appears to be an association between the subjective descriptions and the SPI, they do not overlap completely. For example, most, but not all, children who reported having difficulties making friends said it affected the quality of their lives. This highlights the importance of looking at the two aspects of subjective QOL separately.

Using the Quality of Life Index (QLI), Maddrey et al. (2004) found that there was no significant difference between survivors' ratings of social functioning and population norms. Studies using the PEDSQL generic social subscale found that QOL in survivors was significantly worse when compared to population norms (Poretti et al., 2004; Ribi et al., 2005) and survivors of ALL (Meeske et al., 2004). There was no difference between survivors of BT and survivors of ALL on communication (Meeske et al., 2004).

In their earlier review, Fuemmeler et al. (2002) evaluated nine studies that looked at social functioning and found that BT survivors showed worse social functioning than healthy, non-CNS cancer, and other paediatric control groups. However, the majority of these studies used measures evaluating the objective or subjective description of the social situation for the survivor (as rated by the child themselves, parents, teachers, and researchers), rather then the extent to which that situation caused distress to or was problematic for the child from their own perspective. These findings, taken together with those from the present review suggest that a child surviving a brain tumour is at risk of having impoverished social circumstances, but we do not yet know the extent of the distress that this causes the child.

6.5 Predictors

From the findings presented so far, it appears that some, but not all, survivors of paediatric BTs are at risk for a decreased QOL. It is therefore of value to try to identify particular risk factors so that resources may be directed towards those who are particularly vulnerable to poorer QOL, in order that the impact of such risk-factors can be minimised.

A summary of studies investigating possible predictors of QOL is presented below, and Tables 3 and 4 illustrate which associations were found to be statistically significant and which were not. There were no longitudinal studies and amongst the cross-sectional studies that looked for associations, only a few investigated the same potential correlates, with several having samples too small to be analysed statistically. Therefore the results presented here should be viewed as preliminary findings and the reader should be cautious when using them to make inferences.

6.5.1 Illness-related predictors.

Tumour location and histology: Levisohn, Cronin-Golomb & Schmahmann (2000) observed that all survivors with problems regulating affect and behaviour also had extensive damage to the vermis area, whereas those without such problems did not. However, they were unable to test the significance of this observation as the sample size was too small. In studies where statistical tests could be performed, tumour location was not found to be associated with overall QOL scores (Bhat et al., 2005; Meeske et al., 2004), measures of physical health and fatigue (Meeske et al., 2004), or measures of overall emotional functioning, internalising and externalising problems (Beebe et al., 2005; Copeland et al., 1999; Poggi et al., 2005a). The only

Table 3: Illness- and treatment- related predictors of Quality of Life in survivors of paediatric brain tumours: a summary of associations statistically-tested in the literature.

			Predictors														
			Illness-related			**Treatment-related predictors**											
						Treatments								Complications			
			Tumour location	Histology	Tumour recurrence	Radiation	Chemotherapy		GHT	Surgery		Treatment combination	Currently on/off treatment	Shunt fitted	Pre-surgical	Peri-surgical	Post-surgical
							Use of chemo	Agent		Use of surgery	Extent of resection						
Overall QOL			N^{14} N^{4}	N (child-report)[4] Y(parent report)[4]		$N^{8}N^{20}$	N^{20}		Y^{8}			Y^{4}		Y^{4}			
Physical QOL			N^{14}	Y^{4}		N^{8}						Y^{4}	N^{4}	Y^{4}			
Emotional QOL	Overall		N^{3} N^{6} N^{16}	Y^{4} N^{16}	N^{6}	$N^{8}N^{22}$					N^{6}	Y^{4}			N^{3}	N^{3}	N^{3}
	Internalising	Overall	N^{3} N^{6} N^{16}	N^{16}	N^{6}	$N^{10}N^{16}$		Y^{10}		N^{10}	N^{6}				N^{3}	N^{3}	N^{3}
		Anxiety/ depression	N^{16}	N^{16}		N^{16}		Y^{10}					N^{4}				
		Withdrawal	N^{16}	N^{16}		N^{16}											
		somatisation	N^{16}	N^{16}		N^{16}											
	Externalising	Overall	N^{3} N^{6} N^{16}	N^{16}	N^{6}	$N^{10}N^{16}$		Y^{10}		N^{10}	N^{6}				N^{3}	N^{3}	N^{3}
		Attention problems/ hyperactivity	N^{16}	N^{16}		N^{16}		Y^{10}									
		Aggression	N^{16}	N^{16}		N^{16}											
		Delinquent behaviour	N^{16}	N^{16}		N^{16}											
Social QOL			Y^{4}	Y^{4}								Y^{4}	N^{4}	Y^{4}			

NOTE: "Y" indicates that a significant association was found by a particular study, and "N" indicates that the association was tested, but no significant relationship was found. Some associations were tested by more than one study and hence there are sometimes more than one "Y" or "N" linked to each association. The numbered suffix following each "Y" or "N" indicates which of the reviewed studies each particular "Y" or "N" refers to. The study that each number refers to can be seen in Table 1.

Table 4: Time-related and other predictors of Quality of Life in survivors of paediatric brain tumours: a summary of associations tested in the literature.

			Predictors														
			Time-related						**Other**								
			D_{AGE}	T_{AGE}	A_{AGE}	t_{D-A}	t_T	t_{C-A}	gender	Objective physical appearance	Neurological impairment	Neuropsychological functioning					Parental Regulatory Focus
												FIQ	PIQ	VIQ	Verbal skills	Non-verbal skills	
Overall QOL			N^{20}		N^4N^8	N^4	N^8		N^4 N^{20}	N^{20}		N^{20}					Y^7
Physical QOL					Y^4			Y^{14}									
Emotional QOL	Overall emotional QOL				N^3 Y^{16}	N^6		N^3	N^3 Y^{16}		N^{16}	Y^{16}	N^{16}	N^{16}			
	Internalising	Overall	N^{10}	N^{10}	N^3 Y^{16}	N^6N^{10}		N^3N^{10}	N^3		N^{16}	Y^{16}	Y^{16}	N^{16}	N^5 Y^{10}	N^5	
		Anxiety/ depression			Y^4Y^{16}						N^{16}	N^{16}	N^{16}	N^{16}			
		Withdrawal			Y^{16}	Y^{16}					N^{16}	Y^{16}	Y^{16}	Y^{16}			
		Somatisation									N^{16}	N^{16}	N^{16}	Y^{16}			
	Externalising	Overall	N^{10}	N^{10}	N^3N^{16}	N^6N^{10}		N^3N^{10}	N^3		N^{16}	Y^{16}	N^{16}	Y^{16}	N^5	N^5	
		Attention problems/ hyperactive			N^{16}	Y^{16}					N^{16}	$Y^{10}Y^{16}$	Y^{16}	Y^{16}			
		Aggression			N^{16}						N^{16}						
		Delinquent behaviour			N^{16}						N^{16}						
Social QOL					Y^4												

NOTE: "Y" indicates that a significant association was found by a particular study, and "N" indicates that the association was tested, but no significant relationship was found. Some associations were tested by more than one study and hence there are sometimes more than one "Y" or "N" linked to each association. The numbered suffix following each "Y" or "N" indicates which of the reviewed studies each particular "Y" or "N" refers to. The study that each number refers to can be seen in Table 1.

D_{AGE} = Age at diagnosis, A_{AGE} = age at assessment, t_{D-A} = time between diagnosis and assessment, t_{C-A} = time since treatment completed, t_T = time on treatment, T_{AGE} = Age at start of treatment, FIQ = Full-scale IQ, PIQ = performance IQ, VIQ = verbal IQ

study to find a statistically-significant association between tumour location and an element of QOL was that of Bhat et al. (2005) who found that survivors with tumours located in the infratentorial region of the brain had significantly more problems communicating illness-related issues than those with supratentorial tumours. These findings were in contrast to those reported by Fuemmeler et al. (2002), who found that supratentorial and hypothalamic/chiasmatic regions and areas outside the third ventricle were associated with an increased risk of emotional difficulties.

There were mixed results regarding the impact of tumour histology on QOL. Bhat et al. (2005) found a significant effect of histology on parent-proxy but not child self-report measures of overall, physical and emotional QOL. This effect appeared to reflect a better QOL in those surviving low-grade gliomas than in survivors of other low-grade neoplasms, medulloblastomas or malignant gliomas. However, Poggi et al. (2005a) found no effect of histology on either overall levels of emotional, internalising, and externalising problems, or on specific difficulties such as anxiety, somatisation and aggression.

The way in which tumour location and histology were categorised varied considerably between studies. For example, Beebe et al. (2005) investigated only cerebellar tumours distinguishing between those located in the vermis, the right hemisphere, and the left hemisphere, whereas Bhat et al. (2005) included survivors of tumours located anywhere in the brain, and tested for differences between supratentorial and infratentorial tumours. Therefore it is unsurprising that results differed between studies as they were rarely examining the same feature. This issue is discussed in more detail in the methodological limitations section of this report.

Tumour-recurrence: The impact of tumour-recurrence was tested by Copeland et al. (1999) who found no evidence of an association with levels of overall emotional functioning, internalising or externalising difficulties. However, at the point in the study when emotional functioning was assessed, only 19 of the original 27 participants recruited were alive. Therefore, not only was the sample size relatively small, but the sample was potentially biased as many of those who had suffered from a relapse had died before they were able to be assessed. Furthermore, the specific numbers of recurrences that occurred were not taken into consideration in the analysis and it seems likely that QOL would worsen as the number of recurrences increases. For example, for each additional relapse there could be further damage to the actual structures of the brain (both from the tumour and the treatments), more exposure to frightening and aversive treatment procedures, lengthier periods in hospital resulting in additional time off school, and a worse long-term prognosis. Such factors could lead to, amongst other things, heightened anxiety about the risk of death, fear of impending treatments, and further time away from peers and friends leading to increased social anxieties. Therefore, much about the impact of tumour-recurrence on BT survivors' QOL remains unknown and this is an area that would benefit from future research.

6.5.2 Treatment-related predictors

Treatment stage: Bhat et al. (2005) investigated the possibility of an association between QOL and whether or not the participant was currently receiving treatment. They looked at aspects of physical and emotional QOL (including perceived physical appearance, pain, nausea, procedural anxiety, treatment anxiety, and worry) but did not find a significant association. These findings are rather surprising as it might be

anticipated the QOL would improve once treatment has finished. However, it is possible that whilst some aspects of QOL improve due to the termination of treatment (e.g. pain), others worsen over time as the survivor realises that they are not going to improve further, and recognises the full extent of the deficits they have been left with. This is discussed further in section 6.5.3 (time-related predictors).

Treatments types: Copeland et al. (1999) observed that survivors who had undergone irradiation appeared to have worse emotional functioning than those who had not, but they were unable to test the significance of this due to very small numbers of irradiated participants. Five studies that were able to perform statistical analyses found no significant association between measures of overall, physical and emotional QOL and the use of radiation, dosage, or the extension of the radiotherapy field (Eiser et al., 05; Holmquist & Scott, 2002; Poggi et al., 2005a; Ribi et al., 2005; Sands et al., 2005).

Only two studies investigated the impact of chemotherapy on QOL. Ribi et al. (2005) found no difference in overall QOL between survivors who had undergone chemotherapy and those who had not. However, Holmquist and Scott (2002) found that the type of chemotherapy agent used did account for differences in both internalising and externalising problems experienced by survivors. It is possible that certain agents affect the balance of neurotransmitters in the brain and as such may have a direct impact on certain types of emotional difficulties. Alternatively, different agents could result in different side-effect profiles, and the more severe these are, the greater the impact on QOL would be expected to be. However, Holmquist & Scott (2002) assessed children who had all completed treatment at least 3 years previously,

so it seems unlikely that these explanations can account for the effect observed. A more probable rationale is that the specific treatment agent used is determined by cancer-specific variables (such as severity of tumour) and that it is these variables that are linked to QOL rather than the chemotherapy agents themselves. Such an explanation may also account for the finding that survivors receiving Growth Hormone Treatment (GHT) were reported as having worse overall QOL than those who did not (Eiser et al., 2005). GHT is prescribed to children who have developed Growth Hormone Deficiency (GHD) as a result of their brain tumour and/or treatment. GHD can result in a number of problems, including being substantially shorter than healthy children of the same age. In all children, but particularly in adolescents, being shorter and looking younger than their peers could be very distressing and have a marked impact on the QOL of the survivor. However, it is also the case that GHT requires the survivor to undergo daily injections which can be painful, so this too could impact on QOL ratings.

Neither the use of surgery nor the extent of surgical resection (partial or complete) was found to be associated with overall emotional QOL, or levels of internalising or externalising problems (Copeland et al., 1999; Holmquist & Scott, 2002). On the whole, it seems that with the exception of GHT, simple associations between QOL and whether or not a survivor underwent a specific form of treatment (e.g. radiation, chemotherapy, surgery) were not found to be significant.

Bhat et al. (2005) compared survivors who had received different combinations of treatments, and found that children who had received radiation therapy, with or without surgery, and without chemotherapy had significantly worse QOL on several

domains (overall, physical and emotional) than those who had received either a) no treatment at all, b) surgery only, c) chemotherapy without radiation (with or without surgery) or d) radiation and chemotherapy (with or without surgery). This finding appears to be counterintuitive as not only do survivors exposed to both radiation and chemotherapy have to endure both unpleasant procedures, but it might be expected that they have more severe tumours in the first place. However, the authors propose that the use of chemotherapy allows a smaller radiation dose and field to be administered, the implication being that the benefits of reducing the radiation therapy outweigh the negative consequences of the chemotherapy. This rationale seems reasonable provided the supposition that radiation therapy effects QOL is correct, but the findings from the studies included in the present review do not support this assumption. Further research would need to be conducted to determine whether there is evidence to support this hypothesis.

Treatment complications: Complications such as the development of hydrocephalus, CNS infections, and the requirement of a shunt can occur during treatment. Bhat et al. (2005) found that survivors who had required a shunt to be fitted reported worse overall, physical and social QOL than those who had not. Beebe et al. (2005) found no association between composite scores of complications occurring before, during and after surgery and levels of overall emotional functioning, internalising or externalising problems.

6.5.3 Time-related predictors

There was no evidence of an association between age at diagnosis, age at the start of treatment or time since start of treatment and measures of various aspects of QOL

(Eiser et al., 2005; Holmquist & Scott, 2002; Ribi et al., 2005). However, results were more complicated when age at assessment, time since diagnosis, and time since completion of treatment were considered.

Age at assessment: Studies used different methods to investigate age-effects. Bhat et al. (2005) divided their sample into two age groups, those above the median age of 11 years, and those below. Beebe et al. (2005) and Eiser et al. (2005) both considered age at assessment as a continuous variable and tested for linear associations with measures of QOL. In contrast, Poggi et al. (2005a) divided their sample into three discrete age-groups (0-6, 7-13 and 14-18 years) and compared scores on measures of QOL between these groups, allowing for the detection of linear and non-linear associations.

Bhat et al. (2005), Beebe et al. (2005) and Eiser et al. (2005) found no evidence of a linear association between overall QOL, overall emotional functioning, or levels of internalising or externalising problems and age at assessment. However, when more specific difficulties were considered, Bhat et al. (2005) found that older children reported lower levels of procedural anxiety, higher levels of worry about illness, more difficulty communicating about their illness, worse social QOL and worse QOL related to perceived physical appearance than younger children. It makes sense that different specific aspects of QOL might be more or less affected in children of different ages and that if these aspects balance each other out, age-effects may not be detected on more global measures. For example, a young child may not understand the risks with regard to possible relapse and death following a brain tumour so may not report high levels of anxiety related to these issues. However, they may be more

frightened of painful medical procedures, such as injections and lumbar punctures. Poggi et al. (2005a) also found no effect of age at assessment on global and specific measures of externalising problems, but found significant effects on measures of overall emotional problems, overall internalising problems, withdrawal and anxiety-depression. These effects indicated that 7-18 year olds had worse overall emotional QOL, and higher levels of internalising and withdrawal problems than 0-6 year olds. Interestingly, in terms of anxiety-depression scores, the 7-13 year olds had significantly worse levels of problems than both the 0-6 and 14-18 year olds suggesting the possibility of a non-linear effect.

Time since diagnosis: There was no evidence supporting an association between time since diagnosis and overall QOL, physical QOL, overall emotional QOL, total internalising or externalising problems (Bhat et al., 2005; Copeland et al., 1999; Holmquist & Scott, 2002). However, Poggi et al. (2005a) did report that a longer time since diagnosis was associated with higher levels of withdrawal and "attention and hyperactivity problems".

Time since treatment completion: Meyer & Kieran (2002) observed an increased prevalence of depression in survivors who had been off treatment for less than 1 year compared to those who had been off treatment between 1 and 5 years. Unfortunately, they did not report whether this was a statistically significant observation, but other studies found no significant association between time since completion of treatment and measures of either global or specific emotional QOL (Beebe et al., 2005; Holmquist & Scott, 2002). However, Meeske et al. (2004) reported a quadratic association between physical QOL and time since treatment completion such that

overall physical QOL and levels of fatigue were better for those off treatment for less than 12 months, than for those currently receiving treatment, or those off treatment for more than 12 months. Whilst treatment is ongoing, the survivors' physical functioning will be compromised due to the side-effects of the various treatment procedures, and it is unsurprising that levels of dissatisfaction related to fatigue and physical difficulties are high at this stage. In the months following treatment completion, there is likely to be some improvement in physical functioning, and the survivor is likely to be aware of this improvement and therefore there may be a decrease in levels of dissatisfaction. However, as time goes on, the rate of improvement will tail off, and the survivor will eventually arrive at a more stable level of physical functioning. At this point, if the survivor perceives this level as being unsatisfactory, they may report their physical difficulties as being more problematic for them. If this were the case, then it might be anticipated that other domains of QOL would follow a similar pattern, and this was indeed what was found by Meeske et al. (2004) when they considered a composite score of emotional, social and school functioning. At a later stage, it might be that there is further fluctuation in QOL as the survivor becomes better adapted to their level of ability. If such a non-linear relationship exists, it is unsurprising that other studies that have looked simply for a linear association have not found significant results. At the moment there are no longitudinal studies investigating this and data assessing QOL at multiple time-points are required before conclusions can be drawn.

6.5.4 Other factors

Gender: Poggi et al. (2005a) found that males scored significantly higher (i.e. worse) than females on a measure of overall emotional problems. However, as no other study

found a gender effect (Beebe et al., 2005; Bhat et al., 2005; Ribi et al., 2005) and this was the only significant association out of a large number tested by Poggi et al., it is possible that this result arose from a type I error.

Neuropsychological Functioning: Levisohn et al. (2000) noted that all patients in their sample who had affective difficulties also had some form of cognitive deficit. A small sample size prevented any meaningful conclusions being able to be drawn from this but several other studies have also investigated the links between neuropsychological functioning and elements of QOL.

Poggi et al. (2005a) investigated possible associations between various elements of emotional QOL and intellectual functioning (in terms of verbal, performance and full-scale IQ scores). The data were analysed both considering the sample as a whole (see Table 4 for significance of associations) but also with the sample split into three age groups. Both sets of analyses came up with a variety of significant associations, with more than would be expected to occur purely as a result of type 1 error, suggesting a link between some aspects of intellectual functioning and emotional QOL. Of particular note was the finding that FIQ, PIQ and VIQ were all significantly associated with attention problems and hyperactivity, a finding supported by Holmquist & Scott (2002).

Two studies looked specifically at the impact of verbal skills on emotional QOL. Carey et al. (2001) used several measures of verbal skills, and having used these to develop a single composite verbal ability score found no evidence of an association with levels of either internalising or externalising problems. However, Holmquist &

Scott (2002) used more specific measures and found that long-term verbal memory problems accounted for a substantial proportion (52%) of the variance in internalising behaviour problems.

There are several possible explanations for these findings. Brain damage resulting from the tumour and treatment could cause a decrease in intellectual abilities which in turn could impact upon the QOL of the survivor. For example, a child who had previously been academically confident may need increased educational support at school, or even may have to drop back a year or attend a different school as a result of the intellectual difficulties, all of which could be associated with increasing feelings of frustration, embarrassment, and unhappiness. However, it is also possible that distress arising as a direct result of the cancer experience causes a drop in performance on neuropsychological tasks. Longitudinal data is required to determine the direction of these associations.

Other objective factors: Maddrey et al. (2005) reported that in spite of evidence suggesting significant impairment on several objective indicators of daily functioning (e.g. employment, ability to drive a car, dating history, and education), survivors reported QOL scores within a normal range.

Ribi et al. (2005) found no significant correlation between specific physical symptoms (e.g. alopecia and short stature) and QOL, and there did not appear to be an association between neurological impairment and QOL (Poggi, et al., 2005a). Poretti et al. (2004) looked at the links between objective and subjective descriptions of physical symptoms and whether or not participants felt that such symptoms affected

their QOL (i.e. SPI). Because of small sample sizes it was not possible to draw definitive conclusions, but they observed that some physical symptoms (such as obesity, facial nerve palsy, and strabismus) caused distress or limited QOL in a large proportion (>80%) of survivors, whereas others (e.g. short stature, frequent headaches, and seizures) were not so commonly associated with distress or impaired QOL. These results imply that certain physical symptoms are more likely to cause impaired QOL than others.

Psychological predictors: Only one study looked at what might be considered psychological (as opposed to objective or neuropsychological) predictors. Eiser et al. (2004) looked at parenting styles adopted in both illness-related and more general contexts. They distinguished between prevention-focused parenting (characterised by overly protective concern with potential mishaps and illness occurrence) and promotion-focused parenting (characterised by a focus on accomplishments, aspirations and eagerness in the face of opportunities) and found that the former parenting style was associated with lower QOL in survivors as reported both by child self- and parent proxy-reports. This was particularly true when prevention-focused strategies were adopted in general, everyday contexts. The parents of children treated for cancer face a difficult dilemma: on the one hand they need to encourage their child to participate in the activities expected of a healthy child but at the same time they wish to protect the child from injury and infection. These results may indicate that a promotion-focused parenting style is more desirable and leads to better QOL, but it is also possible that parents of children whose outcome following cancer is particularly bad tend to adopt a more prevention-focused style, and it is the poor outcome rather than parenting style that is truly associated with QOL.

7. SUMMARY AND CRITIQUE

A total of 23 studies investigating overall, physical, emotional and social aspects of QOL in survivors of paediatric brain tumours were reviewed. QOL was defined in a specific way so that studies were included if they elicited information regarding a) emotional difficulties or b) the subjective psychological impact (SPI) of the cancer experience on the individual.

Overall, it seems that survivors of paediatric brain tumours are at risk of a poorer QOL when compared to both healthy populations and survivors of other childhood cancers. BT survivors not only tended to report a poorer global QOL, but they were also at risk of high levels of specific difficulties including fatigue, distress related to physical status, and emotional difficulties resulting in psychiatric hospitalisation both in childhood and later on in adulthood. However, there was considerable discrepancy amongst findings and this was especially the case when considering the emotional domain of QOL. Methodological limitations of the studies reviewed are likely to account for some of the disparity between findings (see discussion in section 7.1), but there was also some evidence that certain subgroups of BT survivors were particularly vulnerable to poorer QOL.

Eleven studies included in the present review attempted to assess the role of an array of variables as predictors of poor QOL. Unfortunately, few studies examined the same hypothesised associations and those that did often had discrepant results making interpretation difficult. There was some evidence that certain treatment- and time-related factors were associated with poorer QOL. These included type of chemotherapy agent used, use of GHT, the requirement of a shunt, age at assessment,

time between diagnosis and assessment, and time between treatment completion and assessment, and there was also evidence that aspects of neuropsychological functioning were associated with poor QOL. Other variables such as tumour location, use of radiation, and treatment complications were typically found not to be related to QOL. Although studies provided some tentative explanations for the results that were observed, the methodological limitations of these studies, together with a general paucity of research in this field, make it very difficult to interpret the findings regarding predictors, and substantially more research is needed before meaningful conclusions can be drawn.

A summary of these limitations is presented below in order that forthcoming studies can seek to minimise such shortcomings. This is followed by a discussion highlighting possible areas of focus for future research initiatives.

7.1 Methodological Limitations

7.1.1 Lack of theory-driven research

One of the most significant problems apparent in the majority of studies included in the current review was the lack of a conceptually-driven basis for the analyses, and this was a problem also noted by Fuemmeler et al. (2002) in their earlier review. For example, several studies tested whether tumour location was associated with different aspects of QOL but only Beebe et al. (2005) developed any basic hypotheses regarding the anticipated impact particular locations would have on QOL. To some extent this lack of theorising is understandable: there is very little research that exists in this area, and the relationship between specific locations and various QOL-related outcomes is likely to be highly complex. Therefore, to some extent, a legitimate aim

for these studies is to attempt to generate hypotheses regarding potential associations rather than to test theories that have already been developed. However, the absence of even basic hypotheses makes it extremely difficult for researchers to determine how to categorise the variables that are being tested. All of these studies looked at tumour location in global terms (for example supratentorial versus infratentorial tumours) and without specific hypotheses regarding the anticipated outcome it is unsurprising that the majority of these studies did not pick up an effect. The conclusion that location does not impact on QOL is misleading and all that can legitimately be deduced is that location, when considered in such global terms, does not appear to account for QOL.

The lack of conceptually-driven research was not just restricted to studies investigating the role of tumour location as a potential predictor of QOL. Many studies did not propose explicit a priori hypotheses, and although the majority reflected "ad hoc" on possible explanations for their findings, they tended not to incorporate these within a wider theoretical framework. Without theoretical foundations to guide predictions, there is a temptation for studies to perform numerous correlational tests to see whether any of the variables measured are significantly associated. Whilst this may be helpful in terms of generating new hypotheses, such practices substantially increase the risk of obtaining type 1 errors, and although some studies adjusted for this (Bhat et al., 2005; Carey et al., 2001) many did not appear to do so.

7.1.2 Study design

Apart from Ross et al.'s population-based study, all the research papers reviewed adopted a cross-sectional design. Similarly, only one study featured in Fuemmeler et

al.'s review utilised a longitudinal design. Whilst cross-sectional studies provide a wealth of information and are quicker and cheaper to run, they are unable to establish direction of causality, and as such it is hard to determine predictors of poor QOL in this population. Such information would be highly valuable in determining where to direct limited NHS resources. However, longitudinal studies in this population are difficult to conduct as sample sizes at initial assessment have to be large in order that attrition rates due to mortality or other factors do not prevent meaningful statistical analyses at follow-up. A further problem is that only eight studies included comparison groups, and although many of the others were able to use normative data this has previously been found to be problematic as it may overestimate the rates of some psychological adjustment problems (Fuemmeler et al., 2002).

7.1.3 Measures

In Fuemmeler et al.'s review, almost half of the studies included used assessment techniques that did not include validated measures. Things have improved somewhat since then and in the present review only a few studies failed to include validated measures (e.g. Martinez-Climent et al., 1994; Pompili et al., 2002). However, a substantial number of studies used instruments, such as the CBCL, that have strong reliability and validity for use with healthy children, but whose validity has been questioned when used with paediatric populations. The high rates of physical deficits in a brain tumour population could have resulted in confounded findings, particularly on somatisation items (Fuemmeler et al., 2002; Tedstone & Tarrier, 2003).

Furthermore, although many studies utilised measures that have both parent proxy- and child self-report versions of the measure, several of these chose only to gather

data from a single informant. Even when information from more than one source was obtained, it was not always made clear in the results whether it was the parent-rating, child-rating or both that was found to be associated with a given factor, making interpretation difficult.

7.1.4 Heterogeneity of samples

There was extensive variability in illness-, treatment- and time-related factors both within and between samples making it difficult to make cross-study comparisons and draw conclusions. Some studies assessed children still receiving treatment (Meeske et al., 2004) whereas others evaluated ten-year survivors (Maddrey et al., 2005). All studies looked at children who had been diagnosed under the age of 18 but the majority of studies had a broad range of ages at evaluation (the largest range being between 4 and 23 years old (Martinez-Climent et al., 1994)). The developmental stage of a child will affect the extent to which they are able to understand and make sense of their experiences, the coping strategies that they have at their disposal, the way in which emotional difficulties manifest, and what is defined as constituting a good quality of life. Therefore, including such wide age ranges of survivors within a single sample can be problematic, and future studies aiming to reduce the heterogeneity of samples in terms of developmental stage may help to elucidate a clearer picture.

7.1.5 Statistical limitations

Several statistical problems were evident. Although some studies gave good descriptions and rationales for the statistical tests used, others did not, making it difficult to ascertain the validity of the conclusions that were being drawn. Many studies had small sample sizes and eight involved survivor group sizes of 20 or less,

making it hard to generalise findings or to determine whether observed associations (or lack of them) resulted from type I or type II errors. Recruitment of sizeable numbers of paediatric brain-tumour survivors can be difficult given the relatively low incidence and high mortality rates, and this is further compounded by the fact that children left with severe cognitive damage following tumour diagnosis and treatment are often excluded from research due to their difficulties. Whilst the use of multiple-sites can help researchers to access more survivors, such studies are expensive to conduct and there are additional problems. Multiple-sites could be used to obtain a more homogeneous sample with regards to a specific variable (for example tumour location), but such methodology increases heterogeneity on other variables (for example treatment protocols may vary between sites).

7.2 Areas for Future Research

There is an urgent need for a clear, coherent body of knowledge regarding the QOL of paediatric brain-tumour survivors. In particular, a good understanding of factors that are specifically associated with an increased risk of poor outcome would be invaluable in terms of informing clinical assessments and interventions, and determining a focus for the direction of resources. However, the scarcity of relevant research and inconsistencies between existing findings illustrates how far we are from establishing such an understanding at the present time.

7.2.1 Theory-driven research

As highlighted earlier, there is a pressing need for theory-driven research aimed at identifying the specific mechanisms which precipitate and maintain a reduced QOL in this population. At present the majority of studies investigating potential predictors

considered the role of objective variables (such as age at assessment, and level of neuropsychological functioning) in predicting QOL. The present review defines QOL from a more psychological perspective, focusing on the emotional domain of QOL, and the subjective psychological impact that brain tumour diagnosis and treatment has on a child's physical and social QOL. Taking this approach to QOL raises the possibility of using psychological theories to derive more psychologically-oriented hypotheses. The application of psychological theory to paediatric cancer populations has begun to be more prevalent in recent years (Barakat, Kazak, Meadows et al., 1997; Brown, Madan-Swain, & Lambert 2003; Kazak, Barakat, Meeske, & Christakis, 1997) but as yet there is virtually nothing that has been directed specifically to a brain tumour population and in the present review, only Eiser et al. (2004) took such an approach.

One such area that might be interesting to investigate would be that of coping styles. In the present review, studies that obtained both self- and parent proxy-reports of QOL showed that whilst there was significant correlation between their responses, parents tended to rate the survivors' QOL as worse than the survivors themselves (Eiser et al., 2004; Eiser et al., 2003; Poretti et al., 2004; Ribi et al., 2005). Some studies found that self-reported QOL was no worse than standards of QOL found in healthy populations, and it is possible that parents have a tendency to "amplify" problems, seeing things as worse than they really are. However, the finding that BT survivors are at increased risk of psychiatric hospitalisation (Ross et al., 2003) suggests that there is a genuine increase in levels of emotional difficulties, and it is therefore possible that the disparity between parent and survivor reports reflects a

tendency for survivors to under-report affective difficulties, rather than for parents to over-report them.

There is evidence that children with cancer typically report few affective difficulties, and, in some instances, report lower levels of emotional problems than are reported by healthy children. Different hypotheses have been proposed to explain this finding. Worchel, Nolan, Wilson et al (1988) suggested that the cancer patients mobilised denial in response to questioning about their emotional state, so that they had some awareness of increased emotional distress but refused to acknowledge it. In contrast, Canning, Canning, & Boyce (1992) suggested the actual absence, or attenuated awareness of emotional distress as part of a global "repressive-adaptive" personality style that has been found to be particularly prevalent in cancer survivors (Phipps & Srivastava, 1997). If it is assumed that personality traits are relatively stable qualities then this hypothesis suggests that a repressive personality profile may actually have a causal role in the development of cancer, and as such is highly controversial. Somewhat less contentious is the suggestion that cancer survivors may endorse a "blunting" attentional coping style which is a consciously avoidant method of coping that acts to limit attention to threatening or distressing stimuli, thus reducing patient exposure to some stressors (Phipps, Fairclough & Mulhern, 1995). These theories have yet to be applied to brain tumour survivors, and to do so may help to identify specific coping-related risk factors for poorer QOL.

Many of the studies included in this review have investigated problems at a global level (for example, looking at overall internalising difficulties rather than at a specific anxiety-disorder) and another area for future researchers is to try to apply

psychological theory to specific difficulties. For example, if the cognitive model of PTSD (Ehlers & Clark, 2000) is applied to this population, it could be hypothesised that particular styles of coping are associated with higher incidence of such problems and as a result a lower emotional QOL.

So far, the impact of familial factors on BT survivors' QOL remains largely unexplored. Eiser et al. (2004) found that prevention-focused parenting style was associated with poorer QOL in BT survivors, and Carlson-Green, Morris & Krawiecki (1995; included in Fuemmeler et al.'s 2002 review) reported that single-parent families and high levels of family stress were associated with increased levels of psychological problems in this population. Research investigating childhood survivors of other types of cancer have reported that greater levels of family support, lower levels of perceived familial chaos, and increased family satisfaction and communication have all been associated with improved QOL (Brown et al., 2003; Pelcovitz, Libov, Mandel et al., 1998; Kazak et al., 1997) and it seems reasonable to anticipate that such associations might also be found within a BT population. It would also be of interest to examine the reciprocal relationship between the QOL of BT survivors and that of their family members.

One area where there has been conspicuously little research focus is on the social domain of QOL for this population. This is largely down to the definition of QOL used in this review and, as such, highlights the need for more investigation regarding the extent to which social deficits observed in this population, and other objective factors (such as physiological sequelae of tumour and treatment, or time off school) impact on the child's own perception of the quality of their life. Qualitative research

in particular could be very helpful in generating hypotheses relating to this area of QOL.

7.2.2 Longitudinal studies

With only a single longitudinal study identified by Fuemmeler et al. (2002), and none found in the present review, this is an obvious area of focus for future research efforts. The profile of QOL in paediatric BT survivors over time can only properly be understood by studies evaluating children at time of diagnosis, during treatment, and at ongoing follow-up intervals. Such studies would be able to determine risk-factors for poor QOL at various stages of the illness and recovery process, which could be invaluable in terms of informing treatment protocols and interventions.

7.2.3 Development of measures

At present there are only a few measures that have been designed specifically for the purpose of assessing psychological difficulties within a paediatric-cancer population. If indicators of psychological difficulties that have been designed for use with healthy children are used with BT samples, a major problem arises due to the significant overlap that exists between symptoms of psychological difficulty and the symptoms and side-effects that occur as a result of a brain tumour and the associated treatment. Future research efforts endeavouring to explore these issues further and develop more appropriate measures would be of great value.

8. CONCLUSION

The diagnosis, treatment, and sequelae of paediatric brain tumours constitute a distressing and chronic life event which impacts on the QOL of the survivor. QOL is a complicated construct and there is no universally agreed upon definition. A psychological perspective of QOL was adopted in the current review such that studies evaluating the emotional domain, or the subjective psychological impact of CNS-cancer on the physical and social domains of QOL were included. Overall it appears that paediatric brain-tumour survivors are at risk of a reduced QOL both when compared to population norms and to other paediatric cancer-populations. Various potential risk factors have been assessed but there is a lack of consistency between findings. This may in part reflect methodological limitations of the studies involved, but may also be due to important psychological mediating factors associated with increased risk of poor QOL that have yet to be identified. Future research efforts should be directed towards developing theory-driven studies aimed at developing the evidence-base in this area so that a better understanding of risk-factors for poor QOL in this population can be established.

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PART II: EMPIRICAL PAPER

Quality of Life in Paediatric Brain Cancer

ABSTRACT

The present study aimed to investigate the Quality of Life (QOL) of paediatric brain tumour survivors and the impact of tumour recurrence, neurological outcome and attentional coping style on QOL. Participants consisted of 52 survivors of paediatric brain tumours, aged 8-16, who completed the Paediatric Quality of Life Scale (Generic and Cancer modules) and the Child Behavioural Style Scale. Survivors' parents also completed the parent-proxy version of the Paediatric Quality of Life Scale. The results showed that survivors had significantly worse QOL than is typically observed in both healthy and chronically ill paediatric populations. Tumour recurrence was not found to impact upon the QOL of the survivor, but poorer neurological status and the increased utilisation of monitoring attentional coping strategies were associated with decreased QOL. An interaction effect between tumour histology and the use of blunting attentional coping strategies was observed such that, for those with craniopharyngioma or medulloblastoma tumours, increased use of blunting strategies was associated with a decrease in QOL. These results highlight the role of subjective psychological variables in moderating the impact of objective outcome on QOL. Further research investigating possible interactions between subjective and objective factors is warranted.

INTRODUCTION

Over the last fifty years, dramatic improvements in the treatment and care of children with cancer have resulted in steadily increasing survival rates and, today, over 70% of children diagnosed with cancer are alive and disease-free ten years after first being diagnosed (Dolgin, Somer, Buchvald & Zaizov, 1999; Fuemmeler, Elkin & Mullins, 2002; Langeveld, Stam, Grootenhuis & Last, 2002; Stiller, Bunch & Lewis, 2000; UK Childhood Cancer Research Group, 2004).

However, survival comes at a cost. The damage done by the cancer itself, together with lengthy and frequently aversive diagnostic, treatment and follow-up procedures can result in a wide range of physiological and psychological sequelae (Armstrong & Horn, 1995; Langeveld et al., 2002). This is particularly true for cancers of the brain. The critical location of a brain tumour together with the iatrogenic effects of treatment can have a profound effect on physical, neurocognitive and psychosocial outcomes which in turn can impact upon the health-related Quality of Life (QOL) of the survivor (Fuemmeler et al., 2002; Moore, 2005; Mulhern, Hancock, Fairclough & Kun, 1992; Patenaude & Kupst 2005).

Brain tumours are the second most common type of paediatric cancer and account for approximately one quarter of all childhood cancers. With a 5-year survival rate of nearly 70% (Stiller, Quinn & Rowan, 2004), QOL in this population is an important construct as it provides information about the experiences of these survivors and can be used as a basis for the development and optimization of treatments (Calaminus & Kiebert, 1999).

QOL is a complicated concept and there is currently no universally accepted definition. The World Health Organisation (WHO) defines QOL as "individuals' perceptions of their position in life in the context of the culture and value system in which they live and in relation to their goals, standards and concerns" (WHO, 1993). This definition places emphasis on the importance of the individual's subjective experience. To determine the QOL of cancer survivors, some researchers have utilised purely objective indicators of QOL (e.g. visual and hearing abilities or type of school attend; Jenkin, Danjoux & Greenberg, 1998). Whilst such methods undoubtedly provide valuable information regarding the objective circumstances that survivors face, they do not describe the survivors' perceptions of their situation and as such do not measure QOL as defined by WHO. Subjective measures may either elicit an individual's subjective description of the situation (e.g. "I have a scar as the result of my operation") or the impact that this situation has on the individual (e.g. "my scar is a sign of my victory in a battle with cancer, I am proud of it"). Arguably it is the latter that affords the truest portrayal of QOL, rather than the subjective description, and it is this definition of QOL that is adopted in the present study.

QOL is generally thought to be a multidimensional concept, but the domains that are considered to be of key importance depend, in part, on the population in question. With an interest in assessing QOL in children with health difficulties, Varni and colleagues developed The Paediatric Quality of Life Scale (PedsQL; Varni, Katz, Seid et al., 1998; Varni, Seid & Kurtin, 2001) specifically for use with a paediatric population. Having reviewed the relevant literature, they concluded that the domains of physical, emotional, school and social functioning were relevant to all children with health difficulties and developed the PedsQL generic core scale to measure

these dimensions of QOL. However they also felt that there were certain domains of relevance to particular disorders, and developed illness-specific modules accordingly. Those domains that they considered to be most relevant to the experience of childhood cancer included pain, nausea, procedural anxiety, treatment anxiety, illness-related worry, cognitive problems, perceived physical appearance and communication.

Matters are somewhat complicated when trying to measure QOL in children. Younger children or children who have been left cognitively impaired following cancer diagnosis and treatment may not be able to answer questions about their experiences, and therefore it may be necessary to use parent-proxy reports to try to determine the impact that particular experiences are having on the child (Calaminus & Kiebert, 1999). Tao & Parsons (2005) highlight the value of parent-proxy reports in paediatric brain tumour populations, but remind the reader that correlations with survivor self-reports are modest and that certain domains (e.g. physical functioning) tend to be more highly correlated than others (e.g. emotional functioning). Therefore studies assessing QOL in paediatric brain tumour survivors should ideally collect both parent-proxy and survivor-self reports although in practice this is not always viable (Tao & Parsons, 2005; Upton, Eiser, Cheung et al., 2005).

A number of studies have investigated QOL in survivors of paediatric brain tumours and the evidence generally suggests that brain tumour survivors have significantly worse QOL than both healthy controls and survivors of other paediatric cancers (Bhat, Goodwin, Buwinkle et al., 2005; Eiser, Eiser & Greco, 2004; Eiser, Vance, Glaser et al., 2005; Eiser, Vance, Horne et al., 2003; Poretti, Grotzer, Ribi, Schonle,

& Boltshauser, 2004; Ross, Johansen, Dalton et al., 2003; Weissenberger, Dell, Liow et al., 2001). However, there are considerable discrepancies between research findings and whilst this may be partially due to methodological limitations and variations between studies, it also appears to be the case that some survivors are particularly at risk for impaired QOL. This is an area of important research focus: if risk factors associated with poor QOL can be identified then resources may be directed towards those who are particularly vulnerable and the impact of such risk-factors can be minimised.

Several studies have attempted to address this issue, and there is preliminary evidence that various treatment- and time-related parameters (including the type of chemotherapy agent used, use of GHT, the requirement of a shunt, age at assessment, time between diagnosis and assessment, and time between treatment completion and assessment) may be associated with survivors' QOL (Bhat et al., 2005; Eiser et al., 2005; Meeske, Katz, Palmer, Burwinkle & Varni, 2004; Poggi, Liscio, Galbiati et al., 2005). However, the paucity of research in this field, together with the methodological limitations of the existing studies makes it very difficult to interpret the findings regarding predictors, and substantially more research is needed before meaningful conclusions can be drawn.

One illness-related variable that has yet to be fully explored is that of tumour recurrence. It might be anticipated that with each relapse, a child is at risk of additional damage to the structures of the brain (both from the tumour itself and subsequent treatments), exposure to further frightening and aversive treatments, additional time spent in hospital, and a poorer long-term prognosis. As a result, the

child may experience frustration following a decline in abilities, heightened anxiety regarding the risk of death, increased fear surrounding the likelihood of future painful treatments, and further time away from peers and friends leading to an increase in social anxiety, all of which are likely to impact on the QOL of the survivor.

To date, no studies have investigated the impact of tumour recurrence on paediatric brain tumour survivors' QOL per se, although Copeland, DeMoor, Moore, & Ater (1999) investigated the impact of recurrence on emotional functioning in this population. Somewhat surprisingly they found no evidence of an association, but this may have been due to the small sample size (n=19) that was employed. The present study aims to evaluate the effect of tumour recurrence on QOL within a paediatric brain tumour population, and it is hypothesised that recurrences will be associated with poorer QOL.

Most research exploring potential predictors of QOL in paediatric brain tumour survivors has focused on the role of objective variables (such as tumour location, age at diagnosis, and neuropsychological outcome). Objective variables are important: they provide a description of the situation faced by survivors, and it seems reasonable to assume that the poorer the situation is (for example, the more severe the neurological impact of the tumour), the higher the chances are that it will impact on the QOL of the survivor. In other words the objective variable may act as a contextual predisposing factor. However, it is important to remember that even when faced with the worst imaginable stressors, people do not always react in the same way, and it seems sensible to propose that whilst the objective severity of the

situation faced by a paediatric brain tumour survivor may impact on their QOL, this impact will be moderated by subjective factors that affect the appraisal of, and response to, the situation.

One such subjective variable for which the impact on health-related outcome has received attention over the years is that of coping style. Various psychological models of coping (e.g. Lazarus & Folkmans' transactional model, 1985; Miller & Schnoll's cognitive-emotional model, 2000) have proposed that specific coping styles have a "buffering" effect on the impact of health-related stressors. The impact of coping on psychological adjustment has been investigated in a range of populations (e.g. breast cancer survivors: Schnoll, Harlow, Stolbach & Brandt, 1998; women who have had an abortion: Major, Richards, Cooper, Cozzarelli & Zubek, 1998). However, the impact of coping style with respect to QOL in a paediatric brain tumour population is, as yet, unexplored and the present study aims to use Miller & Schnoll's model to investigate this.

Miller & colleagues (Miller, 1995; Miller & Schnoll, 2000) considered two specific attentional coping styles that could be adopted when an individual is confronted with a health-threatening situation such as the diagnosis of cancer: "monitoring" (scanning for and magnifying threat cues), and "blunting" (distraction from and down-grading of threatening information).

They suggested that in low-threat situations, monitoring strategies enable an individual to effectively scan for health-related messages and this may improve adherence to medical recommendations, whereas blunting strategies may have the

opposite affect. However, they proposed that as the threat-level grows, the utilisation of monitoring strategies to actively seek out, amplify and focus on threatening aspects of risk information results in a heightened sense of their own vulnerability and risk, resulting in increased anxiety and depression, whereas the adoption of blunting strategies would have a protective effect.

This model has been tested in relation to a number of high-threat health situations (including cardiac catheterization, colposcopy, and cancer treatments) and an increasing ratio of monitoring to blunting strategies adopted has been found to be associated with increasing levels of depression and anxiety, physiological tension and pain during and following treatment procedures and, as such, may be considered to have a negative impact on QOL (Davis, Maguire, Haraphongse & Schaumberger, 1994; Lerman, Rimer, Blumberg et al., 1990; Miller, Buzalgo, Simms, Green & Bales, 1999; Miller & Mangan, 1983; all cited in Lewis & Haviland-Jones, 2000).

Despite improvements in treatment over the last few decades, paediatric cancer remains a high-threat health situation. It therefore seems logical to extend the attentional coping style theory to this population, but to date, very few studies have done this and none have looked specifically at brain tumour survivors. In the paediatric cancer studies, there is evidence that cancer survivors endorse higher levels of blunting than healthy controls (Phipps, Fairclough & Mulhern, 1995; Phipps & Srivastava, 1997), and that increased use of monitoring strategies is associated with increasing emotional dysfunction (Phipps & Srivastava (1997), but studies failed to find an association between the increased use of blunting strategies and emotional wellbeing (Phipps, Fairclough, Tyc & Mulhern, 1998). Although

originally conceived as opposite ends of the same continuum, these findings highlight the importance of considering blunting and monitoring separately as they may be distinct constructs. If blunting and monitoring were poles of a single continuum, it would be anticipated that they would be highly negatively correlated but Phipps et al. (1995) found a small but significant positive correlation between levels of blunting and monitoring strategies adopted by paediatric cancer survivors and hypothesised that this reflected the adoption of a general "coping effort".

The present study aims to investigate the degree to which monitoring and blunting strategies are adopted in a paediatric brain tumour population and the impact of these strategies on the QOL of the survivor. In line with the attentional coping style model, it is hypothesised that the increased use of monitoring strategies will correspond to reduced QOL, and increased blunting strategies will correspond to improved QOL. Furthermore, it is proposed that the impact of objective functional outcome (as measured by the severity of neurological outcome), will be moderated by attentional coping style such that increased use of monitoring strategies will amplify the impact of poor neurological status on QOL, and increased use of blunting strategies will reduce it.

Therefore, in total the following 7 research hypotheses will be investigated:

1. Survivors of paediatric brain tumours will report a worse QOL than healthy children (when compared to standardised normative data), both on parent-proxy and child self-reports.

2. Child self-report and parent-proxy reports of survivors QOL will be correlated.

3. QOL will be reduced in survivors who have experienced tumour recurrences when compared to those who have not.

4. Survivors will endorse significantly higher levels of blunting strategies than healthy children (when compared to standardised normative data).

5. Attentional coping style will be associated with QOL. Specifically, higher levels of blunting will be associated with better QOL, and higher levels of monitoring will be associated with a poorer QOL.

6. The neurological status of the survivor will be associated with QOL such that the worse the neurological status, the poorer the survivor's QOL.

7. The impact of the (objective) neurological status of the survivor on their (subjective) QOL will be moderated by coping style, such that monitoring will amplify the impact of poor neurological status on QOL, and blunting will reduce it.

METHOD

Ethical considerations

A research proposal, detailing the rationale behind this research and the methods intended to be used, was submitted to and approved by the Great Ormond Street Hospital for Children NHS Trust/Institute of Child Health Research Ethics Committee. Copies of the relevant approval letters are provided in Appendix 1.

Participants

This study was conducted in conjunction with another piece of research (Bruce, 2006) and as such all participant recruitment and data collection was done jointly with another researcher. Participants for this study were recruited from Great Ormond Street Hospital, London. A list was formed of all children who had been diagnosed and treated for brain tumours between 1996 and 2004 who met all of the following inclusion criteria: (1) child aged over four-years old at time of diagnosis; (2) child aged between 8 and 16 years old at time of participation; (3) child had completed treatment between 6 months and 7 years prior to participation and was currently disease-free; and (4) there was a parent involved in the child's care during diagnosis and treatment.

A total of 140 children and their parents met the research criteria and were approached via one of two recruitment methods (see procedure section), and 52 survivors and 52 parents were recruited. Of these, 50 parent-child dyads provided QOL data, 1 child provided QOL data where the parent QOL data were unavailable, and 1 parent provided QOL data where the child QOL data were unavailable.

Non-participants did not differ significantly from participants with respect to gender ($\chi^2(1)=1.80$, $p=0.18$) or age at assessment ($t(119)=-0.07$, $p=0.95$). Sample characteristics of participants are outlined in Table 1. Please note that this table is an adapted version of that presented in an associated paper by Bruce (2006).

Procedure

Participants were enlisted using two recruitment strategies: one for those who had a scheduled appointment at the hospital within six months, and one for those who did not. For the latter group, recruitment packs were sent to survivors and their families. Packs consisted of a recruitment letter explaining the purpose of the study, information sheets both for the survivor and for their parent/guardian, questionnaire batteries for both survivor and parent, and a stamped addressed return envelope (see Appendices 2-5). Families who did not respond within three months of this initial approach were sent a reminder letter and an additional recruitment pack.

For those survivors who had a check-up appointment scheduled at the hospital, they and their families were approached directly and invited to participate when they attended their appointment. Families willing to participate were given recruitment packs and were able to choose whether they wished to complete the questionnaire batteries in the clinic or at home (appropriate return envelopes were supplied). Families who agreed to take recruitment packs home were followed-up by phone call if their questionnaire packs were not returned within two months.

Table 1: Sample Characteristics of Childhood Brain Tumour Survivors

Disease and demographic information	Frequency	Percentage
Sex of survivor		
Female	29	55.8
Male	23	44.2
Sex of participating parent		
Female	46	88.5
Male	6	11.5
Ethnicity		
White	44	84.6
Asian	4	7.7
Mixed race	3	5.8
Other	1	1.9
Brain tumour diagnosis		
Astrocytoma	20	38.5
Craniopharyngioma	8	15.4
Ependymoma	6	11.5
Medulloblastoma	5	9.6
Mixed Glioma	4	7.7
DNT	5	9.6
Other	4	7.7
Location		
Infratentorial	20	38.5
Supratentorial	32	61.5
Number of recurrences		
None	38	73.1
1	7	13.5
2	5	9.6
3	2	3.8
Treatment type		
Surgery only	18	34.6
Chemotherapy only	1	1.9
Radiotherapy only	2	3.8
Chemotherapy and radiotherapy only	2	3.8
Surgery and chemotherapy only	2	3.8
Surgery and radiotherapy only	22	42.3
Surgery, chemotherapy and radiotherapy	5	9.6
Use of GHT		
Yes	13	25.0
No	39	75.0
Shunt fitted		
Yes	7	13.5
No	45	86.5
	Mean (S.D)	Range
Age/Time		
Age of child at diagnosis, years	8.1 (2.73)	4 – 13
Age of child at assessment, years	12.7 (2.70)	8 – 16
Age of parent at assessment, years	42.1 (5.02)	31 – 53
Time since diagnosis, years	4.16 (2.11)	1-9
Time since treatment completed, years	3.09 (2.63)	0.5-11.1

All of those approached were offered assistance by a researcher to complete the questionnaire packs and to talk through their experiences with a trainee clinical psychologist if they wished. Of the 140 potential participants, 27 were approached at scheduled hospital appointments and of those 74% (n=20) took part in the study. The remainder of the potential participants were approached via postal recruitment packs and a total of 28% of those (n=32) were successfully recruited. All families who took part in the research were sent a card thanking them for their participation.

Measures

Participant characteristics: Hospital databases were used to obtain data regarding survivor gender, ethnicity, tumour histology, tumour location, number of recurrences, treatments utilised, use of GHT, insertion of a shunt, age of child at diagnosis, age at assessment, and time since diagnosis.

Objective Neurological Status: The Neurological Severity Score (NSS; Ater, Moore, Francis et al., 1996) was utilised as a method of rating the objective neurological status of survivors (see Appendix 6). The NSS includes scores for four time-periods (1) events prior to diagnosis; (2) pre-existing neurological deficits or previous neurological insults; (3) perioperative events including intraoperative complications and events within 1 week postoperatively; and (4) postoperative events secondary to surgery or complications of surgery that persisted beyond 1 week after surgery. Events are each scored on a range from 0 to 3 depending on severity, and for complicated courses points can be awarded for each event that occurs within each time-period.

Although extensive reliability and validity studies have yet to be conducted, the NSS has been found to correlate significantly with neuropsychological abilities (including visual-spatial skills, memory, attention and performance IQ; Ater et al., 1996; Moore, 2005). As it can be rated using information from medical notes, the NSS provides a good alternative to conducting lengthy neuropsychological tests with participants and is considered to be a good tool for investigating the (neuro)-psychological impact of brain tumours and their treatment (Klimo & Kestle, 2005). Information for the scoring of the NSS was obtained from hospital databases and scoring was conducted by a specialist oncology nurse.

Quality of Life: The Paediatric Quality of Life Inventory (PedsQL; Varni, Katz, Seid et al., 1998; Varni, Seid & Kurtin, 2001) is a standardised instrument for measuring health-related quality of life in children and adolescents aged 2 to 18. There are four different versions of the PedsQL corresponding to four distinct age-groups (2-4, 5-7, 8-12, 13-18). The present study used the latter two versions, and administered survivor and parent-proxy versions of the PedsQL to measure QOL. Both the generic core scale (PedsQL-G) and the cancer-specific scale (PedsQL-C) were administered. The generic core scale consists of 23 items, and produces a total QOL score and 4 subscale scores: physical QOL, emotional QOL, social QOL, and school-related QOL. The cancer module consists of 27 items, and produces a total score and 8 subscale scores (pain, nausea, procedural anxiety, treatment anxiety, worry, cognitive problems, perceived physical appearance and communication). All items are rated on a 5-point Likert scale indicating the frequency with which certain experiences (e.g. difficulty running) have been a problem for the survivor in the preceding month. The PedsQL generic scale has been shown to have good internal consistency both for

parent proxy and self-reports on the total QOL score (α=0.90 and 0.88 respectively), and on subscale scores (average α=0.80 and 0.74 respectively; Varni et al., 2001). Similarly, the cancer scale also has good internal consistency for parent and self-reports (average α=0.87 and 0.72 respectively; Varni, Burwinkle, Katz, Meeske, & Dickinson, 2002).

Attentional Coping Style: The Children's Behavioural Style Scale (CBSS; Miller, Roussi, Caputo, & Kruus, 1995) was used to assess monitoring and blunting coping styles. The CBSS consists of four stress-inducing scenarios (e.g. "you are in a class at school. The teacher comes over to you and tells you the head teacher wants to see you at break"). Each scenario is followed by eight potential responses and the child is asked to identify whether or not they would adopt each of these responses in the given scenario. Four responses are representative of monitoring strategies (e.g. "think about what the head teacher did to other kids") and four are blunting-type responses (e.g. "think about other things to get your mind off the head teacher"). The numbers of blunting responses endorsed are summed to derive a blunting score (ranging from 0-16) and similarly a monitoring score is also computed. The CBSS has been shown to yield good internal consistencies (monitoring: 0.85; blunting: 0.77) in a paediatric oncology sample (Phipps & Srivastava, 1997).

RESULTS

Preliminary analyses were conducted to examine interval data with respect to distributional assumptions for parametric analysis. The PedsQL "total generic scale" and "total cancer scale" QOL scores (parent and child) met assumptions for the use of parametric statistics, as did scores on the CBSS (both blunting and monitoring subscales) and NSS, and therefore parametric tests were adopted to examine associations between these variables. However, subscale QOL scores could not be assumed to be approximately normally distributed, and therefore non-parametric tests were adopted when considering these subscales. The exception to this was when mean observed subscale scores were compared with standardised data, and when the survivor and parent-proxy mean subscale scores were compared. In these cases, although the observations themselves were not normally distributed, it was assumed that the distribution of the means would be approximately normal given the relatively large sample size (n=51), and thus parametric t-tests were adopted (Central Limit Theorem: Rice, 1995).

The results are organised into three sections: (i) summary of demographic and illness variables; (ii) QOL in paediatric survivors of brain tumour; (iii) predictors of QOL.

Demographic and Illness Variables

Characteristics: Sample characteristics are presented in Table 1. There were similar numbers of male (n=23) and female (n=29) survivors although the majority of parents who provided proxy information were female (n=46). Most survivors were white (n=44). There was a variety of histological diagnoses, the most common being astrocytoma (n=20). Of the tumours, 38.5% (n=20) were located infratentorially (i.e.

in the lower part of the brain). The most common location of infratentorial tumours was the posterior fossa, but other locations (e.g. brainstem) were also observed. Supratentorial tumours (i.e. those in the upper part of the brain) were found in 61.5% (n=32) of participating survivors. Common supratentorial locations included the cerebral hemispheres, third ventricle and suprasellar regions. Thirty-eight patients had experienced no recurrence of the tumour, but 14 had experienced at least one relapse with 2 children experiencing 3 recurrences. Most survivors had been treated either with surgery alone (n=18) or with a combination of surgery and radiotherapy (n=22), although all treatment combinations of surgery, chemotherapy and radiotherapy were observed. Seven children (13.5%) had required a shunt to be fitted, and 13 children (25%) were prescribed Growth Hormone Treatment (GHT). The mean age at diagnosis was 8.1 years and mean age at time of assessment was 12.7 years. Mean time since diagnosis was 4.16 years.

Associations between demographic and illness variables and QOL: Significant associations between various demographic and illness variables and total or subscale PedsQL scores were tested for using one-way analysis of variance (ANOVA; for total scores) and Kruskal-Wallis tests (for subscale scores). Due to the number of tests involved, significance was set at $p<0.01$ to reduce the probability of type 1 error. Where significant effects were found, post-hoc tests were conducted to identify the specific nature of the effect.

Parental gender, ethnicity, tumour location, recurrence, treatment combination, use of GHT, presence of a shunt, age of child at diagnosis, age of child at assessment, age of parent at assessment, time since diagnosis and time since treatment

completion were not found to be significantly associated with QOL scores. However, tumour histology was found to be associated with parental responses on the PedsQL generic total score ($F(6, 44)=3.89$, $p=0.003$), physical functioning subscale score ($\chi^2(6)=18.94$, $p=0.007$), school functioning subscale score ($\chi^2(6)=18.37$, $p=0.005$), and nausea subscale score ($\chi^2(6)=20.21$, $p=0.003$), and with child responses on the PedsQL generic total score ($F(6, 44)=3.73$, $p=0.004$). The nature of these associations was such that those survivors with a diagnosis of either craniopharyngioma or medulloblastoma tended to have worse QOL than those with other histologies (possible explanations for this finding are discussed in later sections of this paper). Child gender was found to be associated with child responses on the procedural anxiety subscale score such that females tended to report higher levels of procedural anxiety than males ($U=178.50$, $p=0.006$). Therefore where appropriate, the effect of these variables was accounted for in following analyses.

QOL in paediatric survivors of brain tumour

Comparison of QOL scores with standardised norms: Child self-report and parent-proxy mean total and subscale scores obtained on the PedsQL generic scale were compared to UK population norms (child: total, M=83.89; physical, M=88.5; emotional, M=78.49; social, M= 87.65; school, M=78.97; parent-proxy: total, M=84.61; physical, M=89.06; emotional, M=78.28; social, M=86.82; school, M=81.52; Upton et al., 2005). Significant differences ($p<0.01$) were observed such that on all total and subscale scores, children with brain tumour were reported (by self-report and parent-proxy) as significantly worse than standardised norms. These results are presented in Table 2.

Table 2: Obtained scores on psychological variables, and comparisons with standardised normative data, and between survivor and parent-proxy reports.

	Experimental Data				Standardised norms[b]		Difference between experimental data and standardised norms			
	Survivors N=51 Mean (SD)	Parent-proxy N=51 Mean (SD)	Survivor and parent correlations[a]		Test of difference between survivor & parent means		Survivor Mean	Parent-proxy Mean	Survivor		Parent	
Psychological Variables			r/ρ	p-value (2-tailed)	t-score	p-value (2-tailed)			t-score	p-value (2-tailed)	t-score	p-value (2-tailed)
PedsQL-G: (possible range 0-100)												
Total	**69.78(20.06)**	**67.43(20.85)**	**r=0.83**	**0.000***	**t(49)= -1.24**	**0.220**	**83.89**	**84.61**	**t(50)=-5.02**	**0.000***	**t(50)=-5.88**	**0.000***
Physical	71.14(27.02)	69.79(28.49)	ρ=0.86	0.000*	t(49)= -0.51	0.612	88.51	89.06	t(50)=-459	0.000*	t(50)=-4.83	0.000*
Emotional	69.51(23.33)	66.57(21.55)	ρ=0.52	0.000*	t(49)= -0.98	0.333	78.49	78.28	t(50)=-2.75	0.008*	t(50)=-3.88	0.000*
Social	72.75(22.50)	69.80(24.00)	ρ=0.72	0.000*	t(49)= -0.96	0.343	87.65	86.82	t(50)=-4.73	0.000*	t(50)=-5.06	0.000*
School	64.90(21.71)	62.16(20.86)	ρ=0.72	0.000*	t(49)= -1.23	0.227	78.87	81.52	t(50)=-4.59	0.000*	t(50)=-6.63	0.000*
PedsQL-C: (possible range 0-100)												
Total	**69.52(17.38)**	**70.56(15.30)**	**r=0.72**	**0.000***	**t(49)= 0.61**	**0.546**	-	-	-		-	
Pain	75.49(31.91)	76.23(26.84)	ρ=0.56	0.000*	t(49)= 0.33	0.740	-	-	-		-	
Nausea	80.20(19.67)	82.84(18.15)	ρ=0.59	0.000*	t(49)= 0.92	0.361	-	-	-		-	
Procedural anxiety	57.68(36.32)	59.31(38.32)	ρ=0.80	0.000*	t(49)= 0.67	0.509	-	-	-		-	
Treatment anxiety	76.96(26.44)	76.80(24.85)	ρ=0.60	0.000*	t(49)=-0.31	0.756	-	-	-		-	
Worry	73.83(23.45)	77.12(23.50)	ρ=0.47	0.001*	t(49)= 1.28	0.208	-	-	-		-	
Cognition	64.80(21.54)	61.96(20.42)	ρ=0.59	0.000*	t(49)= 0.24	0.814	-	-	-		-	
Perceived physical appearance	61.11(26.96)	61.93(24.68)	ρ=0.52	0.000*	t(49)= 0.85	0.398	-	-	-		-	
Communication	64.27(27.23)	67.81(31.71)	ρ=0.57	0.000*	t(49)=-0.99	0.328	-	-	-		-	
CBSS: (possible range 0-16)												
Monitoring	**8.7 (3.50)**	-	-		-		**8.48**	-	**t(51)=0.437**	**0.664**	-	
Blunting	**6.6 (3.25)**	-	-		-		**3.92**	-	**t(51)=5.895**	**0.000***	-	
NSS: (possible range: [0, ∞))	**2.60 (1.94)**											

*=p<0.01; p-values given are for2-tailed tests.

[a] = spearman's rho (ρ) correlations are used for all associations except PedsQL-G total, and PedsQL-C total where Pearson's r is adopted. Correlations are performed using n=50 parent-survivor dyads.

[b] = standardised norms for the PedsQL are from Upton, Eiser, Cheung et al. (2005). Those for the CBSS are from Phipps, Fairclough, & Mulhern (1995).

Note: All QOL total and subscale scores are rated on a scale between 0 and 100, where better QOL is indicated by a higher score(e.g. the higher the score on the pain subscale, the less pain is experienced).

Comparison of parent proxy and self-report QOL scores: Significant positive correlations ($p<0.001$) were observed between child self- and parent proxy-report scores on all of the PedsQL total and subscales scores (see Table 2). Scatterplots of equivalent child and parent PedsQL scores were drawn. For those subscales where histology or child gender had been found to be associated with QOL, discrete markers indicating either histological tumour type or gender were utilised, but the correlations observed did not appear to be affected by these factors.

Appropriate paired sample tests were used to test for significant differences between child and parent proxy-reports on the PedsQL generic and cancer total and subscale scores (see Table 2). No significant differences were observed although parents tended to rate survivors' QOL worse than survivors themselves on the generic scale scores, but for the reverse to be the case on the majority of the cancer scale scores.

Predictors of QOL

The impact of tumour recurrence on QOL: Fourteen of the 52 children had experienced a recurrence: 7 children had a single recurrence, 5 had 2 recurrences, and 3 children had 3 recurrences. Due to small numbers, it was not possible to test the impact of increasing numbers of recurrences on QOL, so all children who had experienced one or more recurrences were pooled together and a comparison was made with children who had not had any tumour recurrence.

Students t-tests were used to compare children who had experienced recurrence with those who had not on the PedsQL generic total, and cancer total scores (parent and child) and these are shown in Table 3. Contrary to expectations, there were no

significant differences observed on these total scores. Mann-Whitney U tests were used to make comparisons on the PedsQL subscale scores, and these too failed to reach significance. This remained the case even when tumour histology and child gender were accounted for in the subscales where those variables had previously been shown to have an impact. It is interesting to note however, that even though statistical significance was not achieved, the direction of the effect for the majority of mean QOL scores was such that children who had experienced at least one recurrence had poorer QOL than those who had not experienced recurrence.

Comparison of levels of blunting and monitoring endorsed with standardised norms: The current sample of paediatric brain tumour survivors endorsed significantly more blunting responses than standardised normative data from a) healthy children ($M=3.92$; $t(51)=5.90$, $p<0.01$) and b) paediatric oncology survivors ($M=4.75$; $t(51)=4.05$, $p<0.01$; Phipps, Fairclough & Mulhern, 1995). There were no significant differences in the utilisation of monitoring coping responses between the current sample and the aforementioned populations.

Association between attentional coping style and QOL: Table 4 shows correlations between QOL scores and levels of blunting and monitoring. There was little evidence of any association between attentional coping style and parent-proxy rated QOL, but this was not the case on the survivor reported QOL measures. As predicted, an increase in survivors' use of monitoring strategies was modestly but significantly ($p<0.01$) correlated with a decrease in QOL as measured by the total cancer scale score ($r=-0.440$, $p=0.001$), and several subscale scores (emotional, $\rho=-0.527$, $p<0.001$; procedural anxiety, $\rho=-0.528$, $p<0.001$; worry, $\rho=-0.372$, $p=0.008$;

Table 3: QOL comparisons between survivors who have experienced at least one recurrence versus those who have not.

	Child report Mean score		Difference		Parent report mean score		Difference	
	0 recurrence	≥1 recurrence	t-value/ U-value	p-value (2-tailed)	0 recurrence	≥1recurrence	t-value/ U-value	p-value (2-tailed)
PedsQL-Generic								
Total	**71.25(20.24)**	**65.47(19.67)**	**t=0.90**	**0.375**	**68.28(20.10)**	**64.97(23.61)**	**t=0.490**	**0.626**
Physical	72.53(27.68)	67.07(25.63)	U=208	0.397	70.23(28.84)	68.51(28.54)	U=230	0.704
Emotional	72.76(22.74)	60.00(23.27)	U=167	0.083	68.29(20.18)	61.54(25.36)	U=209	0.410
Social	73.29(22.34)	71.15(23.82)	U=232	0.744	71.32(23.67)	65.38(25.37)	U=216	0.498
School	65.66(23.05)	62.69(17.87)	U=229	0.688	62.11(19.51)	62.31(25.30)	U=243	0.931
PedsQL-Cancer								
Total	**71.27(16.46)**	**64.41(19.64)**	**t=1.23**	**0.223**	**71.83(14.07)**	**66.85(18.55)**	**t=1.01**	**0.315**
Pain	78.29(28.43)	67.31(40.68)	U=218	0.512	78.95(23.45)	68.27(34.84)	U=214	0.450
Nausea	82.76(17.62)	72.69(23.95)	U=179	0.134	82.50(18.91)	83.85(16.35)	U=245	0.956
Procedural anxiety	59.43(36.05)	52.56(38.09)	U=228	0.679	61.40(37.83)	53.21(40.62)	U=218	0.518
Treatment anxiety	82.02(24.39)	62.18(27.56)	U=139	0.015	77.41(24.27)	75.00(27.43)	U=232	0.734
Worry	77.25(20.28)	64.10(29.54)	U=180	0.175	80.92(17.43)	66.03(34.44)	U=197	0.266
Cognition	63.42(23.48)	68.85(14.46)	U=204	0.351	60.53(20.49)	66.15(20.43)	U=203	0.340
Perceived physical appearance	61.62(27,98)	59.61(24.73)	U=238	0.845	65.57(21.59)	51.28(30.59)	U=176	0.121
Communication	65.57(26.51)	60.46(30.02)	U=225	0.632	70.18(32.40)	60.90(29.73)	U=103	0.331

Note: All QOL total and subscale scores are rated on a scale between 0 and 100, where better QOL is indicated by a higher score(e.g. the higher the score on the pain subscale, the less pain is experienced).

Table 4: Associations between QOL and survivors' attentional coping style and neurological severity scores.

	Survivor			Parent-proxy report		
	Correlation with CBSS Blunting r/ρ p-value (2-tailed)	Correlation with CBSS Monitoring r/ρ p-value (2-tailed)	Correlation with NSS r/ρ p-value (2-tailed)	Correlation with CBSS Blunting r/ρ p-value (2-tailed)	Correlation with CBSS Monitoring r/ρ p-value (2-tailed)	Correlation with NSS r/ρ p-value (2-tailed)
PedsQL-Generic						
Total	**r=-0.184 0.196**	**r=-0.355 0.011**	**r=-0.286 0.042**	**r=-0.125 0.383**	**r=-0.430 0.765**	**r=-0.318 0.023**
Physical	ρ=-0.116 0.418	ρ=-0.245 0.083	ρ=-0.151 0.289	ρ=-0.025 0.864	ρ=-0.060 0.674	ρ=-0.210 0.140
Emotional	ρ=-0.149 0.297	ρ=-0.527 0.000*	ρ=-0.241 0.088	ρ=-0.047 0.743	ρ=-0.131 0.359	ρ=-0.385 0.005*
Social	ρ=-0.094 0.513	ρ=-0.353 0.011	ρ=-0.307 0.029	ρ=-0.031 0.830	ρ=-0.074 0.604	ρ=-0.225 0.113
School	ρ=-0.143 0.318	ρ=-0.305 0.030	ρ=-0.336 0.016	ρ=-0.205 0.149	ρ=-0.002 0.988	ρ=-0.348 0.012
PedsQL-Cancer						
Total	**r=-0.258 0.068**	**r=-0.440 0.001***	**r=-0.362 0.009***	**r=-0.182 0.201**	**r=-0.210 0.131**	**r=-0.183 0.198**
Pain	ρ=-0.108 0.449	ρ=-0.128 0.371	ρ=-0.188 0.188	ρ=0.020 0.889	ρ=0.043 0.764	ρ=-0.109 0.444
Nausea	ρ=-0.344 0.013	ρ=-0.323 0.021	ρ=-0.202 0.155	ρ=-0.217 0.125	ρ=0.004 0.980	ρ=-0.154 0.282
Procedural anxiety	ρ=-0.308 0.028	ρ=-0.528 0.000*	ρ=-0.221 0.119	ρ=-0.223 0.116	ρ=-0.364 0.009*	ρ=-0.139 0.331
Treatment anxiety	ρ=-0.086 0.547	ρ=-0.327 0.019	ρ=-0.163 0.253	ρ=-0.060 0.674	ρ=-0302 0.257	ρ=-0.064 0.656
Worry	ρ=-0.201 0.162	ρ=-0.372 0.008*	ρ=-0.256 0.073	ρ=-0.073 0.611	ρ=-0.243 0.326	ρ=-0.32 0.823
Cognition	ρ=-0.118 0.410	ρ=-0.369 0.008*	ρ=-0.335 0.016	ρ=-0.061 0.671	ρ=-0.146 0.308	ρ=-0.173 0.225
Perceived physical appearance	ρ=0.006 0.964	ρ=-0.286 0.042	ρ=-0.249 -0.078	ρ=0.156 0.273	ρ=-0.180 0.207	ρ=-0.032 0.822
Communication	ρ=-0.111 0.439	ρ=-0.132 0.356	ρ=-0.327 0.019	ρ=0.042 0.769	ρ=0.002 0.990	ρ=-0.140 0.327

Note: All QOL total and subscale scores are rated on a scale between 0 and 100, where better QOL is indicated by a higher score(e.g. the higher the score on the pain subscale, the less pain is experienced).

cognition, ρ=-0.369, p=0.008). Furthermore, the associations between monitoring and the majority of the other survivor-report QOL scores also approached significance (generic total score, r=-0.355, p=0.011; physical subscale, ρ=-0.245, p=0.083; social subscale, ρ=-0.353, p=0.011; school subscale, ρ=-0.305, p=0.030; nausea, ρ=-0.323, p=0.021; treatment anxiety, ρ=-0.327, p=0.019; perceived physical appearance, ρ=-0.286, p=0.042). There were only two subscales whose association with monitoring did not approach significance (pain, ρ=-0.128, p=0.371; communication, ρ=-0.132, p=0.356).

In contrast, there was no evidence to support the hypothesised association between blunting and QOL. None of the associations reached significance ($p<0.01$) and for those that approached significance (total cancer, r=-0.258, p=0.068; nausea, ρ= -0.344, p=0.013; procedural anxiety, ρ=-0.308, p=0.028) the direction of the association was actually the opposite of what was predicted, so that an increase in the utilisation of blunting strategies was associated with a *decrease* in QOL.

Association between neurological status and QOL: The results of correlational tests of association between survivors' NSS scores and QOL are shown in Table 4. For survivor-rated QOL, total cancer score was significantly negatively correlated with NSS score such that as neurological outcome worsened (i.e. NSS score increased), QOL decreased (r=-0.362, p=0.009). Although not strictly statistically significant, survivor rated total generic QOL also tended to decrease as NSS score increased (r= -0.286, p=0.042). None of the associations between NSS and the subscale QOL scores reached significance (at $p<0.010$) but several approached significance (social,

ρ=-0.307, p=0.029; school, ρ=-0.336, p=0.016; cognition, ρ=-0.335, p=0.016; communication, ρ=-0.327, p=0.019).

For parent-proxy reports of QOL there was no evidence of an association between NSS score and total cancer QOL score, although the negative correlation between total generic QOL score and NSS score approached significance (r=-0.318, p=0.023). When associations between NSS and PedsQL subscale scores were considered, only one reached significance (emotional functioning, r=-0.385, p=0.005).

Moderating effect of attentional coping style: The potential moderating effect of attentional coping style on the impact of objective outcome on QOL scores was considered using multiple regression. Given the lack of association between parent-proxy QOL scores and either NSS scores or attentional coping style scores, only survivor self-report scores were considered. Two separate regression equations were investigated to correspond to two distinct response variables: (i) child PedsQL generic total score and (ii) child PedsQL cancer total score. Given the earlier finding that tumour histology impacted on QOL, this factor was also entered into the regression equation as a further index of neurological status, measured by a dichotomous variable classifying tumour type. The two categories for this variable were "medulloblastoma or craniopharyngioma" versus "other tumour histologies". The decision was made to dichotomise the variable in this way because the mean QOL scores for participants with either a medulloblastoma or craniopharyngioma were significantly lower than for participants with other tumour types. Medulloblastoma and craniopharyngioma are both particularly unpleasant tumours which typically cannot be treated with surgery alone, and require additional

chemotherapy and irradiation treatments. Furthermore, both types of tumour are associated with a wide range of often quite severe neurological sequelae (see discussion section for more details), and therefore although this effect of histology was not predicted a priori, it was felt that classifying histology in this way was justified.

For each of the response variables, monitoring, blunting, NSS and histology were first entered as main effects (model 1) and then the interactions were added (model 2) to see whether interaction effects independently accounted for the variation in the response variable. The results of these regression analyses are presented in Table 5.

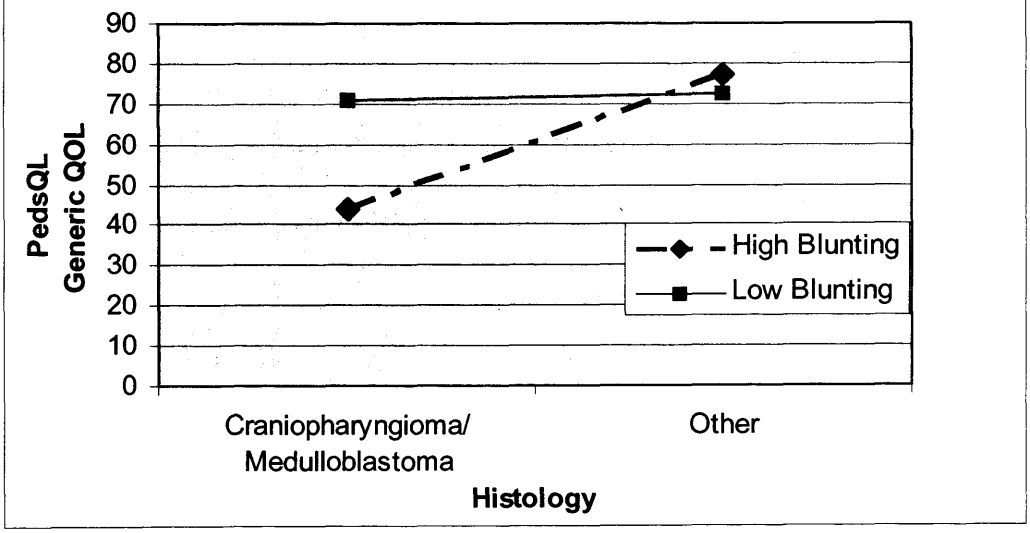
For PedsQL generic total score, the regression model was significantly improved by adding the interactions (F-change=2.986, p=0.029) and this second model (model 2) was significant ($F(8, 42)=5.007$, $p<0.001$). Within this model, the only significant interaction was that of blunting x histology ($\beta = 0.363$, $p=0.038$). For PedsQL cancer total score, the initial regression model (model 1) was not significantly improved by adding the interactions (F-change=0.1456, p=0.233).Therefore for survivor-rated generic, but not cancer QOL scores, there was an independent and significant interaction effect of blunting and histology. Survivors were divided into two groups, high and low blunters, using a median split and Figure 1 shows the nature of the interaction effect where PedsQL generic score is the response variable. If diagnoses of craniopharyngioma and medulloblastoma are taken to be indicative of poor objective outcome, it can be seen that when outcome is poor, the impact of high levels of blunting is actually opposite to that which was hypothesised, and is such that blunting amplifies the effect of poor outcome to reduce QOL.

Table 5: Multiple regression analyses explaining variation in survivor-rated QOL scores

Dependent Variable	Predictor Variables	Standardised regression coefficient β	p-value	R^2	R^2 change	F-change F-change	p-value
PedsQL Generic TOTAL	Model 1:			0.343	0.343	5.993	0.001
	Monitoring	-0.272	0.034				
	Blunting	-0.062	0.618				
	NSS	-0.266	0.032				
	Histology	0.375	0.003				
	Model 2:			0.488	0.146	2.986	0.029
	Monitoring	-0.303	0.014				
	Blunting	-0.082	0.492				
	NSS	-0.227	0.061				
	Histology	0.379	0.002				
	Monitoring x NSS	-0.006	0.964				
	Monitoring x Histology	-0.151	0.202				
	Blunting x NSS	-0.217	0.124				
	Blunting x Histology	0.363	0.003				
PedsQL Cancer TOTAL	Model 1:			0.358	0.358	6.413	0.000
	Monitoring	-0.372	0.004				
	Blunting	-0.115	0.354				
	NSS	-0.334	0.007				
	Histology	0.178	0.144				
	Model 2:			0.436	0.078	1.456	0.233
	Monitoring	-0.377	0.004				
	Blunting	-0.097	0.439				
	NSS	-0.350	0.007				
	Histology	0.189	0.119				
	Monitoring x NSS	0.113	0.410				
	Monitoring x Histology	-0.144	0.246				
	Blunting x NSS	-0.059	0.689				
	Blunting x Histology	2.139	0.038				

β = standardised regression coefficient; PedsQL = Paediatric Quality of Life Scale (survivor self-report).

Figure 1: The interaction effect of blunting and histology on Generic QOL



DISCUSSION

The aim of this study was to investigate the QOL of survivors of paediatric brain tumours. QOL scores were compared to standardised normative data, and the impact of specific objective (e.g. tumour recurrence and neurological status) and subjective (e.g. monitoring and blunting attentional coping styles) variables on QOL were investigated. Interaction effects between these variables were also examined.

QOL total and subscale scores were significantly worse for the brain tumour survivors than has previously been found in standardised normative populations, both when rated by parent-proxy and survivor self-reports, and this is in line with existing literature (Bhat et al., 2005; Eiser et al., 2005; Poretti et al., 2005). The survivors included in the present study had all been off treatment for at least 6 months, and in some cases there had been up to 7 years between treatment completion and assessment. Time since completion of treatment was not found to be associated with QOL scores and, although longitudinal data are required to determine the QOL profile of survivors over time, these findings suggest that QOL deficits may extend well beyond the initial year following treatment completion and highlight the need for the long-term follow-up of these patients.

As expected, parent-proxy and child self-reports of QOL were significantly correlated, although the correlation was perhaps higher than was originally anticipated. In healthy populations, correlation coefficients for scores on the PedsQL generic scale have generally been found to fall in the range 0.20-0.42 (Upton et al., 2005), whereas in the current study, correlation coefficients ranged from 0.52 to 0.86 (all significant at $p<0.01$). Upton et al. (2005) found that the correlation between

parent- and child-reported QOL was better when the child had a chronic health condition and suggested that this increased association may have reflected a tendency for parents and children to share more information about an issue if there is a perceived problem. It might be expected that this would be particularly true when a child has experienced a brain tumour, given the range and extent of difficulties that the child may face as a result. However, as many participants in the current study returned their questionnaires by post, rather than having them administered by a researcher, it is also possible that parent and child participants influenced each others' responses and this should be taken into consideration when interpreting these findings.

It was hypothesised that the QOL of survivors who had experienced one or more tumour recurrences would be impaired in comparison to those who had not but, in agreement with the results found by Copeland et al. (1999), this was not the case. It makes intuitive sense that recurrences would be associated with reduced QOL and it is difficult to imagine why this would not occur. It is conceivable that the survivors who had experienced relapse were utilising some form of effective coping strategy to compensate for the effects of the recurrence or alternatively were in denial about the impact of the recurrence, but it seems more likely that these findings reflect type 2 errors (particularly as differences on two subscales in the present study approached significance). Copeland et al. (1999) utilised a sample size of 19, only 11 of whom had experienced a relapse, and in the present study only 14 of the 52 survivors had experienced a recurrence. These sample sizes may have yielded insufficient power to detect an effect and future research should seek to recruit larger numbers of participants to be able to determine the impact of relapse on QOL.

As predicted, the brain tumour survivors in the current sample employed significantly higher levels of blunting attentional coping strategies than has been found in both standardised normative populations, and generic paediatric cancer samples (Phipps et al., 1995). These findings are consistent with the idea, proposed by Phipps and colleagues (Phipps et al., 1995; Phipps & Srivastava, 1997), that paediatric cancer survivors utilise a greater number of blunting strategies in an attempt to deal with the stress of the cancer experience. As is consistent with previous literature, there was no evidence of an increased endorsement of monitoring strategies in this population.

In concordance with Miller & Schnoll's model of monitoring and blunting (Miller & Schnoll, 2000) it was hypothesised that the increased utilisation of blunting strategies, and decreased utilisation of monitoring strategies, would be associated with improved QOL. There was evidence to support this hypothesis with regards to the effect of monitoring, but there was no significant association found between levels of blunting strategies endorsed and QOL. Furthermore, for those QOL subscale scores where the association between blunting and QOL approached significance, the direction of the effect was actually the opposite of that which was predicted, so that as use of blunting strategies increased, QOL decreased.

Whilst these findings go against, in part, what is proposed by Miller & Schnoll's model, they can perhaps be understood using a cognitive-behavioural model of coping. There is some confusion regarding the different terminologies adopted to describe coping behaviours, and Phipps et al. (1995) note that although there may be some differences between "blunting", and "avoidance", and between "monitoring",

"information-seeking" and "hypervigilance", these are largely overlapping constructs. Cognitive-behavioural theory proposes that both "hypervigilance" and "avoidance" may play a role in the maintenance of psychological difficulties, as they can result in an individual being more aware of problems, and less able to test out dysfunctional assumptions held, than they otherwise would have been (Hawton, Salkovskis, Kirk & Clark, 2001). Furthermore, avoidance is thought to have a key role in the development of posttraumatic stress disorder (PTSD) which has been found to be present in a substantial number of paediatric brain tumour survivors (Bruce, 2006) and it would be anticipated that the presence of this and other psychological difficulties would significantly reduce QOL reports.

Neurological status as measured by the NSS was found to be significantly associated with QOL such that as neurological status got worse, QOL diminished. Histology too was found to be associated with QOL scores and as such was included post-hoc as another objective measure of outcome.

The effect of histology was such that those survivors who had experienced medulloblastoma or craniopharyngioma reported worse QOL than those with other diagnoses. Although this effect was not predicted, it does make sense. Medulloblastoma are malignant tumours and as surgery alone is often insufficient to treat these tumours, children with medulloblastoma typically have to endure chemotherapy and irradiation treatments as well. Furthermore, about 25% of children with these tumours develop posterior fossa syndrome or cerebellar mutism: conditions associated with difficulty producing voluntary movements, irritability and emotional lability, and, in the case of cerebellar mutism, little or no ability to speak.

Although children do get well from this syndrome, there can be substantial variability in the rate of recovery and sometimes it can be a frustrating process lasting months or even years (Gordan, 2006; Pollack, 2001; Turkel, Chen, Nelson et al., 2004). Craniopharyngioma are benign tumours but their affects can be of a widespread and "malignant" nature. They are typically located near the pituitary stalk and their proximity to vital structure can make surgical resection difficult, resulting in the frequent need for chemotherapy and radiation treatment. Endocrine dysfunction is common and weight gain with an associated poor body image can be one of the many problems encountered by survivors of these tumours (Muller, Emser, Faldum et al., 2004; The Pituitary Foundation, 2006; Williams, 2004). In contrast, astrocytoma tumours (which accounted for over 50% of tumours in the "other histology" category adopted in the present study) are typically benign and slow-growing and can frequently be removed completely by surgery, resulting in less exposure to aversive treatments, less time in hospital, and a lower risk of long term cognitive or adaptive deficits (Beebe, Ris, Armstrong et al., 2005).

The final hypothesis considered in this paper concerned the possible interaction effect between objective outcome and attentional coping style. The regression analysis revealed that in addition to the main effects of monitoring, NSS score and histology on QOL (as rated by the PedsQL generic total score) there was also a significant independent effect of the interaction between blunting and histology. The direction of this effect was such that for those survivors with a worse objective outcome (i.e. survivors of medulloblastoma and craniopharyngioma), the utilisation of a high level of blunting strategies amplified this poor outcome. This was the opposite direction to that which was hypothesised, but as highlighted earlier, this can

be understood if blunting is considered as synonymous with avoidance in the context of cognitive-behavioural theory.

This effect described above may be partially due to incidences of PTSD in the survivors. As highlighted earlier, survivors of medulloblastoma and craniopharyngioma typically encounter a wider range of potentially traumatic scenarios than other survivors and therefore it could be argued that they have a greater chance of developing PTSD. The cognitive model of PTSD (Ehlers & Clark, 2000) proposes that PTSD develops and is maintained by attempts to avoid thoughts regarding the traumatic incident. Therefore, the increased utilisation of blunting (or "avoidant") strategies in a specific population that is exposed to high levels of traumatic incidents may result in higher incidence of PTSD in that population, which in turn could be associated with decreased QOL. This is a hypothesis that could be investigated in future research projects.

To date, the majority of research examining the QOL of paediatric survivors in brain tumours has focused on the role of objective predictors of QOL, but these results highlight the need to consider subjective psychological factors, both in their own right and also as moderators of the impact of objective factors on QOL.

There were several methodological limitations to the current research and these should be taken into account when considering the empirical validity and clinical utility of the findings presented here. The cross-sectional design of the study, whilst time- and cost-effective, prevented the direction of causality of correlational associations being ascertained. For example, whilst it may be the case that when

outcome is poor, the increased use of blunting strategies results in a poorer QOL, the converse could also be true, and longitudinal research is required to determine the direction of this association. However, longitudinal psychological research is difficult to conduct in this population. Large samples of survivors would be required in order that attrition rates due to mortality or other factors do not prevent meaningful statistical analyses at follow-up. As paediatric brain tumours are a relatively rare phenomenon, a multi-centre trial would almost certainly be required, and this would increase both the cost of the study and the heterogeneity within the sample. Furthermore, the speed with which medical advances occur poses a challenge for psychological longitudinal research. Phipps (2005) eloquently summarises this difficulty: "Our primary recourse is to hitch our wagons to the shooting star of the prevailing medical advances and follow where it leads. To do so is not easy. Psychosocial research takes time to develop, and having a moving target does not help". Whilst the rapid development of medical techniques and knowledge is to be applauded, it does mean that research data can quickly become "out of date" and this would be particularly true in the case of long-term longitudinal research. Phipps highlights the need for researchers to try to strike a balance between utilising monies to fund research in this important area whilst at the same time not using up valuable resources when it becomes apparent that the research question being conducted is no longer as relevant as it first was. This requires researchers to be flexible: they need to "choose (their) target and have it, but be prepared for change" (Phipps, 2005).

Another difficulty encountered was the relatively low recruitment rate of 37%. Efforts were made to improve recruitment by utilising two strategies, and individuals

attending the host hospital for a routine appointment were approached in person in the hope that this strategy would have a higher response rate than that which is typically found with postal questionnaires. However, the recruitment rate was still somewhat low, and together with the fact that survivors who would be unable to complete the questionnaire battery were excluded, the extent to which the sample of participants was representative of the population from which it was drawn is questionable.

Another limitation of the study was that of the differing methods by which the data were collected. Some participants chose to complete the questionnaires at home and return them by post, but others requested that the researcher administer them. Whilst the use of more than one mode of administration has been recognised as being beneficial for practical reasons (Tao & Parsons, 2005) there may be differences between responses depending on the method of data collection. Although it was not done in the present study, future researchers may wish to test the impact of the mode of data collection on the outcome variables of interest.

In comparison to other single-site studies in this field, the present study employed a relatively large number of participants, but an even larger sample size could have increased the sensitivity of the tests and reduced the risk of type II error. The large number of associations tested for in the present study also substantially increased the risk of type I error, although attempts were made to compensate for this by setting significance at 0.01 level.

Finally, a difficulty common to many research programmes conducted with paediatric brain tumour survivors is the lack of available measures that have been developed and tested specifically for use with this population. Although the PedsQL has been tested extensively for use with healthy children, children with chronic illness, and children with generic cancer, it has only had limited exposure in the paediatric brain tumour population. Reliability and validity tests for the brain tumour population are desperately needed, particularly given the higher risk of cognitive impairment found in this population.

CONCLUSION

The current findings showed that paediatric brain tumour survivors are at risk for impaired QOL both when compared to healthy children and to survivors of generic cancer. Whilst tumour recurrence did not appear to impact upon QOL, neurological status and tumour histology did. The effect of attentional coping style on QOL was investigated and it was found that an increased use of monitoring strategies was associated with poorer QOL. There was no main effect of blunting strategy utilisation on QOL, but a significant interaction between histology and blunting was observed such that for those diagnosed with arguably more severe tumours, the impact of this diagnosis on QOL was amplified by the utilisation of an increased number of blunting strategies.

Although there is a substantial amount of research concerning QOL in the generic paediatric cancer literature, this type of research is in its infancy in the brain tumour population and as such there is a considerable need for future research investment.

Longitudinal research would be invaluable in determining survivors' QOL profiles over time, and efforts to develop measures specifically for use with a brain tumour population would be of great use. The findings regarding the impact of attentional coping style on QOL merit further investigation and attempts to replicate these results are warranted. Furthermore, the consideration of other potential interaction effects between objective and subjective predictors of QOL would be beneficial.

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PART III: CRITICAL APPRAISAL

Quality of Life in Paediatric Brain Cancer: A Reflection on the Process of Conducting Research with this Population

INTRODUCTION

The process of conducting empirical research is complex. Researchers are typically called upon to make difficult decisions in the face of numerous constraints and dilemmas, and the choices that are subsequently made can significantly affect the results obtained. The aim of this paper is to review the process of conducting the empirical research presented in the current thesis. In particular, I aim to take a reflective stance and to consider some of the specific dilemmas that arose and the effect these had both on the research as a whole, and on the researchers themselves.

These issues are considered in 2 sections: the first discusses the different agendas that were encountered during the research process, and the second considers the impact of the research process on the researcher.

BALANCING AGENDAS

One of the difficult yet essential tasks of a researcher is to be able to balance competing agendas that occur during the research process and I found that often it was necessary for a balance to be struck between ethical and research integrity. Furthermore, I discovered that not only was it necessary to balance my own agenda as a researcher with those of the participants and my colleagues, but also the different agendas that I held within me: that of the "scientist" versus that of the "practitioner". Finding a balance between these different agendas was, at times, challenging and I feel that this aspect of the research process warrants explicit consideration.

Joining an Established Research Project: One Researcher or Two?

I conducted this research in collaboration with another trainee clinical psychologist who was in the year above me at college. At the point at which I joined the project, he had obtained ethical approval for a study investigating the occurrence and predictors of PTSD in a paediatric brain tumour population and was about to start data collection. He was keen to work alongside another trainee and after an initial meeting we agreed that I would join the project to look at the issue of Quality of Life with respect to this population.

There were numerous advantages to taking this approach: we effectively halved much of the workload as we were able to split tasks such as photocopying questionnaire packs, approaching and interviewing participants, and creating and entering data into a database. I was also able to save time on the paperwork required to set up a research project as I could submit an amendment to an approved ethics application, rather than having to complete the ethics application process from the beginning. Furthermore, we were able to support each other at difficult or stressful points in the research process (see later section on "impact of research on the researcher") and I found it invaluable to have someone to share the "highs" and "lows" of the research experience with.

In order to be able to make this collaboration effective, however, we had to consider our similar, but not synonymous, research agendas, the main difficulty being the different time scales that we were operating on. At the point that I joined the research project, I had just completed my first year of clinical training and thus had two years until I needed to complete my research. However, my colleague was entering his

third and final year of his training and as such there was a pressing need for him to collect data quickly. There were a limited number of potential participants that we could approach to participate in our research and therefore it was important that we were able to administer questionnaires relevant to both studies to the same set of research participants. We felt that it would be unethical to approach the participants on two separate occasions so it was necessary for me to make quick decisions regarding my hypotheses and the questionnaires that I wanted to utilise, so that both mine and my colleague's measures could be included in the research packs.

My colleague was fortunately very patient with me given the time pressures he was under, and he and our research supervisors helped me to become familiar with relevant literature as quickly as possible. However, given that this was an area of research that was completely new to me, this inevitably entailed certain compromises to be made. In hindsight, had I had longer to get to grips with current research in the area, I may have conducted certain aspects of the study differently, for example, including other measures of coping style in addition to the CBSS.

Another issue we faced was that as a second year trainee, I was entitled to only one day per fortnight to dedicate to the research project, whereas my final year colleague typically had two days a week. This meant that it was easier for him to see potential participants attending the host hospital during the day, and I was concerned that this might lead to the distribution of work between us being unbalanced. However, we came to an agreement that whilst he would do the majority of the contacts that were to be conducted in the hospital setting during the daytime, I would do most of the

home visits that needed to be done in the evenings or weekends. This balance worked well and we were able to share out the workload fairly.

Overall, I am extremely glad that I was able to work together with another trainee in conducting this study as I felt that the pros of working with another researcher far outweighed the cons. Joint working in this way highlighted for me some of the practical issues that must inevitably face clinical psychologists when working collaboratively together on research, such as how tasks are delegated and time managed on a day to day basis.

Language Issues: Cancer, Tumours, or Lumps?

This project involved interviewing children who had all experienced brain tumours and it became apparent at the study's inception that the language used when referring to the diagnosis warranted careful consideration. Rowland (2005) comments on the importance of being attentive to language when talking about cancer and its treatment especially to a paediatric population. A consultant paediatric psychologist and a specialist paediatric oncology nurse involved in the research also raised this issue, reporting that in their experience, many parents would avoid using the word "cancer" when discussing the tumour with the child. They said that parents often worried that their child would immediately associate the word cancer with imminent death and that parents wanted to spare the child this anxiety (particularly given the already considerable stress that the child was subjected to due to hospital admissions, exposure to painful procedures, and being separated from friends and family).

Whether or not the avoidance of the word "cancer" is actually effective in reducing a child's distress or anxiety is perhaps debatable. Furthermore, the idea that a diagnosis of cancer is considered to be synonymous with death raises the possibility of a role for some form of health-education within the general population as, thanks to hugely improved diagnostic and treatment procedures, this is not necessarily the case. However, whilst these are perhaps issues for consideration elsewhere, it was felt that in the present study it was essential that the (anticipated) wishes of parents should be respected and therefore it was decided that the word "cancer" would not be used and the term "brain tumour" would be adopted instead (this was the term reported to be commonly used by professionals when discussing diagnoses with parents and children).

In practice, this meant that the Paediatric Quality of Life Measure (PedsQL: Varni, Katz, Seid et al, 1998; Varni, Seid & Kurtin, 2001) had to be slightly adapted. For example, in the Cancer Module, question 2 of the worry subscale was changed from "I worry that my cancer will come back or relapse" to "I worry that my tumour will come back or relapse", and researchers had to be mindful not to use the word cancer when discussing the study with potential participants. This alternative appeared to be acceptable to most parents although in one case a parent requested that "lump" was used instead of "tumour" as that was the language they had always adopted with their child. Furthermore, there was one instance when a parent requested that the entire "worry" subscale be left out as they did not want the child to become aware of the possibility of relapse. By adapting a well-established measure there may be an impact on the reliability and validity of the measure but it was felt that this was a concession that was necessary for us to make for ethical reasons. It was hoped that

because the adaptations were relatively minor, the impact on the integrity of the measure would be small but the impact such changes may have had on the overall results should not be discounted altogether.

It is worth noting that these types of "language dilemmas" are not restricted to research conducted with paediatric cancer populations, and can be found throughout psychological research (e.g. when conducting research with people diagnosed with psychotic illness but who don't have insight into their illness, or disagree with the diagnosis that has been made). Clinical psychologists are typically well practiced at adopting the client's own language (as opposed to imposing their own) as this is routinely done in therapy as a way of improving understanding, collaboration and rapport with the client. The transferability of a psychologist's skills from the therapeutic setting to the research arena is perhaps one of the advantages of adopting the scientist-practitioner model of clinical psychology.

The Family Agenda

As a researcher, one of my key objectives in this study was to be able to recruit enough participants in order that I had a sufficient sample size to test my research hypotheses. However, again this agenda had to be balanced with those of the participants and the two did not always synchronise.

During one interview with a family, for example, it became apparent that the child did not want to answer the research questions, and that the parents had asked me to come to see them because they were feeling intense distress and despair in relation to the severe disabilities that their child had been left with following his brain tumour.

On this occasion it became evident very quickly that my agenda as a researcher (i.e. to get the questionnaires completed) would need to be abandoned as this was unimportant in comparison to ensuring the welfare of the family. I ended up staying with the family for several hours, which was how long it took for them to "offload" their considerable anger and distress and for me to feel that their distress had reduced sufficiently for it to be appropriate for me to leave. (Notably in this situation my experience as a therapist was of great value and the benefits of having a dual scientist-practitioner role were again evident).

The possibility of this type of situation occurring had been foreseen by the research team and it had been agreed that in such circumstances an immediate referral would be made to the consultant clinical psychologist supervising this research and that she would arrange an appointment with the family to offer appropriate support and therapeutic input. Whilst the family's welfare in such circumstances is of primary importance, it is also important to remember that these situations can impact upon the feelings of the researcher and these issues are discussed in more detail later on in this paper.

A different type of family agenda that I also encountered was that of the survivors' siblings. On several occasions I found that siblings of the child that I was interviewing wanted to be part of the interview too. Numerous studies have investigated the impact of paediatric cancer on survivors and their parents, but the psychological adjustment of siblings has received less attention. There is some evidence that siblings of children with cancer typically experience family separation and decreased social contact and support from parents whose focus may unavoidably

be directed towards their sick child (Barrera, Fleming & Khan, 2004). Therefore it is perhaps unsurprising that the sibling feels anxious about being "left out" of the attention that their brother or sister receives. The ways in which the parents in the present study managed these situations varied. All parents recognised the sibling's need for attention but whilst some parents dealt with this by spending time themselves with the sibling whilst the interview was conducted with the survivor in a separate room, others encouraged the sibling to be present and an active participant during the interview. This was another occasion where the ethics versus research integrity dilemma arose. On the one hand, having a sibling present who voices their opinion may affect the survivor's responses to the research questions, but on the other hand it felt unethical to refuse to include the sibling when they obviously wanted to take part. In practice I tried to handle these situations sensitively and ethically, whilst still maintaining as much research integrity as possible. If the family were keen for the sibling to be in the room during the interview then I would typically try to engage the sibling in a task not related to the interview (such as drawing me a picture), and made sure that I frequently reinforced their efforts with praise so that they felt included and valued. If this was not possible (for example when a sibling wanted to be directly involved in the interview) then I tried to be creative and engage them in the research process in a way that would have as little impact on the survivor's responses as possible (e.g. asking the sibling to read out questions).

In general, I felt that I was fairly successful with these strategies, and was able to limit the impact that the presence of siblings had on the data provided by the survivor. However, on occasions, parents too wanted to be present during the

interview and whilst this was a reasonable request and one which had to be respected, it was somewhat harder to control the effect that the parent's presence had on the survivor's responses. Although most parents were happy to allow space for their child to provide a response, some parents tended to answer for the child, or even "correct" the child when they felt that the child had got the answer "wrong". Although I tried to encourage parents to allow their child the chance to respond without being corrected, just by being present parents may have inadvertently affected the child's answers. This is also likely to have been the case for respondents who returned postal questionnaires, where the parent may have helped the child to complete the measures, and such factors are likely to have shaped the research outcomes to some extent.

From my experiences in conducting research in this area I would suggest that further research into the impact of childhood cancer on siblings could be an important area to develop. In addition, more exploration of parental influences on children's narratives about cancer could also be invaluable

The Scientist versus the Practitioner: who am I again?

The scientist-practitioner model is one that has been endorsed by the majority of clinical psychologists, and there are many advantages to be found in taking such an approach (Kennedy & Lewellyn, 2001) some of which have already been discussed. However, such a model is not without its difficulties and this also became apparent when conducting the present research.

The data for the empirical paper was collected during my second year of clinical psychology training, and therefore at a time when, for three days a week, I wore my "practitioner's" hat, conducting assessments and therapeutic interventions whilst on clinical placement. Such work requires the development and maintenance of an ongoing therapeutic relationship with a client, which is different to the type of relationship developed between the researcher and research participant during a single research oriented interview.

Although both situations require the fostering of a safe environment in which the other can feel comfortable discussing personal issues, it is vital to hold in mind that the research participant is not a client who has approached services for therapy, and the researcher will not have an ongoing therapeutic relationship with the participant. Therefore, it is important that specific boundaries are adopted to ensure that the research participant does not disclose too much personal information that could leave them feeling vulnerable and exposed and without the support of a therapeutic relationship.

In practice, this proved to be a somewhat difficult balance to achieve. For those participants who had requested a personal interview (rather than responding by postal questionnaire) it was necessary to engage in some "small talk" in order to set both the parent and the child at ease. Furthermore, specific questions in the interview pack often prompted recollections of certain incidents and participants frequently wanted to recount these memories in order to give me the best understanding that they could of their situation. I felt that it was important to allow the participant to express their responses in the manner they felt most comfortable with, and that it would have been

inappropriate to insist on answers being given in a strict "yes-no" format without allowing a discursive element. However, at times I found that my instinct was to react to these more discursive responses from a "practitioner" rather than a "scientist" stance. I often had to consciously remind myself that I was not conducting therapy with a client and to steer myself away from asking the types of probing questions that I would have utilised in a therapeutic situation. This could be frustrating as it was sometimes evident that there was an issue that might benefit from therapeutic input, and having built up rapport with the participant (albeit over only a single session) I sometimes wanted to discard my "scientist" role and revert to adopting the "practitioner" hat that I generally feel more comfortable in. At times (such as the occasion discussed earlier when the parents were extremely distressed) it was appropriate to do this, but in general it was important to maintain the "scientist's stance" rather than allow myself to be drawn into acting as a "practitioner".

Supervision, both from my research supervisor and peer support from the other trainee clinical psychologist with whom I jointly conducted the research was of great importance in helping me to deal with such dilemmas. We reflected on ways in which it was possible to respond to participants in a respectful and interested way whilst still being able to provide the containment necessary, and this was of enormous use, particularly in the earlier stages of data collection when the task of swapping between the roles of scientist and practitioner was still relatively new to me. This experience did again remind me of the difficulties facing psychologists working both clinically and in research, especially where this is in the same setting, and the dilemmas they must frequently face regarding where to draw the line between these dual "scientist" and "practitioner" roles.

THE IMPACT OF RESEARCH ON THE RESEARCHER

It is always important to consider the impact of choices made by a researcher on the outcome of the research, and this is usually well documented in empirical research papers. However, less commonly discussed but still of importance, is the converse relationship: the effect that the research has on the researcher.

As a trainee clinical psychologist I regularly come into contact with clients who have experienced traumatic life events and are distressed by their experiences, and I am used to dealing with my own emotions that arise in response to working with these clients. However, at the time when I collected the data for the current research, I had not had previous experience of working with children, and I was unsure of what my personal response would be in relation to children who had faced, and may still face, a life-threatening illness. I anticipated that there may be times when this work would give rise to negative feelings such as sadness and helplessness, and this was indeed the case. I did also, however, experience positive feelings of hope and admiration, which, whilst perhaps more unexpected, have made an equally lasting impression on me. A discussion about some of the particular "highs" and "lows" that I experienced is presented below.

The Lows

I inevitably experienced a certain amount of sadness whilst working with this group. It was clear that some of the participants in the study had been deeply affected by their experience of cancer, and one of the children has since died following a further relapse. Although referrals were made to clinical psychologists and other services where appropriate, I still experienced feelings of powerlessness in relation to my

inability to offer help, and it was difficult to come to terms with the enormity of the situation that these often very young children had encountered. A telling example is the following comment that was written by a survivor on one of the questionnaires returned by post: "I have short term memory loss. My life is horrible. I want to go to school, I want a childhood but I don't see no-one".

For those families requesting a personal interview it was often necessary to visit them at their homes in the evenings and weekends in order to minimise disruption to the child's daily routine (which typically had already been severely disrupted at the time when the tumour was initially diagnosed and treated). Whilst I was keen to be as flexible as possible (both to ensure the wellbeing of participants, and to recruit sufficient numbers for analyses), conducting interviews in my free-time, particularly in an evening following a day of providing therapeutic interventions at my clinical placement, was sometimes stressful and tiring. This was exacerbated by the fact that several participants lived outside of the London region (as a centre of national excellence, the host hospital receives nationwide referrals) and so interviews were often preceded and followed by a lengthy journey.

One of the most helpful ways that I found to cope with this stress was to telephone the other trainee clinical psychologist involved in this research immediately after I had completed an interview and to talk through what had occurred. From the project's inception we had agreed post-visit telephone calls were vital in order to ensure the safety of the researcher conducting the interview. However, it soon became apparent that this phone call also provided a forum for informal peer supervision, where the person who had conducted the interview was able to offload,

discuss issues of transference that had occurred, and if necessary draw up a plan of action for how to help the family if they needed further assistance from services.

Formal supervision was attended on a regular basis, and I also adopted personal coping strategies (e.g. ensuring that I took time out to relax, and where possible arranging interviews on days when I did not also have a lot of therapeutic work to do) but it was perhaps these post-interview phone calls that I found most helpful in coping with my own distress. In general I felt that I successfully kept my own emotions in check during the interviews and therefore I do not feel that they would particularly have influenced the responses of the participants, but it is of course possible that some of the participants picked up that I felt sad for them and minimised the distress that they reported accordingly.

Although feeling sad about the situation that the survivors and their families faced was the predominant negative emotion that I experienced during this research process, there were also times when I felt frustrated. This was typically at times where I was reliant on a response from someone else before I could proceed any further with the study (for example when waiting for my honorary contract to come through, or for permission to use a specific questionnaire). I found that together with talking through my frustrations in supervision, it was helpful to adopt a mindful approach to this experience, acknowledging that delays are part and parcel of the researcher's experience, are inevitable, and to try to accept them as such.

The Highs

Whilst there were some points during the research process where I felt low and frustrated, these moments were outweighed by the incredibly positive experiences I encountered when working with this population. Many of the families I met reported being happy and content despite all that they had been through, and the astonishing capacity that families had to find a silver lining around even the darkest cloud never ceased to amaze me.

A particularly striking example of this bravery and determination to adopt a positive outlook was shown in a letter that I received from a mother, which she wrote to accompany the questionnaires that she completed and returned to us. In the preceding few years, not only had her child been diagnosed and treated for a brain tumour but her husband had died suddenly and unexpectedly. In the letter she wrote "The past eight years have been hard and sometimes surreal yet also enlightening and wonderful, and I know that our experience has enriched the way we look at 'life': we have learned a lot".

I feel that this quote sums up the bravery, integrity and resiliency of the participants that I met whilst conducting this study and it was an honour to have worked with such people. The majority of research in this field is problem-focused and investigates the disability and distress encountered following diagnosis and treatment of a brain tumour. Whilst these are obviously important areas of research interest, it would also be valuable to examine the positive narratives that survivors and their families develop when faced with such adverse circumstances.

SUMMARY

This paper has discussed the dilemmas that arose throughout the research process and the ways in which responses to these dilemmas impacted upon both the outcome of the research, and the researchers themselves.

It is clear that a researcher has to acknowledge and balance a host of competing demands made by their own research agenda, other personal agendas that they may hold, and the agendas of their colleagues and participants. It is essential that the researcher adopts a reflective position so that they are aware of these differing demands and are able to negotiate a compromise.

The participants in this study were paediatric survivors of brain tumours and their parents and research with this population requires the careful consideration of a number of factors. Care needs to be taken with the language used when discussing the cancer experience with survivors and their families so as not to cause undue distress. Although some attention has been paid to the narratives of adult cancer survivors (Ford & Christmon, 2005; Van der Molen, 2000), I am unaware of any research directed at eliciting paediatric survivors' narratives, and this is an area that would certainly be worthy of future research. As well as investigating the specific words and language that children and their families use to describe their cancer experience, and the rationale behind this, it would also be valuable to investigate the positive narratives that families develop in the face of adversity, and future researchers could consider using a qualitative approach to begin to investigate these issues.

In the present research, the dilemmas that arose frequently required a trade off to be made between ensuring ethical practice was conducted and preserving the integrity of the research. For example, in my inclusion of family members that wanted to be present during the survivor's interview, I had to make decisions about balancing the needs of the particular family with my need to collect reliable and valid research data that could usefully inform the care and treatment of many future families. Clearly conducting ethically sound research is always of paramount importance but it is crucial that whilst protecting the research participants from further distress as much as possible, the researcher tries to be creative so that the loss to the integrity of the research can be minimised.

Work with any distressed population is always challenging, for the researcher and clinician alike but arguably this is particularly true when working with a paediatric population who have faced, and may again face, a life-threatening illness. In the present research study, there were a number of strategies that were found to be helpful in managing my own distress but perhaps the one that stood out as most beneficial was that of peer supervision from my fellow trainee clinical psychologist who was also involved in the research work. Despite the difficulties inherent in undertaking research of this nature, the benefits I gained from this experience, both personally and professionally, were considerable and I look forward to the opportunity of undertaking other research initiatives in the future.

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APPENDICES

Appendix 1:

Letters of Ethical Approval

Great Ormond Street Hospital for Children NHS Trust / The Institute of Child Health Research Ethics Committee

Institute of Child Health
30 Guilford Street
London
WC1N 1EH

Tel: 020 7905 2620
Fax: 020 7905 2201

30th April 2004

Department of Psychological Medicine
GOSH

Dear

Full title of study: Post-traumatic stress symptoms in childhood survivors of brain tumours and their parents: Moderating effects of coping styles and parent-child interactions
REC reference number: 04Q0508/9
R&D number: 04BS10

Thank you for your letter of 20th April 2004, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chairman.

Confirmation of ethical opinion
On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

The favourable opinion applies to the following research site:

Site: *Great Ormond Street Hospital for Children NHS Trust/The Institute of Child Health*

Principal Investigator:. *Consultant Clinical Psychologist*

Conditions of approval
The favourable opinion is given provided that you comply with the conditions set out in the attached document. You are advised to study the conditions carefully.

Management approval
The study may not commence until final management approval has been confirmed by the organisation hosting the research.

Statement of Compliance
The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

Yours sincerely,

Research Ethics Coordinator

Enclosures: Standard approval conditions

Great Ormond Street Hospital for Children NHS Trust / The Institute of Child Health Research Ethics Committee

Institute of Child Health
30 Guilford Street
London
WC1N 1EH

Tel: 020 7905 2620
Fax: 020 7905 2201

19th November 2004

Dr
Department of Psychological Medicine
GOSH

Dear

Full title of study: Post-traumatic stress symptoms in childhood survivors of brain tumours and their parents: Moderating effects of coping styles and parent-child interactions
REC reference number: 04/Q0508/9
R&D number: 04BS10

Amendment date: 29 October 2004
Amendment: adding Louise Isham as an additional researcher and adding an extra measure (Child Report, and Parent Report for Children).

The above amendment was reviewed by the Sub-Committee or the Research Ethics Committee at the meeting held on 17 November 2004.

Ethical opinion
The members of the Committee present have a favourable ethical opinion on the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents
The documents reviewed and approved at the meeting were:
Correspondence dated 28 October
Questionnaires as above

Membership of the Committee
The members of the Ethics Committee who were present at the meeting are listed below:
Dr and Dr

Management approval
Before implementing the amendment, you should check with the host organisation whether it affects their approval of the research.

Statement of compliance (from 1 May 2004)
The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

Yours sincerely,

Research Ethics Coordinator

Copy to: R&D Department

Appendix 2:

Recruitment Letters

Great Ormond Street Hospital for Children NHS
NHS Trust

Great Ormond Street
London WC1N 3JH

Tel: 020 7405 9200

Initial solicitation letter

Address

Date

Dear .....

Project Title: How children and their parents cope with the experience of childhood brain tumours

My colleagues and I are conducting a study which attempts to explore the different ways children diagnosed and treated for brain tumours and their parents cope with this experience. In particular, we are keen to discover how coping styles and child-parent relationships affect adjustment to such experiences.

As you and your child are "experts" in this area we are very interested to hear about your experiences. In sharing these individual experiences with us, we hope that we will then be able to better assist the emotional adjustment of other families who are facing similar situations.

We have enclosed an information sheet for you and your child, which outlines the study in more detail. If you agree to take part then we would be very grateful if you and your child could complete the enclosed questionnaires and sign the consent forms and return the following in the stamped addressed envelope provided:

a) **The completed "Parent/Guardian Questionnaire Pack"**
b) **The completed "Child Questionnaire Pack"**
c) **Signed child and parent consent forms**

Whilst participation in this study does not require a meeting, if you would like one of us to assist you and/or your child completing the packs or would like the opportunity to discuss your experiences further then we would be happy to meet with you. This can

either take place at Great Ormond Street Hospital or in your home. We would be happy to visit you during the working day, in the evening or at the weekend; whichever is best for you.

We would like you to know that these questionnaires are invaluable for helping us support other parents and children who may face similar experiences in the future.

If you wish to find out more about the study before deciding to take part please contact one of us on the numbers below and we will be happy to talk to you.

Many thanks and best wishes,

Louise Isham
Trainee Clinical Psychologist

NB:
You do not have to take part in this study if you do not want to. If you do decide to take part you may withdraw at any time without having to give a reason.

All proposals for research using human subjects are reviewed by an ethics committee before they can proceed. This proposal was reviewed by the Institute if Child Health Research Committee.

Delete as appropriate

YES, I / my child would like some assistance in completing the forms.

YES, I / we would like an opportunity to discuss our experiences with a researcher

I would like to meet at: Home (tick if applicable) ☐

Hospital (tick if applicable) ☐

I / we can be contacted on the following telephone number/s:

Home (if applicable): .....

Mobile (if applicable): .....

Great Ormond Street Hospital for Children NHS
NHS Trust

Great Ormond Street
London WC1N 3JH

Tel: 020 7405 9200

Reminder letter

Address

Date

Dear .....

Project Title: How children and their parents cope with the experience of childhood brain tumours

You may recall receiving a letter from us in *...(month)...* asking whether you would be willing to take part in a study looking at different ways children diagnosed and treated for brain tumours and their parents cope with this experience.

Understanding your experience, and your child's, will provide enormous help in assisting and supporting other families who are facing similar situations.

You are "experts" in this area and we would still be very interested to hear about you and your child's experiences and thus are writing to invite you to participate.

If you do have time to take part then we would be very grateful if you and your child could complete the questionnaires and return the following in the stamped addressed envelope provided in the original pack by the **31st of March 2005**:

a) **The completed "Parent/Guardian Questionnaire Pack"**
b) **The completed "Child Questionnaire Pack"**
c) **Signed child and parent consent forms**

Whilst participation in this study does not require a meeting, if you would like one of us to assist you and/or your child completing the packs or would like the opportunity to discuss your experiences further then we would be happy to meet with you. This can either take place at Great Ormond Street Hospital or in your home. We would be happy

to visit you during the working day, in the evening or at the weekend; whichever is best for you.

We would like you to know that these questionnaires are invaluable for helping us support other parents and children who may face similar experiences in the future. If you wish to find out more about the study before deciding to take part please contact one of us on the numbers below and we will be happy to talk to you.
Many thanks and best wishes,

Louise Isham
Trainee Clinical Psychologist

NB:
You do not have to take part in this study if you do not want to. If you do decide to take part you may withdraw at any time without having to give a reason.
All proposals for research using human subjects are reviewed by an ethics committee before they can proceed. This proposal was reviewed by the Institute if Child Health Research Committee.

Delete as appropriate
YES, I / my child would like some assistance in completing the forms.
YES, I / we would like an opportunity to discuss our experiences with a researcher
I would like to meet at: Home (tick if applicable) ☐

Hospital (tick if applicable) ☐
I / we can be contacted on the following telephone number/s:
Home (if applicable): .....

Mobile (if applicable): .....

Appendix 3:

Information sheets

PARENT / GURADIAN INFORMATION SHEET

How children and their parents experience the diagnosis and treatment of childhood brain tumours

The aim of the project
To explore how children and their parents cope with the experience of childhood brain tumours.

Why is the project being done?
Research has suggested that diagnosis and treatment of childhood brain tumours can be very stressful for patients and their families. Such levels of stress can have a negative impact on individuals' emotional functioning. This project attempts to investigate whether certain coping styles and parent-child interactions decrease the levels of stress experienced by individuals following treatment of childhood brain tumours. We may then be able to advise patients and families about specific coping styles (or strategies) and ways of interacting with each other that help reduce stress levels and promote healthy emotional adjustment following diagnosis and treatment.

How is this project to be done?
This study hopes to gain the views of a sample of children and their parents about their experience of childhood brain tumours. You and your child will each be asked to fill in some short questionnaires. These may be completed at the hospital or at home. If you or your child would like some assistance in completing these questionnaires we would be happy to arrange a convenient time to meet, either at the hospital or at your home.

What are the risks and discomforts?
There will be no physical risks or discomforts from taking part. Some of the questions might ask about experiences related to the diagnosis or treatment that may be uncomfortable or upsetting for you and your child to think about. If completing the questionnaire makes you or your child upset you are free to stop at any point and withdraw from the study. In addition, we can also arrange for you or our child to see a psychologist here at the hospital if you feel that such support would be helpful (but we will advise you about such facilities in more detail should you find the questionnaires distressing).

What are the potential benefits?
It is hoped that this study will be able to highlight certain coping styles and ways of interacting with each other, which increase the likelihood of patients and their families adjusting well emotionally following diagnosis and treatment of brain tumours. This information may therefore be used to advise families about specific ways (or strategies) of coping and interacting during the course of the illness which promotes optimum emotional adjustment. There may not be any direct benefits to you and your child from taking part. However, if this project gives us any information that might help your doctors and other healthcare professionals to take care of you and your child, we can pass this information back to them if you are happy for us to do so.

Please turn over

Who will have access to the case/research records?
Only the researchers and a representative of the Research Ethics Committee will have access to the data collected during this study. The use of some types of personal information is safeguarded by the Data Protection Act 1998 (DPA). The DPA places an obligation on those who record or use personal information, but also gives rights to people about whom information is held. If you have any questions about data protection, contact the Data Protection officer via the switchboard on 020 7405 9200 extension 5217.

What are the arrangements for compensation?
This project has been approved by an independent research ethics committee who believe that it is of minimal risk to you. However, research can carry unforeseen risks and we want you to be informed of your rights in the unlikely event that any harm should occur as a result of taking part in this study. No special compensation arrangements have been made for this project but you have the right to claim damages in a court of law. This would require you to prove fault on the part of the Hospital and/or any manufacturer involved.

Do I have to take part in this study?
If you decide, now or at a later stage, that you do not wish to participate in this research project, that is entirely your right and will not in anyway prejudice any present or future treatment.

Who do I speak to if problems arise?
If you have any complaints about the way in which this research project has been, or is being conducted, please, in the first instance, discuss them with the researcher. If the problems are not resolved, or you wish to comment in any other way, please contact the Chairman of the Research Ethics Committee, by post via the Research and Development Office, Institute of Child Health, 30 Guildford Street, London, WC1N 1EH, or if urgent, by telephone on 020 7905 2620, and the Committee administration will put you in contact with him.

If you have any queries you can telephone or email any of us and we will be happy to answer your questions.

Louise Isham
Trainee Clinical Psychologist

CHILD INFORMATION SHEET *(Ages 8 - 12)*

How children and their parents experience the diagnosis and treatment of childhood brain tumours

You are invited to take part in a project about children and their families who have experienced childhood brain tumours. Please read this information sheet because it tells you why we are doing this project and what we will ask you to do if you want to take part.

Why are we doing the project?
Lots of children have to come to hospital to be treated for their illnesses. Because of this we want to find out what that it like for them as well as their families. We hope that what you tell us will help us understand how to look after children who find the experience of going to hospital frightening or stressful. We are interested to hear what every child and their parent has to say.

Why have I been chosen?
We are inviting all children between the ages of 8 - 16 who have experienced having a brain tumour and have had to go to hospital for treatment.

Do I have to do it?
You do not have to take part in the project if you do not want to. If you take part and then want to change your mind then that's OK and you won't have to tell us why you wanted to stop. If you decide not to take part it will not change anything that happens to you in hospital. If you do take part then we would like you to sign a form stating that you are willing to be involved in the project.

What will I have to do?
If you decide to take part in the project we would like you to fill in some short questionnaires. But don't worry, if you find them a bit tricky one of us can help you fill them in.

Are there any risks?
We don't think there are any risks, but there might be a small chance that some children will get a bit upset when thinking about what happened to them. If this happens, we will tell you about somewhere that you could go to talk to someone who can help.

Why will it be good to take part?
The things that you and other children (and parents) tell us will be very useful and will help us find out how to help other children who have might also have the same illness in their childhood.

Please turn over

What will happen to the questionnaires?
Whatever you tell us will be kept confidential; that means that no one will see the questionnaires except for the people doing the project (the names below). Also they will not tell anyone else what you said.

What if something goes wrong?
We do not expect anything to go wrong, but if it does we will talk to your mum or dad about what they can do.

What happens to the results of the project?
We hope to write a report for other people to see so that they can help other children who have had an illness like yours. Your name will not be on the report.

Louise Isham
Trainee Clinical Psychologist

PARTICIPANT INFORMATION SHEET *(Ages 13-16)*

How children and their parents experience the diagnosis and treatment of childhood brain tumours

You are invited to take part in a project about adolescents and their families who have experienced childhood brain tumours. Please read this information sheet because it tells you why we are doing this project and what we will ask you to do if you want to take part.

Why is the project being done?
Research has suggested that diagnosis and treatment of brain tumours can be very stressful for young people as well as their families. This study attempts to investigate whether certain coping styles and family communication styles decrease the levels of stress experienced by the family following treatment of brain tumours.

Why I have I been chosen?
We are inviting all young people between the ages of 8 - 16 who have experienced having a brain tumour and have had to go to hospital for treatment.

Do I have to do it?
You do not have to take part in the project if you do not want to. If you take part and then want to change your mind then that's OK and you won't have to tell us why you wanted to stop. If you decide not to take part it will not change anything that happens to you in hospital. If you do take part then we would like you to sign a form stating that you are willing to be involved in the project.

What will I have to do?
If you decide to take part in the project we would like you to fill in some short questionnaires. If you need help doing this we will be pleased to help you.

Are there any risks?
There will be no physical risks or discomforts from taking part. Some of the questions might ask you about experiences related to the diagnosis or treatment you received which may be uncomfortable or upsetting for you to think about. If completing the questionnaire makes you upset you are free to stop and withdraw from the project.

What are the possible benefits?
The things that you and other young people tell us about having an illness and going to hospital, including the way they coped with these experiences, will be very useful. It will help us find out how to help other young people cope if they ever have the illness in their lifetimes.

Please turn over

What will happen to the questionnaires?
Whatever you tell us will be kept confidential and no one will see the questionnaires except for the people doing the project (the names below) and that they will not tell anyone else what you said.

What if something goes wrong?
We do not expect anything to go wrong, but if it does we will talk to your mum or dad about what they can do.

What happens to the results of the project?
We hope to write a report for other health care professionals so that they can help other young people have experienced an illness like you did. Your name will not be on the report.

If you have any queries you can telephone or email any of us and we will be happy to answer your questions.

Louise Isham
Trainee Clinical Psychologist

Appendix 4:

Consent forms

PARENT CONSENT FORM

Title of project:
How children and their parents experience the diagnosis and treatment of childhood brain tumours

Name of Principal investigator:

	Please initial box
1. I confirm that I have read and understood the information sheet for the above project and have had the opportunity to ask questions.	☐
2. I confirm that I have had time to consider whether or not want to be included in the project.	☐
3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	☐
4. I understand that responsible individuals from GOSH may look at sections of my child's medical notes. I give permission for these individuals to have access to my child's records.	☐
5. I agree to take part in the above project.	☐

Name of participant _____ Date _____ Signature _____

Louise Isham

Researchers (to be contacted if there are any problems)

CHILD CONSENT FORM

Title of project:
How children and their parents experience the diagnosis and treatment of childhood brain tumours

Name of Principal investigator:

	Please put your initials in the boxes if you agree box
1. I have read and understood the information sheet have asked any questions that I wanted to.	☐
2. I have had enough time to decide if I want to take part in the project.	☐
3. I understand that I only need to take part if I want to and that I am free to stop doing the project at any time, without giving any reason.	☐
4. I understand that the people doing the research project may look at my hospital notes if they need to. This is OK if my parent lets them.	☐
5. I agree to take part in this project.	☐

Name of participant _____ Date _____ Signature _____

Louise Isham

Researchers (to be contacted if there are any problems)

Appendix 5:

Parent/guardian and child questionnaire packs

Child Questionnaire Pack[3]

Thanks for agreeing to fill in this questionnaire pack!

There are a number of short questionnaires we would like you to fill in. Below is a list of the questionnaires in the pack

1. **PACHIQ-R-P**: This questionnaire asks about the way you get on with your mum, dad or guardian.

2. **Impact of Events Scale**: This questionnaire asks about whether you still think about the time you had a brain tumour.

3. **Child Coping Style Scale**: This questionnaire asks about the way you deal with difficult times.

4. **PedsQL**: This questionnaire asks about how you are getting on after the time you had a brain tumour.

Before you begin, try to remember:

- There are **no** "right" answers to any of these questions.
- If you want to stop filling in the questionnaires you can. You don't have to tell us why you wanted to stop either.
- We are happy to answer any questions you might have, just ask us!

[3] NOTE: Questionnaires 1 & 2 were included in the questionnaire packs as these were the measures used in the study by Bruce (2006) which was run in conjunction with the present study. These questionnaires have not been included here, as they are not relevant to the present study.

CBSS - Child Version (Revised)

Imagine that:

I. Your parent takes you to the doctor's because you are sick. You are sitting in the waiting room waiting for the doctor. Would you:

Circle "yes" or "no"

1)	Play with toys or a game in the waiting room	yes	no
2)	Talk to your parent about how sick you feel	yes	no
3)	Play with other children in the waiting room	yes	no
4)	Think about what the doctor might do to you	yes	no
5)	Look at a book, either by yourself or with your parent	yes	no
6)	Close your eyes and think about where in your body you feel sick	yes	no
7)	Think about something else to get your mind off being sick	yes	no
8)	Think about what the doctor did to you the last time you were sick	yes	no

II. You're playing in the living room with a friend and you accidentally break a lamp. Your parent will be home soon. While you are waiting with your friend for your parent to come home, would you:

9)	Keep looking at the pieces and think about what happened	yes	no
10)	Go outside and play until your parent gets home	yes	no
11)	Think about what will happen when your parent gets home	yes	no
12)	Just play at home and forget the lamp	yes	no
13)	Talk about it with your brother or sister or your friend	yes	no
14)	Go and watch TV	yes	no
15)	Think about the look on your parent's face	yes	no
16)	Get your mind off what happened by thinking about other things	yes	no

III. You are in class at school. Your teacher comes over and tells you the head teacher wants to see you at break. While you are waiting for break, would you:

17)	Think about other things to get your mind off the head teacher	yes	no
18)	Think about what you did to make the head teacher want to see you	yes	no
19)	Think about what the head teacher might say or do	yes	no
20)	Continue with your class pretending you don't know	yes	no
21)	Think about what the head teacher did to other kids	yes	no
22)	Try to keep your mind on your school work	yes	no
23)	Pretend the head teacher will say something good to you	yes	no
24)	Watch the faces of your teacher and the other children to see what they might think about it	yes	No

IV. You are sitting in the dentist's chair. The dentist has gone out of the room to get something, but soon will come back and start working on your teeth. You feel worried about what the dentist will do. While you are waiting, would you:

25)	Look around to see what tools the dentist will use	yes	no
26)	Think about what the dentist did when you were there before	yes	No
27)	Think about what you don't want the dentist to do	yes	No
28)	Keep looking at the pictures on the wall	yes	No
29)	Think about other things to get your mind off the dentist	yes	No
30)	Close your eyes and pretend you are someplace else	yes	No
31)	Think of things you want to ask the dentist	yes	No
32)	Think about being with friends or your parent	yes	No

ID# _____

Date:_____

PedsQL™

Paediatric Quality of Life Inventory

Version 4.0 & 3.0 – UK English

CHILD REPORT (ages **8-12**)

DIRECTIONS

On the following page is a list of things that might be a problem for you. Please tell us **how much of a problem** each one has been for you during the **PAST MONTH** by circling:

0 if it is **never** a problem
1 if it is **almost never** a problem
2 if it is **sometimes** a problem
3 if it is **often** a problem
4 if it is **almost always** a problem

There are no right or wrong answers.

If you do not understand a question, please ask for help.

*In the **PAST MONTH**, how much of a **problem** has this been for you ...*

About My Health and Activities *(PROBLEMS WITH...)*	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. It is hard for me to walk more than a couple of streets (about 100m)	0	1	2	3	4
2. It is hard for me to run	0	1	2	3	4
3. It is hard for me to do sports activities or exercise	0	1	2	3	4
4. It is hard for me to lift heavy things	0	1	2	3	4
5. It is hard for me to have a bath or shower by myself	0	1	2	3	4
6. It is hard for me to do chores around the house	0	1	2	3	4
7. I have aches and pains	0	1	2	3	4
8. I feel tired	0	1	2	3	4

About My Feelings *(PROBLEMS WITH...)*	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. I feel afraid or scared	0	1	2	3	4
2. I feel sad	0	1	2	3	4
3. I feel angry	0	1	2	3	4
4. I have trouble sleeping	0	1	2	3	4
5. I worry about what will happen to me	0	1	2	3	4

How I Get On with Others *(PROBLEMS WITH...)*	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. I have trouble getting on with other children	0	1	2	3	4
2. Other children do not want to be my friend	0	1	2	3	4
3. Other children tease me	0	1	2	3	4
4. I cannot do things that other children my age can do	0	1	2	3	4
5. It is hard to keep up when I play with other children	0	1	2	3	4

About School *(PROBLEMS WITH...)*	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. It is hard to pay attention in class	0	1	2	3	4
2. I forget things	0	1	2	3	4
3. I have trouble keeping up with my schoolwork	0	1	2	3	4
4. I miss school because of not feeling well	0	1	2	3	4
5. I miss school to go to the doctor or hospital	0	1	2	3	4

*In the past **ONE month,** how much of a **problem** has this been for you ...*

Pain	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. I ache or hurt in my joints and/or muscles	0	1	2	3	4
2. I hurt a lot	0	1	2	3	4

Nausea	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. I become sick to my stomach when I have medical treatments	0	1	2	3	4
2. Food does not taste very good to me	0	1	2	3	4
3. I become sick to my stomach when I think about medical treatments	0	1	2	3	4
4. I don't feel hungry	0	1	2	3	4
5. Some foods and smells make my stomach upset	0	1	2	3	4

Procedural Anxiety	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. Needle sticks (i.e. injections, blood tests, IV's) hurt me	0	1	2	3	4
2. I get scared when I have to have blood tests	0	1	2	3	4
3. I get scared about having needle sticks (i.e. injections, blood tests, IV's)	0	1	2	3	4

Treatment Anxiety	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. I get scared when I am waiting to see the doctor	0	1	2	3	4
2. I get scared when I have to go to the doctor	0	1	2	3	4
3. I get scared when I have to go to the hospital	0	1	2	3	4

Worry	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. I worry about side effects from medical treatments	0	1	2	3	4
2. I worry that my tumour will come back or relapse	0	1	2	3	4
3. I worry about whether or not my medical treatments are working	0	1	2	3	4

*In the past **ONE month,** how much of a **problem** has this been for you ...*

Cognitive Problems	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. It is hard for me to figure out what to do when something bothers me	0	1	2	3	4
2. I have trouble solving math problems	0	1	2	3	4
3. I have trouble writing school papers or reports	0	1	2	3	4
4. It is hard for me to pay attention to things	0	1	2	3	4
5. It is hard for me to remember what I read	0	1	2	3	4

Perceived Physical Appearance	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. I feel I am not good looking	0	1	2	3	4
2. I don't like other people to see my scars	0	1	2	3	4
3. I am embarrassed when others see my body	0	1	2	3	4

Communication	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. It is hard for me to tell the doctors and nurses how I feel	0	1	2	3	4
2. It is hard for me to ask the doctors and nurses questions	0	1	2	3	4
3. It is hard for me to explain my illness to other people	0	1	2	3	4

Parent / Guardian Questionnaire Pack[4]

There are a number of short questionnaires we would like you to complete. Below is a brief explanation of what each questionnaire is about.

1. **PACHIQ-R-P**: This questionnaire asks about the way you get on with your child

2. **Impact of Events Scale**: This asks about how the experience of having a child with a brain tumour has affected you

3. **Miller Behavioural Style Scale**: This questionnaire asks about the way you generally cope with stressful situations

4. **General Health Questionnaire**: This asks about your current general health and day-to-day functioning

5. **Strengths and Difficulties Questionnaire**: This asks about the strengths and difficulties you think your child has following his/her brain tumour

6. **PedsQL**: This questionnaire looks at how you feel your child is getting along since having a brain tumour

Just before you begin, please remember:

- There are **no** "right" answers to any of these questions. They are simply a quick way of getting an understanding your experiences and views which are very valuable to us.

- If at any point during the completion of these questionnaires you wish to discontinue you are free to do so without giving a reason.

- If there is anything that you would like to ask or if you have any worries or queries about any of the questions please contact any one of us about them (our contact details are on the information sheets).

[4] NOTE: Questionnaires 1-5 were included in the questionnaire packs as these were the measures used in the study by Bruce (2006) which was run in conjunction with the present study. These questionnaires have not been included here, as they are not relevant to the present study.

ID# _____

Date:_____

PedsQL™

Paediatric Quality of Life Inventory

Version 4.0 & 3.0 – UK English

PARENT REPORT for **CHILDREN** (ages **8-12**)

DIRECTIONS

On the following page is a list of things that might be a problem for **your child**. Please tell us **how much of a problem** each one has been for **your child** during the **past ONE month** by circling:

0 if it is **never** a problem
1 if it is **almost never** a problem
2 if it is **sometimes** a problem
3 if it is **often** a problem
4 if it is **almost always** a problem

There are no right or wrong answers.
If you do not understand a question, please ask for help.

*In the past **ONE month,** how much of a **problem** has your child had with ...*

Physical Functioning ***(PROBLEMS WITH.....)***	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. Walking down the road a little bit	0	1	2	3	4
2. Running	0	1	2	3	4
3. Participating in sports or running	0	1	2	3	4
4. Lifting heavy things	0	1	2	3	4
5. Having a bath or shower by him or herself	0	1	2	3	4
6. Tidying up around the house	0	1	2	3	4
7. Having hurts or aches	0	1	2	3	4
8. Feeling very tired	0	1	2	3	4

Emotional Functioning ***(PROBLEMS WITH...)***	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. Feeling afraid or scared	0	1	2	3	4
2. Feeling sad or unhappy	0	1	2	3	4
3. Feeling angry or cross	0	1	2	3	4
4. Trouble sleeping at night	0	1	2	3	4
5. Worrying about what will happen to him or her	0	1	2	3	4

Social Functioning (PROBLEMS WITH...)	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. Getting on with other children	0	1	2	3	4
2. Other kids not wanting to be his or her friend	0	1	2	3	4
3. Getting bullied by other children	0	1	2	3	4
4. Not able to do things that other children his or her age can do	0	1	2	3	4
5. Keeping up when playing with other children	0	1	2	3	4

School Functioning (PROBLEMS WITH...)	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. Paying attention in class	0	1	2	3	4
2. Forgetting things	0	1	2	3	4
3. Keeping up with schoolwork	0	1	2	3	4
4. Having days off school because of not feeling well	0	1	2	3	4
5. Having days off school to go to the doctor or hospital	0	1	2	3	4

*In the past **ONE month,** how much of a **problem** has your child had with ...*

Pain	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. Aches in joints and/or muscles	0	1	2	3	4
2. Having a lot of pain	0	1	2	3	4

Nausea	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. Becoming nauseated during medical treatments	0	1	2	3	4
2. Food not tasting very good to him/her	0	1	2	3	4
3. Becoming nauseated while thinking about medical treatments	0	1	2	3	4
4. Not feeling hungry	0	1	2	3	4
5. Some foods and smells making him/her nauseous	0	1	2	3	4

Procedural Anxiety	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. Needle sticks (i.e. injections, blood tests, IV's) causing him/her pain	0	1	2	3	4
2. Getting anxious about having blood drawn	0	1	2	3	4
3. Getting anxious about having needle sticks (i.e. injections, blood tests, IV's)	0	1	2	3	4

Treatment Anxiety	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. Getting anxious when waiting to see the doctor	0	1	2	3	4
2. Getting anxious about going to the doctor	0	1	2	3	4
3. Getting anxious about going to the hospital	0	1	2	3	4

Worry	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. Worrying about side effects from medical treatments	0	1	2	3	4
2. Worrying that the tumour will reoccur or relapse	0	1	2	3	4
3. Worrying about whether or not his/her medical treatments are working	0	1	2	3	4

*In the past **ONE month,** how much of a **problem** has your child had with ...*

Cognitive Problems	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. Figuring out what to do when something is bothering him/her	0	1	2	3	4
2. Solving math problems	0	1	2	3	4
3. Writing school papers or reports	0	1	2	3	4
4. Difficulty paying attention to things	0	1	2	3	4
5. Remembering what he/she reads	0	1	2	3	4

Perceived Physical Appearance	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. Feeling that he/she is not good looking	0	1	2	3	4
2. Not liking other people to see his/her scars	0	1	2	3	4
3. Being embarrassed about others seeing his/ her body	0	1	2	3	4

Communication	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. Telling the doctors and nurses how he/she feels	0	1	2	3	4
2. Asking the doctors or nurses questions	0	1	2	3	4
3. Explaining his/her illness to other people	0	1	2	3	4

Appendix 6:

Neurological Severity Scale

NEUROLOGICAL SEVERITY SCORE (Ater et al., 1996)

A: Events Prior to Diagnosis

0-Mild symptoms not affecting mental status, without abnormality on neurological examination

1-Mild neurological symptoms and signs not affecting function performance status

2-Onset of seizures controlled by anticonvulsants; significant neurological deficit resulting in loss of developmental milestones

3-Near herniation requiring emergency ventriculostomy, respiratory arrest, status epilepticus > 1 hr, cerebellar fits with posturing; surgery done as emergency procedure because of signs of impending herniation (if more than one of these severe events occur, the score should be multiple)

B: Pre-existing neurological deficits

0-None

1-Pre-existing known borderline intelligence

2-Pre-existing neurological deficit from head trauma, central nervous system infection, or other (e.g. mental retardation caused by meningitis in earlier childhood, Down's syndrome, etc.); pre-existing visual or auditory impairment (for known pre-existing mental retardation, score 3=mild, 4=moderate, 5=severe).

C: Perioperative events

0-Biopsy only without any complication; no change between preoperative and postoperative neurological status

1-Craniotomy with open biopsy or attempted surgical resection; uneventful postoperative recovery with discharge in < 1 week

2-Postoperative period complicated by persistent fever, headache, or vomiting; hydrocephalus requiring shunting; syndrome of inappropriate secretion of antidiuretic hormone (SIADH) leading to seizures or requiring desmopressing (DDAVP); new neurological deficit not present preoperatively.

3-Impending herniation postoperatively requiring preoperative mannitol or second surgical resection; hypotension during surgery due to bleeding; postoperative central nervous system haemorrhage or infarction; not awakening postoperatively for >24 hrs; postoperative meningitis caused by identified organism (if more than one of these severe events occur, the score should be multiple).

D: Postoperative events, due to surgery

0-After discharge, neurological status continues to improve, no further seizures, not receiving anticonvulsants or dexamethasone after 1 month postoperatively

1-Same as above, but receiving anticonvulsant and/or tapering doses of dexamethasone >1month postoperatively, no generalised seizures.

2-Continued poorly controlled seizures; significant neurological deficits affecting performance status, e.g. hemiparesis, severe ataxia, visual/hearing impairment

3-Persistent mutism, somnolence, or hypothalamic dysfunction (temperature instability, hyperphagia, disordered thirst)

TOTAL SCORE =