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Caregivers' Experiences and Coping Strategies Relating to Patient's Subjective
Treatment-Related Cognitive Impairment following Haematopoietic Stem Cell
Transplant (HSCT)

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*Submitted in partial fulfilment of the requirements for the degree of
Doctorate in Clinical Psychology (D.Clin.Psy)*

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Chapter 1: Systematic Review

Psychological Factors Associated with Psychological Adjustment following Stem Cell Transplant

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ABSTRACT

Objective: The literature regarding correlates of adjustment to cancer is abundant; however there has been no systematic review of the literature to identify which psychological variables are associated with adjustment specifically to stem cell transplantation. The aim of this study was to identify the risk and protective factors for psychological adjustment to stem cell transplant. These factors can inform the development/implementation of specific interventions for this increasing population.

Method: Five databases were systematically searched for quantitative research articles examining associative/predictive factors of adults' psychological adjustment to Haematopoietic Stem Cell Transplantation (HSCT). A narrative synthesis was conducted. Studies were appraised for quality using the Downs & Black (1998) checklist for non-randomised studies.

Results: Eleven studies were identified reporting on a total of 2751 individuals. Seven studies were longitudinal and four were cross-sectional. All studies used correlation and/or regression approaches. A broad range of instruments were used to measure adjustment. No studies were rated as low quality. Evidence from moderate to high quality studies suggests that factors associated with poorer adjustment include avoidance-based coping strategies; high anxious preoccupation with the illness; lack of motivation to overcome the illness; low social support; high social constraint and pre-transplant distress/past psychiatric history. Factors associated with better adjustment include approach coping strategies, good social support, resilience, self-efficacy, optimism, a sense of coherence and a sense of personal control.

Conclusion: A psychosocial assessment should be performed at the point of diagnosis to identify individuals who may be at risk of poor post-transplant adjustment as a result of previous/current mental health, personality traits, coping style and level of support. The provision of interventions which enhance factors that are associated with good adjustment and modify factors associated with poor adjustment should be explored and made available to all potential transplant patients prior to commencing treatment.

Keywords: psychological adjustment, stem cell transplant

INTRODUCTION

A steady and gradual reduction in the mortality rate from cancer has occurred over the past few decades¹. This is attributable to earlier detection rates and more effective medical interventions². One intervention increasingly being used to treat a number of blood and bone marrow malignancies is haematopoietic stem cell transplantation, of which two types exist – autologous and allogeneic³.

In an autologous transplant, stem cells are harvested from the patient. In an allogeneic transplant they are harvested from a donor. Prior to receiving the transplant, patients receive high dose chemotherapy and, occasionally, total body irradiation (TBI) both of which are used to destroy unhealthy blood cells. Stem cells are then placed back into the body whereby they find their way back to the bone marrow and begin to make healthy blood cells again⁴. This is an increasingly successful treatment, however the intensity of the treatment has been found to cause considerable and prolonged distress, more so than might be experienced by other oncology patients with less intense treatment regimens³. Stressors include lengthy hospital stays, hospital readmission as a result of physical complications such as graft vs. host disease, fear of transplant failure and fear of death⁵. These treatment-related stressors have been found to contribute to psychiatric morbidity beyond that reported in the general oncology population⁶.

In the general oncology literature, approximately 40% of patients experience clinically significant levels of distress following cancer treatment⁷. This distress takes many forms including post-traumatic stress symptoms, depression and anxiety. Prevalence of depression has been reported to be around 10-25% by Cooke *et al.*⁶ and up to 40% by Carlson *et al.*⁸. The prevalence of anxiety and depression has been found to be four times greater than in the general population^{9,10}. Other researchers however have found anxiety and depression rates similar to those in non-patient populations¹¹.

Attempts to explain such differences in psychological adjustment to cancer has focused on demographic (age, sex, socio-economic status) medical (type of cancer, stage and severity of cancer and physical side effects) and psychosocial factors¹².

Among the psychosocial factors, one consistent finding is that patients who consider themselves well supported experience less distress and greater wellbeing than those with little support¹³. Another area of investigation includes dispositional factors such as coping styles and personality traits. In a study of advanced cancer patients, having controlled for functional status, Miller *et al.*¹⁴ found that optimism was strongly and positively associated with well-being and inversely related to distress, while avoidance coping was positively associated with distress. Similarly, van't Spiker *et al.*'s¹⁵ meta-analysis found that approach coping strategies contribute to positive adjustment while avoidant coping is associated with poorer adjustment. Other factors reported to affect post-transplant adjustment include pre-transplant distress. Research in organ transplantation has shown that pre-transplant psychiatric disorders are significant predictors of poor post-transplant quality of life (QoL)¹⁶. Similarly, high pre-surgery depression scores in breast cancer patients predict poorer post-surgical adjustment two years later¹⁷.

Because of the unique nature of the transplant experience, HSCT patients may be more likely to experience a higher prevalence of distress (anxiety, depression and post-traumatic stress symptoms) at the pre-transplant stage when compared to other oncology populations⁶. A prevalence of 50% of pre-transplant global psychological distress has been documented in the transplant population compared to 30% outwith the transplant population¹⁸. This distress has been documented to persist for up to 5 years post-transplant with up to 36% of patients reporting moderate to severe depressive symptoms during the first year following transplant¹⁹ and 19% reporting mild depressive symptoms at five years post-transplant²⁰. The experience of such distress has been associated with decreased quality of life⁶.

In view of the increasing success and use of stem cell transplantation, and the acknowledgment of the prevalence and longevity of distress in this population, it would be clinically beneficial to systematically review the literature on psychological risk and protective factors associated with psychological adjustment. A better understanding of these factors can help to identify those at risk of developing psychological morbidity. This can then inform the content of interventions to help

patients manage the psychological consequences they may experience as a result of the treatment.

Although a broad concept, psychological adjustment can be described as 1) the absence of psychopathology such as anxiety, depression and trauma symptoms or 2) the presence of wellbeing as indicators of positive adaptation (e.g. self-esteem, self-efficacy, quality of life and life satisfaction)²¹. In addition, as social support has been conceptualised as a form of coping in that it aids individuals, when social support is measured as a factor associated with adjustment it will also be reported on²².

Research question

What psychological factors are associated with psychological adjustment following stem cell transplant?

METHODS

Search strategy

Five databases (Medline, Embase, CINAHL, Psyc Info and the Cochrane Database) were searched in April 2016 by the researcher. Articles pertaining to psychological adjustment and stem cell transplant were identified by using the following search terms. These were developed in consultation with a librarian from the Greater Glasgow and Clyde Maria Henderson Library and with a clinician working in Oncology Services at the Beatson West of Scotland Cancer Centre (BWoSCC). Medical Subject Headings (MeSH) 'bone marrow transplantation' OR 'hematopoietic stem cell transplantation' were combined with keywords which included 'bone marrow adj2 transplant*' OR 'hematopoietic adj2 stem cell transplant*' OR 'haematopoietic adj2 stem cell transplant*'. These terms were combined with MeSH terms 'adaptation psychological' OR 'emotional adjustment' OR 'coping behaviour' OR 'mental stress' and key words 'emotional or psychological' adj 'wellbeing or coping'. The search was limited to adult human subjects and English language (See Appendix 1.2 for a full search strategy).

To increase the sensitivity of the search the reference lists of included studies were hand searched for further articles. No further articles were found following the hand search. The researcher independently screened first by title, then by abstract and finally by reading the full text of articles. Studies that did not meet the inclusion criteria were excluded with reasons provided at the full text level. See Figure 1 for an illustration of the systematic selection process.

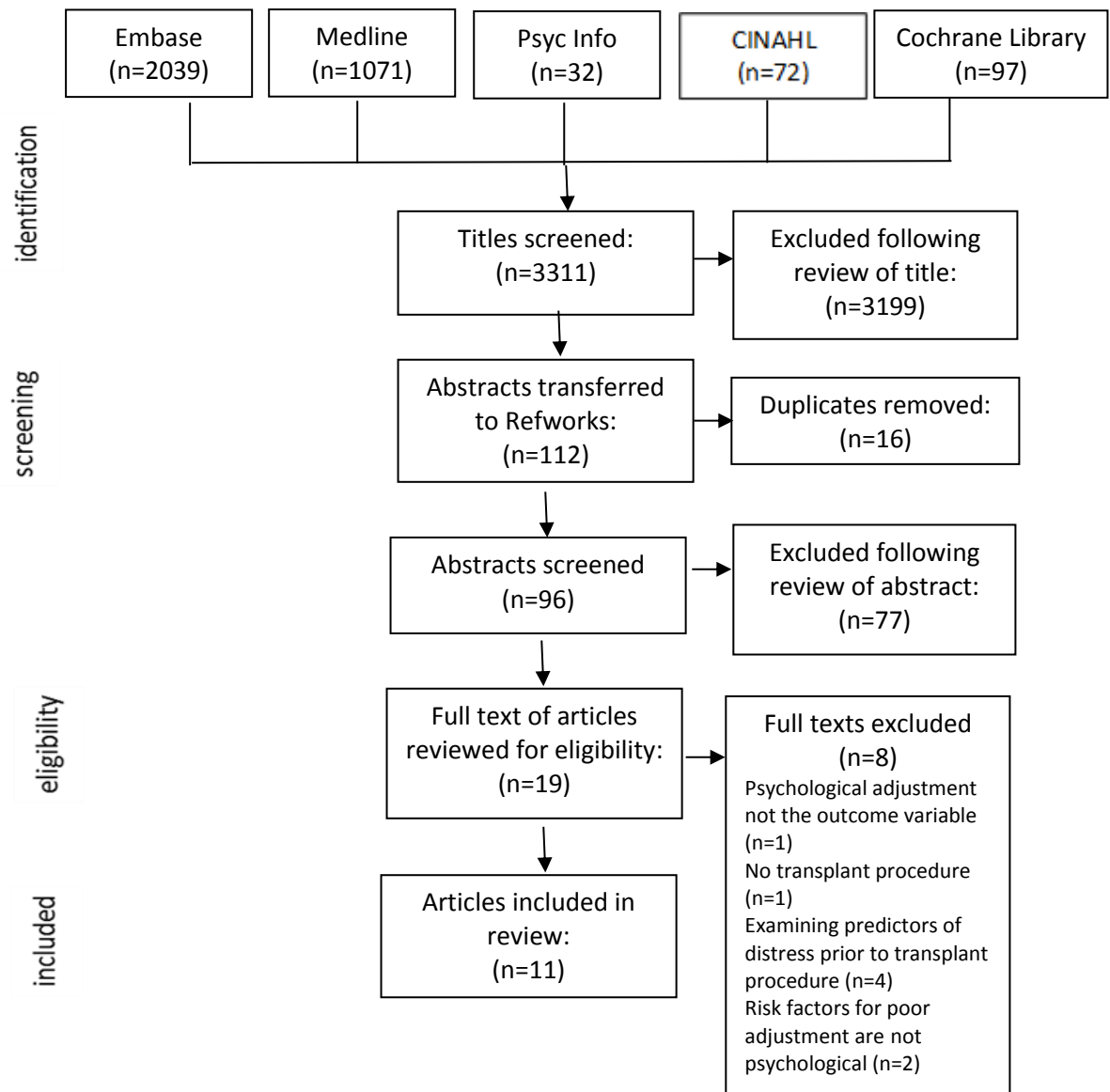


Figure 1. Flow diagram of the systematic selection process.

Inclusion and exclusion criteria

Articles were included if they explored psychological variables associated with psychological adjustment (consistent with the definition given in the introduction) to a bone marrow transplant (BMT) or haematopoietic stem cell transplant; were published in English, using quantitative methods and published in a peer reviewed journal. Articles were excluded if there was no reference to transplant procedure as part of the cancer treatment e.g. chemotherapy only; if no measures of psychological adjustment were reported; if only non-psychological (i.e. physical and demographic) variables were studied as associates of adjustment; if they employed qualitative methods and if they were reviews, case studies, dissertations or conference proceedings. See Appendix 1.3 for reasons for exclusion at the full text level.

Data extraction and quality assessment

It is accepted that there is no one single approach to assessing quality that is appropriate for all types of systematic review²³. The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) suggests using a domain approach that illustrates common sources of bias that may influence results. A modified version of the checklist developed by Downs and Black (1998)²⁴ was used to assess the methodological quality of the included studies (Appendix 1.4). The National Collaborating Centre for Methods and Tools has recognised this as a valid and reliable quality rating tool for non-randomised studies²⁵. In addition, a systematic review of the methodological quality of assessment tools for non-experimental studies reported that Downs and Black (1998) checklist assesses five of the six content domains considered essential when assessing methodological quality (with the exception of funding) and it is suitable cross-sectional designs²⁶.

No experimental studies were included in this review; therefore, nine of the 27 questions relating to intervention studies were removed from the checklist (questions 4, 7, 8, 13, 14, 15, 19, 23, and 24). This left 18 items which were given a score of '1' if the study met the criteria and '0' if the study did not, or if it was not possible to determine whether the study met the criteria based on the information provided. Following these modifications, the maximum possible score was 18. Articles with a score of ≥ 14 (75% of the maximum attainable score) were classified as high quality, those with a score of 9-13 (50-74%) were classified as moderate quality and those with

a score of ≤ 8 (below 50%) were classified as low quality. Inter-rater reliability was achieved by having an independent rater review 55% of the included papers (n=6). Overall agreement was 91%. Any disagreements were resolved through discussion (See Appendix 1.5 for quality ratings of included studies).

RESULTS

Participant Characteristics

The studies reported on 2751 patients who had undergone BMT or HSCT (1414 males, 1337 females). Rosenberg *et al.*²⁷ who recruited 1823 patients skews this number. Ages ranged from 18-76, although Hochhausen *et al.*²⁸ did not report age ranges. One thousand and forty-eight patients received an autologous transplant, 1632 received an allogeneic transplant. Goetzman *et al.*²⁹ did not report the transplant type. Ethnicity was not reported by four studies²⁹⁻³². When ethnicity was reported, the majority were white (n=2186).

Assessment of psychological adjustment

Psychological adjustment was measured in a number of different ways in the included studies. These include the absence of anxiety, depression, anger, uncertainty and PTSD symptoms; presence of quality of life, life satisfaction, social and emotional wellbeing and self-efficacy. As a result, there was considerable variability in the instruments used to measure adjustment. Fourteen different measures were used, four more commonly. Four studies used the PTSD Checklist Civilian Version (PCL-C)³³⁻³⁶; three studies used the Hospital Anxiety and Depression Scale (HADS)³¹⁻³³; three studies used the Medical Outcomes Short Form-36^{27,29,34} and two studies used the Centre for Epidemiological Studies of Depression (CES-D)^{28,37}. (See Appendix 1.6 for a full list of outcome measures used). Due to the heterogeneous nature of the studies identified in terms of description and measurement of adjustment and study design, a narrative synthesis was considered more appropriate than a meta-analysis.

Study characteristics and methodological quality

Among the studies, four were cross-sectional^{27,31,35,36} and seven were longitudinal^{28,29,30,32,33,34,37}. Warchala *et al.*³² did not report the time points examined, only reported 'pre and post BMT'. No studies were conducted in the UK. The quality of studies ranged from 13-18, with a median of 15. Two studies received 'moderate quality' scores^{30,32}. The remaining nine studies received 'high quality' scores^{27,28,29,31,33,34,35,36,37}.

Methodological shortcomings in both 'moderate quality' studies arose from being unable to determine the representativeness of the population. This was owing to a lack of information regarding the proportion of people who were asked to participate but declined, compared to the proportion who were asked to participate and agreed to take part. As the characteristics of those who did not take part were not described, it was not possible to determine if those invited versus those recruited differed in any way. In addition, it was also unclear if potential confounding variables such as medical and demographic factors were investigated or controlled for in the analysis. Furthermore, there was a lack of clarity from Warchala *et al.*³² regarding how long after transplant follow up took place and if this was the same for all participants. One of Fife *et al.*'s³⁰ main findings was not presented in a table making it difficult to determine the importance of its contribution and its meaning in the context of the other results.

Synthesis of findings

Social support

Six studies examined relationship between social support and adjustment. A lower perception of support pre-transplant was associated with increased PTSD symptom severity post-transplant³⁴ as was an increased perception of social constraint (an unsupportive environment)³⁶. Low social support was also predictive of poor general life satisfaction at one year post-transplant²⁹. Good social support was a predictor of emotional wellbeing and reduced post-transplant depression²⁸, negatively correlated with post-transplant depression³⁰ (the availability of material aid in particular)³⁷ and associated with reduced anxiety, anger and uncertainty³⁰.

Coping strategies

Five studies examined the relationship between coping strategy and adjustment. Two studies found an association between avoidant coping (behavioural disengagement, denial, distraction³⁶ cognitive avoidance, resignation, seeking alternative rewards)³⁴ and PTSD symptom severity. The remaining three studies found a relationship between avoidant coping on post-transplant anxiety³⁰ and depression^{32,37}. Wells *et al.*³⁷ found that post-transplant anxiety was positively correlated with the use of avoidance coping, in particular, resignation. Similarly, Warchala *et al.*³² found that post-transplant anxiety was significantly predicted by pre-transplant lower 'fighting spirit' (motivation regarding overcoming the illness). Post-transplant depression was predicted by lower 'fighting spirit' and high anxious preoccupation regarding the illness pre-transplant. Conversely, depression was negatively correlated with approach coping strategies such as problem solving³⁷ and positive reframing³⁰.

Jacobson *et al.*³⁴ found an interaction between coping and social support. At high levels of avoidance coping, those with low social support had more severe PTSD symptoms than those who were high in both avoidance coping and high in social support. This accounted for 7% of the variance in PTSD symptoms not already explained by social support, avoidance coping and psychological distress mentioned above. Conversely, at a low level of avoidance coping there was no significant relationship between social support and PTSD symptom severity.

Pre-transplant distress/past psychiatric history

Five studies examined the relationship between pre-transplant distress or psychiatric history on adjustment. Two studies found that a past psychiatric history (anxiety or mood disorder) was associated with increased severity of PTSD symptoms post-transplant^{34,36}. Jacobson *et al.*³⁴ found that this accounted for 30% of the variability in PTSD symptom severity. Two studies found that those most distressed pre-transplant (anxiety and anger) continued to be most distressed at post-transplant³⁰ and those most distressed pre-transplant (anxiety and depression) continued to be most distressed post-transplant when compared to non-distressed patients (81% vs 13%)³³.

Goetzman *et al.*²⁹ found that pre-transplant distress was predictive of poor general life satisfaction post-transplant.

Optimism

Two studies examined the relationship between optimism and adjustment. Results revealed that high optimism pre-transplant is a significant predictor of low anxiety²⁹ and depression^{28,29} and higher social and emotional wellbeing post-transplant²⁸.

Resilience

Two cross-sectional studies examined the relationship between resilience and adjustment. They found a negative relationship between resilience and anxiety and depression^{27,31} and a positive relationship between resilience and mental health related QoL, global QoL and self-efficacy³¹. Furthermore, individuals grouped as 'highly resilient' based on a median split were found to have higher QoL, emotional functioning, self-efficacy and lower anxiety and depression than less resilient individuals³¹.

Sense of coherence/global meaning

Two studies examined the relationship between a sense of coherence, a concept that Park and Folkman (1997) labelled 'global meaning' defined as "the general sense that one's life has purpose and coherence" on adjustment (Johnson-Vickberg *et al.*³⁵ p.30). They found that global meaning was inversely related to anxiety and depression^{29,35}, inversely related to BMT related distress (PTSD symptoms associated with transplantation)³⁵ and positively related³⁵/predictive²⁹ of low anxiety and depression post-transplant.

Self-efficacy

Hochhausen *et al.*²⁸ found that higher self-efficacy was a significant predictor of social and emotional wellbeing and lower depression severity one year post-transplant.

Personal control

Fife *et al.*³⁰ found that personal control accounted for 50% of the variance in anxiety, depression, anger and uncertainty at one year post-transplant.

Table 1. Summary of factors associated with psychological adjustment

Associated factors	Post-transplant adjustment
Pre-transplant: <ul style="list-style-type: none"> • avoidance coping • low social support • high social constraint • distress (anxiety, depression) Past psychiatric history (anxiety or mood disturbance)	Increased PTSD
Pre-transplant sense of coherence/global meaning	Decreased PTSD
Pre-transplant: <ul style="list-style-type: none"> • avoidance coping • anxiety • low fighting spirit Post-transplant anxious pre-occupation	Increased anxiety
Resilience Pre and during transplant personal control Pre-transplant: <ul style="list-style-type: none"> • Social support • Optimism • Sense of coherence/global meaning 	Decreased anxiety
Pre-transplant: <ul style="list-style-type: none"> • Depression • low fighting spirit Post-transplant high anxious preoccupation	Increased depression
Pre-transplant: <ul style="list-style-type: none"> • approach coping • social support • optimism • sense of coherence/global meaning • self-efficacy Pre and during transplant personal control Resilience	Decreased depression
Resilience	Increased quality of life
Resilience	Increased self-efficacy
Pre transplant: <ul style="list-style-type: none"> • Anxiety • Depression • Low social support 	Decreased life satisfaction
Pre-transplant: <ul style="list-style-type: none"> • Social support • optimism • self-efficacy 	Increased social/emotional wellbeing
Pre and during transplant personal control During transplant family support Pre-transplant approach coping	Decreased anger
Pre and during transplant personal control During transplant family support Pre-transplant approach coping	Decreased uncertainty

Although the focus of this review was to determine what factors are associated with post-transplant adjustment, two studies examined factors associated with pre-transplant distress. Given that the included studies have found an association between pre-transplant distress and post-transplant adjustment, these findings are worth noting. Warchala *et al.*³² found that pre-transplant anxiety was predicted by high anxious pre-occupation, low 'fighting spirit' and low optimism. These factors accounted for 51% of variation in pre-transplant anxiety. Similarly, pre-transplant depression was predicted by low global quality of life and low 'fighting spirit', accounting for 36% of variation in pre-transplant depression. Wells *et al.*³⁷ found that higher avoidance coping and lower social support explained 24% of the variance in pre-transplant depression and 26% of the variance in pre-transplant anxiety.

Table 2. Data extraction table of studies investigating psychological factors associated with psychological adjustment following stem cell transplant.

Author, year origin	Quality rating	Sample characteristics	Design / Measurement points	Psychological adjustment outcome measure	Associated factors measures	Results
Fife et al. (2000) USA	13/18	N=100 Male -67 Female-33 Age range-20-59 Autologous-78 Allogeneic-22 Multi-site	Longitudinal T1- baseline pre- transplant T2-1-2 days pre- transplant T3-7 days post- transplant T4-14 days post- transplant T5-1 month post- transplant T6-3 months post- transplant T7-1 year post- transplant	Depression, anger, anxiety, uncertainty (Bi-Polar POMS)	Perception of social support (PFPFSS + HCPSS) Coping style (WCC) Perception of personal control in life (Mastery Scale) Perception of impact of transplant on life (MIS)	-Greater personal control, associated with reduced anxiety, depression anger and uncertainty from T3 to T7. -Individuals most distressed at baseline were most distressed 1 year post-transplant (anxiety $r=0.28$ and anger $r=0.40$ only) At time points T3/T4: -avoidant coping associated with increased anxiety. -approach coping (positive re-framing) associated with reduced depression, anger, uncertainty. -family support associated with reduced anxiety, depression, anger, uncertainty.
Goetzmann et al. (2007) Germany	15/18	N=76 (28 BMT patients) Male-49 Female-27 Age range 18-67 Single centre	Longitudinal T1-2 days prior to hospital stay T2-1 year post- transplant	Overall quality of life mental health subscale (SF-36) Questions on Life Satisfaction questionnaire	Extent to which it is believed ones environment is predictable/explicable and resources can meet demands (SOC-13) Optimism (LOT) Anxiety and depression (HADS) Perceived and anticipated social support (F-SozU)	-high sense is of coherence pre-transplant is predictive of better mental health ($\beta=0.36$) post-transplant. -high optimism pre-transplant is a predictor of good mental health post- transplant ($\beta=0.26$). -anxiety ($\beta=0.37$) depression ($\beta=-0.30$) and low social support ($\beta=0.39$) are predictors of poor general life satisfaction post-transplant.

Author, year <i>origin</i>	Quality rating	Sample characteristics	Design / Measurement points	Psychological adjustment outcome measure	Associated factors measures	Results
Hochhausen et al. (2007) <i>USA</i>	14/18	N=87 Male-46 Female-41 All allogeneic Multi-site	Longitudinal T1-Baseline (four days prior to transplant T2-1 year post- transplant	Depression (CES-D) Health Related Quality of Life in cancer patients (FACT -G)	Social support (MOS) Optimism (LOT) Self-efficacy (CBI-L)	-higher social support ($\beta=0.368$), higher optimism ($\beta=0.256$), higher self- efficacy ($\beta=0.417$) all significant predictors of HRQoL and lower scores on the CES-D ($\beta=-.370$), ($\beta=-0.235$) and ($\beta=-0.422$) respectively.
Jacobson et al. (2002) <i>USA</i>	14/18	N=70 Male-16 Female-54 Age 23-65 White non-hispanic – 93% Autologous-83% Allogeneic-17% Country-USA Site not reported	Longitudinal T1-1 month pre- transplant T2-5 months post- transplant	DSM-IV PTSD symptom criteria (PCL-C)	Coping responses (CRI) Psychological distress (anxiety, depression, anger) (POMS) Social support (ISEL-SF)	-Higher avoidance coping ($\beta=0.24$) and lower social support ($\beta=0.26$) pre-transplant related to increased PTSD symptom severity. -Higher psychological distress pre-transplant ($\beta=0.55$) related to greater PTSD symptom severity.

Author, year <i>origin</i>	Quality rating	Sample characteristics	Design / Measurement points	Psychological adjustment outcome measure	Associated factors measures	Results
Lee et al. (2005) <i>USA</i>	15/18	N=61 Male-31 Female-30 Age range 20-72 White- 60 Autologous-27 Allogeneic-34 Single centre	Longitudinal T1-Prior to hospital admission T2-first clinic visit after discharge T3-100 days post- transplant	Depression (BDI-II) Anxiety and depression (HADS) DSM-IV PTSD symptom criteria (PCL-C)	Depression (BDI-II) Anxiety and depression (HADS) DSM-IV PTSD symptom criteria (PCL-C)	-38 pre-transplant assessments returned – 21 (55%) in distressed range for anxiety and/or depression at pre-transplant. -Of the 21 distressed pre-transplant, 13/16 (81%) were still distressed post-transplant. -Of the 17 non-distressed 2 of 16 (13%) had become distressed. Therefore, those distressed pre-transplant are more likely to screen for distress post-transplant (81 vs 13%).
Rosenberg et al. (2015) <i>USA</i>	16/18	N=1823 Male-957 Female-866 Age range-24-76 White-1646 Asian-68 African/American-47 Non-hispanic-1737 Hispanic-47 Autologous-672 Allogeneic-1151 Total body irradiation (TBI)-795 No TBI-952 Single centre	Cross-sectional	Overall quality of life mental health subscale (SF-36) Anxiety, depression, cancer related distress (CTD)	Resilience (CDRS)	-resilience scores correlated with psychological distress ($r=-0.51$) and HRQoL composite score ($r=0.62$). -each additional resilience point associated with 0.8 higher mental composite score. -individuals reporting lowest quartile of resilience scores had the highest odds of psychological distress (odds ratio, 3.0; 95% CI, 2.1-4.3).

Author, year origin	Quality rating	Sample characteristics	Design / Measurement points	Psychological adjustment outcome measure	Associated factors measures	Results
Warchala et al. (2015) Poland	13/18	N=60 Male-26 Female-34 All allogeneic transplants Single centre	Longitudinal Time points not reported	Anxiety and depression (HADS)	Acceptance of Illness (AIS) Anger, depression, anxiety expression (CECS) Coping responses in patients with cancer (MAC) Optimism (LOT)	-pre-transplant anxiety predicted by high anxious preoccupation ($\beta=0.23$) low 'fighting spirit' ($\beta=-0.20$) and low optimism ($\beta=-0.09$). These explained 51% of variation in pre-transplant anxiety ($R^2=0.51$). -post-transplant anxiety predicted by pre-transplant anxiety ($\beta=0.43$), low pre-transplant 'fighting spirit', ($\beta=-0.10$) and post-transplant high 'anxious preoccupation' ($\beta=0.05$) These explained 77% of variation in post-transplant anxiety ($R^2=0.77$). -pre-transplant depression predicted by low 'fighting spirit' ($\beta=0.14$), low global quality of life ($\beta=0.22$). These explained 36% of variation in pre-transplant depression ($R^2=0.36$). -post-transplant depression predicted by low pre-transplant 'fighting spirit' ($\beta=0.14$), high pre-transplant depression ($\beta=0.07$) high post-transplant 'anxious preoccupation' ($\beta=0.38$), low post-transplant global QoL ($\beta=0.10$) and low pre-transplant QoL ($\beta=0.12$). These explained 81% of variation in depression post-transplant ($R^2=0.81$).
Wells et al. (2009) USA	16/18	N=212 Male-113 Female-101 (discrepancy here) Age range 21-73 White non-Hispanic-181 African american-20 Hispanic-11 Autologous-172 Allogeneic-42 Single centre	Longitudinal T1-pre-transplant T2-6 months post-transplant	Depression (CES-D) Anxiety (STAI -SAS)	Coping responses (CRI) Social support (ISEL-SF)	<u>Coping:</u> -pre-transplant depression positively correlated with cognitive avoidance ($r=0.23$) resignation ($r=0.32$) and negatively correlated with problem solving ($r=-0.15$). -pre-transplant anxiety positively correlated with cognitive avoidance ($r=0.33$) and resignation ($r=0.36$). -post transplant anxiety was positively correlated with resignation ($r=0.19$). <u>Support:</u> -pre-transplant depression negatively correlated with tangible ($r=-0.29$) appraisal ($r=-0.25$) belonging support ($r=-0.25$) -pre-transplant anxiety negatively correlated with tangible ($r=-0.27$) appraisal ($r=-0.21$) belonging support ($r=-0.24$) -post-transplant depression negatively correlated with tangible support ($r=-0.15$).

Author, year origin	Quality rating	Sample characteristics	Design / Measurement points	Psychological adjustment outcome measure	Associated factors measures	Results
						<u>Support & coping</u> -higher resignation ($\beta=0.27$), lower problem solving ($\beta=-0.18$), lower perception of tangible ($\beta=-0.16$) and belonging support ($\beta=-0.13$) associated with increased depression pre-transplant. -higher resignation ($\beta=0.25$) higher cognitive avoidance ($\beta=0.16$) and lower tangible ($\beta=-0.14$) and belonging ($\beta=-0.17$) support associated with increased pre-transplant anxiety.
Widows et al. (2000) USA	18/18	N=102 Male-23 Female-79 Age range 21-70 White-91% Allogeneic-17% Autologous-83% Single centre	Cross-sectional	Assessment of Axis 1 psychiatric disorders on DSM-IV criteria non- patient edition (SCID- I/NP) DSM-IV PTSD symptom criteria (PCL-C)	Coping styles (Brief COPE) Social support (ISEL-SF) Perception of constraint in discussing thoughts and feelings with others (SCS) Perceptions of trauma associated with BMT (TEQ – developed for this study)	<u>Past psychiatric history</u> Individuals with history of anxiety/mood disorder pre-transplant, reported greater PTSD severity ($M=33.22$, $SD=12.48$) than participants with no history ($M=28.36$, $SD=9.01$), $t=-2.16$. <u>Coping</u> increased use of avoidance based coping related to increased PTSD severity—behavioural disengagement ($r=0.34$) self-distraction ($r=0.21$), denial ($r=0.39$). <u>Social support</u> -Decreased perceptions of social support related to increased PTSD severity -tangible ($r=-0.36$), appraisal ($r=-0.21$), and belonging support ($r=-0.41$). -increased perceptions of social constraint from a significant other ($r=0.28$) and other people ($r=0.39$) related to higher PTSD severity.

All reported results were indicated to be statistically significant in original articles at $p<0.05$ level or below.

DISCUSSION

This is the first systematic review of the literature to identify psychological factors associated with post-transplant psychological adjustment to stem cell transplant. Factors associated with poorer adjustment i.e. an increase in psychological distress include avoidance-based coping strategies; high preoccupation with the illness; lack of motivation to overcome the illness; lack of social support and pre-transplant distress/past psychiatric history. Factors associated with better adjustment include good social support, resilience, self-efficacy, optimism, a sense of coherence and a sense of personal control.

Methodological critique of included studies

Limitations of the studies included relatively small sample sizes, apart from Rosenberg *et al.*²⁷ whose sample accounted for over 50% of all participants in the review. Patient attrition is a problem commonly found in studies of cancer patients, often owing to symptom burden or mortality³⁸. Participant attrition resulted in only 48% of Fife *et al.*'s.³⁰ sample completing final questionnaires, 47% of Goetzman *et al.*'s.²⁹ and 45% of Lee *et al.*'s.³³ sample. Attrition also arose from a desire not to take part. Participants reported no longer wanting to think about it³⁰ or wanting to move on³⁵. Similarly, a number of participants eligible to take part chose not to³⁴. Although the majority of studies determined that there were no significant differences between participants and non-participants with regards to demographic and medical factors (type of cancer, length of hospitalisation, transplant type) it is uncertain if there were differences between groups with regards to psychological variables. Together, these factors indicate a potential selection bias in that those who declined to take part and those who opted out during the study may have been experiencing greater distress. Furthermore, this may mean that those in most need of intervention are not being captured by research.

In addition, these relatively small samples comprise individuals with various diagnoses. Of those who reported cancer type, 18 types were reported, comprising individuals who had received different transplant types (autologous or allogeneic) and treatment regimens (chemotherapy and/or TBI). It is possible that different intensity of treatment regimens contribute to variability in the psychological adjustment of patients. For example, one might expect an individual who has undergone high dose conditioning chemotherapy, TBI and an allogeneic transplant (which is associated with a higher

incidence of mortality) to experience more distress. Predominantly single centre studies with little racial diversity and largely from the USA also limit the generalizability of the findings to individuals who have undergone stem cell transplantation from other ethnic groups and in other countries.

Four included studies were cross-sectional, all of which were rated as high quality. These studies found moderate to large relationships between resilience, a sense of coherence, avoidance coping and social support on psychological adjustment, however it is impossible to infer causality in these studies. These results do not illustrate whether low resilience predisposes an individual to poor adjustment, or whether poor adjustment affects self-reported resilience at that time point. Furthermore, it is possible that these variables are related owing to shared associations with another unmeasured variable. Nevertheless, these associations now identified can be more rigorously studied using longitudinal designs. The data collection points in the cross sectional studies also varied considerably in the time period since transplantation, between 3 months³⁶ to 11 years³⁵. Therefore psychological status may have been impacted by a number of life events/environmental stressors in the preceding months and years and cannot be solely attributed to BMT/HSCT. Widows *et al.*³⁶ attempted to account for prior psychopathology and/or life events which may contribute to psychological adjustment by using the Structured Clinical Interview for DSM-IV (SCID) to assess lifetime and current psychiatric diagnoses. They requested that participants separately consider their experiences of cancer diagnosis and treatment when responding to questions in order to distinguish PTSD symptoms related to their cancer experience from those related to other traumatic experiences.

Limitations of current review

This review noted heterogeneity in the measurement and description of psychological adjustment. Owing to the limited research in this area, it was not possible to limit the included studies to only those which defined psychological adjustment in one way e.g. absence of depression or to those which measured adjustment using one outcome measure e.g. BDI-II. Greater consistency regarding instruments used to measure adjustment would facilitate comparison across studies or the combination of results in a meta-analysis. A meta-analysis would help to overcome the small sample sizes in

cancer research therefore increasing the power to detect effect and in turn, provide a rational for the design/implementation of interventions to target those variables.

Conclusions

Consistent with previous general oncology literature, the current review found that good social support and optimism pre-transplant was associated with reduced distress post-transplant i.e. better adjustment, while avoidance coping was associated with increased distress i.e. poorer adjustment. The current findings also reflect those of organ transplantation research which found that pre-transplant psychiatric history and pre-surgery depression scores are associated with low post-transplant quality of life and poorer post-surgical adjustment respectively¹⁶. Additionally, one moderate quality³² and one high quality³⁷ study found that pre-transplant depression and anxiety were associated with high anxious pre-occupation, low motivation regarding overcoming the illness, low optimism, low global quality of life, low social support and high avoidance coping.

Recommendations for future research and practice

The finding that personal dispositions such as optimism and coping styles are associated with pre-transplant distress and that past psychiatric history and pre-transplant distress contribute to poorer post-transplant adjustment, together, suggest that it may be beneficial for all patients undergoing this treatment to complete a psychiatric history, routine screening for current psychological distress and an assessment of personality characteristics. This might identify those who are at risk of poor adjustment who can then be monitored and offered support throughout the treatment journey. Social support was consistently associated with better adjustment which highlights the need for a psychosocial assessment and provision of social support via health, social care and third sector services where required. Larger samples would enable more homogenous groups' to be studied e.g. comparing adjustment of allogeneic and autologous transplant patients to determine if different transplant/treatment regimens differentially affects adjustment. This systematic review has identified the factors associated with psychological adjustment to BMT/HSCT. Following on from this, the use of qualitative methods may help determine in what ways and in what context these factors are important and contribute to adjustment. This would also omit the use of commonly used self-report measures which are not specifically developed for this population.

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Chapter 2: Major Research Project

Caregivers' Experiences and Coping Strategies Relating to Patient's Subjective Treatment-Related Cognitive Impairment following Haematopoietic Stem Cell Transplant (HSCT)

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Plain English Summary

Caregivers' Experiences and Coping Strategies Relating to Patient's Subjective Treatment-Related Cognitive Impairment following Haematopoietic Stem Cell Transplant (HSCT)

Background

The treatments involved in cancers of the blood and bone marrow, such as stem cell transplantation can be physically and psychologically challenging and be associated with side effects such as memory and concentration difficulties, known as “chemo brain” (Evans & Eschiti, 2009). The severity of these side effects varies widely but when it occurs, it can significantly impact the patient's quality of life by interfering with their daily activities, relationships and future plans. Cancer has been described as a “family disease” which indicates that these challenges are also faced by the patients' loved ones. This has prompted a great deal of research exploring caregivers' experiences of caring for a loved one with cancer, however, no research so far has explored caregivers' experiences related specifically to the cognitive effects or “chemo brain” their loved one has experienced following stem cell transplantation.

Aims

The aims of this study were to investigate caregivers' experiences of the cognitive effects in their loved ones who have undergone stem cell transplant, how they coped with their experiences and what supports they believe could help.

Methods

The study involved interviewing five participants (all female caregivers) and asking them to describe their experiences. Two participants requested a face-to-face interview and three requested a telephone interview. The interviews were audio-recorded and then typed up word for word. This was then analysed for experiences shared by participants.

Findings

The results illustrated 4 main themes shared by participants.

1. Noticing change. Caregivers' experienced increasing recognition of their spouse's memory difficulty which initially went unnoticed. This was also accompanied by an increasing recognition of a change in their spouse's behaviour. This included a lack of confidence in themselves and a desire to isolate themselves.
2. Managing expectations. Caregivers' experienced uncertainty about their future. There was concern regarding how the changes in their spouse would affect their lives. Caregivers dealt with this uncertainty by planning for the future, trying to prevent deterioration of their spouse's memory and trying to keep their day-to-day lives as normal as possible.
3. Managing personal feelings. Caregivers' experienced a sense of loss. Loss of their partner, loss of friendships and loss of aspirations for the future. They also experienced frustration with their spouse's limitations. They dealt with this frustration by reminding themselves the limitations were not their spouse's fault. They also coped with these feelings by talking to others, distracting themselves and making the most of their time together.

4. Commitment. Despite experiences of uncertainty, loss and frustration, there was a sense of enduring responsibility to their spouses.

Conclusions

The “next steps” booklet that patients receive explaining long term effects of HSCT could be supplemented with a discussion with patients and their partners/family members about potential late side effects of treatment, such as changes in memory and behaviour. This might help caregivers to feel more prepared and reduce the uncertainty they experience. Caregivers and patients are likely to have different needs, therefore future research should consider exploring the experiences of individuals as a couple in order to identify any mutual needs, where interventions are likely to create optimum impact.

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ABSTRACT

The treatments involved in cancers of the blood and bone marrow can be physically and psychologically challenging and be associated with adverse secondary effects, including cognitive impairment. The incidence and severity of treatment-related cognitive impairment varies widely, however it can significantly impact quality of life by interfering with patients' activities of daily living, relationships and future plans. It can also pose challenges for the patients' caregivers, an area which has received comparatively less research attention. The aim of this study was to investigate caregivers' experiences of treatment-related cognitive impairment in patients who have undergone Haematopoietic Stem Cell Transplant (HSCT); how they coped, both practically and emotionally, and what supports they believe could help them. Participants were caregivers to individuals who had undergone HSCT within the past 20 years and who had reported cognitive changes at the HSCT Late Effects Clinic, Beatson West of Scotland Cancer Centre. Five participants completed a single semi-structured interview. The data was then analysed using Interpretative Phenomenological Analysis (IPA). Results of this analysis illustrated four super-ordinate themes: noticing change; managing expectations, managing personal feelings and commitment. Findings from the current study highlighted the importance of caregiver education regarding post HSCT cognitive and behavioural changes and providing caregiver emotional support. Future research should explore the mutual needs of both care recipient and caregiver.

INTRODUCTION

More than one in three people in the UK will develop some form of cancer during their lifetime, of which there are more than 200 types, each with different causes, symptoms and treatments¹. For many cancers, the treatments involved can be physically and psychologically challenging and associated with lasting adverse secondary effects².

Approximately 26,700 cases of the three most common blood cancers (leukaemia, lymphoma and myeloma) are diagnosed in the UK every year, 94% of which occur in adults¹. Haematopoietic Stem Cell Transplant (HSCT) can be used to treat these diseases. Allogeneic stem cell transplant involves transferring stem cells from a healthy person (the donor) to the affected individual following their conditioning therapy (high-intensity chemotherapy and/or total body irradiation). This treatment is highly burdensome. Even an 'uncomplicated' allogeneic HSCT may involve up to 4 weeks hospitalization and up to 4 months outpatient management³. Physical and psychological recovery may take several years for HSCT recipients and for some, cure of the cancer may not be accompanied by full restoration of health⁴.

In addition to physical complications, patients may experience cognitive difficulties, often referred to as "chemo brain"⁵ (p.661) long after their treatment has ended. Changes commonly occur in the domains of executive functioning, memory and attention⁶. For some patients, cognitive impairment is present up to twenty years following treatment⁷. This is most often seen in patients who require high dose chemotherapy and/or total body irradiation⁸. The exact incidence of its occurrence is unknown, however at present it is estimated that treatment-related cognitive impairment affects between 17-78%⁷. Changes can occur as early as the first chemotherapy session and/or accumulate and develop over subsequent treatments⁹.

In a two year prospective study of cognitive functioning on 242 HSCT recipients and 98 healthy controls, Bosworth and Bhatia¹⁰ found that executive functioning,

processing speed and verbal fluency were all significantly worse in HSCT participants. With regards to the duration of symptoms, Booth-Jones *et al.*¹¹ examined patients six months after HSCT, finding at least mild cognitive deficits in 51% and moderate to severe impairment in 28%. As evident in the aforementioned studies, for those who do develop treatment-related cognitive impairment, the duration and severity are highly variable. Nevertheless, even mild cognitive difficulties can have practical and psychological consequences⁹. Jim *et al.*'s.¹² study exploring what patients' wish they had known about quality of life following allogeneic HSCT revealed a desire for education about late effects as these were experienced as unexpected and were reported to have significantly impacted their quality of life. One respondent noted *"...that's what I am hoping will come out of this [study], is that you have support groups that would focus on key areas: neurological side effects, orthopaedic side effects, you know, mental emotional side effects."*¹²(p.301).

Cancer has been described as a "family disease"¹³ (p.194) which indicates that challenges are rarely faced in isolation. Rather, caregivers must adapt. Recognition of this has prompted a great deal of research investigating caregivers' experiences of the caring for a loved one with cancer. During the acute phase of the transplant process caregivers report unmet needs such as finding time for themselves and ways to deal with the stress they are experiencing¹⁴. They also describe feeling responsible for their loved one's care and putting the needs of their loved one before their own³. Although this may be necessary during the acute transplant phase, this is likely to extend beyond the transplant period if late effects of treatment are experienced and may cause a relationship imbalance, and in turn, caregiver distress. Boyle *et al.*¹⁴ found that "dealing with physical and mental complications" (p.200) post-transplant was ranked most difficult by both caregiver and patient.

Equity theory is a useful framework for understanding the experiences of caregivers. This theory suggests that within a relationship, individuals strive to maintain a balance between what they provide and what they receive. It asserts that inequity in either direction causes distress and attempts to restore equity¹⁵. In oncology literature, the perception of being under benefitted (either because they provide too much for the patient or receive too little) has been linked to higher caregiver burden¹⁵. This theory has been supported by results of Langer *et al.*'s.¹⁶ study in which

caregivers report significant changes to marital dynamics, with approximately 49% experiencing decreased marital satisfaction one year following HSCT owing to caregiver burden, with female caregivers at greatest risk for decreased satisfaction¹⁶.

In the context of distress, Lazarus and Launier (1978) cited by Ogden¹⁷ describe coping as the process of managing stressors that have been appraised as exceeding an individual's resources. Coping skills can be categorised into three subtypes, appraisal focussed, problem focussed and emotion focussed. Research has indicated that several factors influence strategy selection. These include problem type, gender, controllability and resources. Findings from studies examining coping strategies in relation to caregiver distress indicate that avoidance coping (whether cognitive or behavioural) is consistently associated with higher levels of emotional distress¹⁸. Coping is typically thought of as an individual task, however, research has demonstrated that couples respond to stressors as units, rather than individuals¹⁹. One relationship-focussed coping strategy is 'protective buffering'. This involves strategies such as hiding anger, denying worries and avoiding disagreement. Langer *et al.*²⁰ found that increased buffering from caregivers to and from their loved one resulted in decreased relationship satisfaction and poorer mental health for both parties.

Advances in medicine have improved outcomes for HSCT patients, with more than 54% of patients surviving one year post-transplant compared to 42% ten years ago²¹. Given the increasing number of cancer survivors who have undergone HSCT, the clinical relevance of treatment-related cognitive impairment is considerable. Following the transplant, aftercare is provided at home and in 50-91% of the cases, the spouse is the primary caregiver¹⁸. As a result, the responsibility on the caregiver and their requirement to adapt to the changes in their spouse is ever increasing.

A body of research exists exploring patient's quality of life following HSCT¹²; the experiences of caregivers whose spouses are undergoing HSCT²² or in the acute phase of HSCT²³. To the author's knowledge, no study has examined caregivers experiences related specifically to the cognitive late effects their spouse has experienced following HSCT.

AIMS

The primary aim of this study was to investigate caregivers' experiences of treatment-related cognitive impairment in patients who have undergone a HSCT. Secondary aims included gaining an understanding of how the caregivers coped with their experiences and what supports they believe could help them.

SUBJECTS AND METHODS

Ethical considerations

The research project was assessed and sponsored by the West of Scotland Research Ethics Service (WoSRES). Ethical approval was also granted by the Beatson West of Scotland Cancer Centre (BWoSCC) Research Ethics Committee. Management approval was granted by NHS Greater Glasgow and Clyde Research and Development department. Approval for amendments to widen the recruitment procedure was granted. This allowed for information packs to be sent to patients who met the inclusion criteria but who had attended the Late Effects Clinic within the year prior to the study commencing.

Design

Interpretative Phenomenological Analysis (IPA) has been informed by three key philosophies: 1. phenomenology, a philosophical approach to the study of experience; 2. hermeneutics, a method of interpretation and 3. idiography, a focus on the particular or unique. IPA involves a two-stage process in which the researcher aims to explore what personal and social experiences mean to the individuals who experience them and to make sense of what the individual is telling us i.e. to make interpretations about those experiences²⁴. IPA is also being increasingly used in health psychology research owing to an increasing recognition of the constructed nature of illness and therefore, the importance of understanding individuals' perceptions and interpretations of illness²⁵. For both of these reasons, IPA was considered to be the approach most able to address the aims of this study. A semi-structured topic guide was developed following the guidelines by Smith *et al.*²⁴. Given the scarcity of reports of caregivers' experiences of cognitive impairment following HSCT, the topic guide was modelled on one which explored caregivers experiences of the neurocognitive and neurobehavioural changes associated with brain tumours²⁶.

Sample

In accordance with IPA methodology, purposive sampling was used. Participants (caregivers) were recruited from the Beatson West of Scotland Cancer Centre (BWOSCC) Late Effects Clinic. A caregiver was defined as the person who most often provides physical and emotional support to the patient. Clinicians working at the BWOSCC identified that in most cases, the primary caregiver is a partner or spouse. Consultant Haemato-oncologists and a Senior Nurse identified individuals who were a caregiver to somebody who:

- Reports experiencing a degree of cognitive impairment which they associate with their Bone Marrow Transplant. Cognitive difficulties are identified by using the 'Patient Distress Thermometer'. (This is a self-assessment which alerts clinicians to memory and concentration difficulties that the patient is experiencing).
- Has undergone total body irradiation, high dose chemotherapy or a combination of these within the last 20 years.
- Has no known psychiatric or neurological problems likely to lead to cognitive impairments e.g. schizophrenia, previous head injury, organic cognitive decline.
- Has no current use of psychotropic medication.
- Has no known learning disability.

Participants were excluded from the study if:

- Their loved one had received total body irradiation, high dose chemotherapy or a combination of these within the last year.
- Their loved one lacked the capacity to consent for their caregiver to take part.
- They did not speak fluent English.

Justification of sample size

IPA is an idiographic approach and therefore has a commitment to detail and depth of analysis when attempting to understand a particular phenomenon in a particular context. Consequently, the use of small sample sizes when employing IPA is recommended. According to Smith *et al.*²⁴, the typical number of interviews to be completed as part of a professional doctorate employing IPA is between four and ten. This allows the researcher to gain an in-depth understanding of the individual experiences of the participants²⁴. This recommendation is also in keeping with Braun and Clarke²⁷ who recommend carrying out enough interviews to demonstrate

patterns across a data set, whilst retaining a focus on the experience of individual participants.

Recruitment procedure

Patients who have undergone a Bone Marrow Transplant (BMT) attend the Late Effects Clinic annually to identify any difficulties they may be experiencing following their cancer treatment. These include physical, emotional, practical, spiritual and relationship difficulties. These are identified using the NHS Greater Glasgow & Clyde Haematopoietic Stem Cell Transplantation Services 'Patient Distress Thermometer'. Recruitment took place between February 2016 and June 2016. During this time, if any patient attending the Late Effects Clinic identified a memory or concentration difficulty, an information pack was given to them. Patients who did not attend the Late Effects Clinic between February and June 2016, but were known by the Clinical Team to have experienced these symptoms, were also provided with an information pack. This contained a cover letter detailing the rationale and aim of the study, information sheets for both the patient and their caregiver and a joint consent form to be signed by both parties. This ensured that caregivers could not take part without their spouse's permission (Appendices 2.9-2.12). Participants who returned their consent forms were contacted to arrange a suitable time to conduct an interview.

Telephone interviews were offered to all participants as it is recognised that caregivers to individuals who have undergone a HSCT have a number of competing demands and responsibilities²³. It was acknowledged that telephone interviews may result in the loss of non-verbal information which could impact upon rapport. Conversely however, it has been suggested that a telephone interview may allow the participant to feel more relaxed and comfortable to disclose sensitive information²⁸. In addition, as the unrelated allogeneic transplant service serves the whole of Scotland, it was hoped that a telephone interview would help facilitate participants to take part who lived some distance from Glasgow. Three of five participants chose this option.

Interviews took place at the BWoSCC in Glasgow. Participants completed a single interview lasting between 30 minutes to 70 minutes (mean 47 minutes). Telephone interviews also took place from the BWoSCC. Interviews were recorded (for

telephone interviews via a Sony Electret Condenser Microphone which enabled the recording of the conversation onto the digital voice recorder) and transcribed verbatim. To help ensure the validity of the interview guide, the first three interviews were anonymised and reviewed by the primary researcher and academic supervisor to ensure that they were eliciting data consonant with the aims of the study. The topic guide was thought to be appropriate and these three pilot interviews were used as part of the data set. The topic guide was used in further interviews without modification (Appendix 2.13). All further interviews were anonymised for references to people and places.

Data analysis and quality assurance

Datum were analysed using IPA. The six step process described by Smith *et al.*²⁴(p.82-106) was followed. See Appendix 2.16 for a description of the process of data analysis. Owing to the subjective nature of qualitative research, it is essential to be mindful of factors that are characteristic of high quality qualitative research. Yardley's²⁹ evaluative criteria include *sensitivity to context; commitment and rigour, transparency and coherence*, and *impact and importance*. See Appendix 2.17 for a description of the ways in which the principles of quality assurance were demonstrated in the current project.

RESULTS

The central phenomenon was the caregivers' lived experience of their spouse's cognitive impairment. Four super-ordinate themes emerged from the data: noticing change; managing expectations; managing personal feelings and commitment. These are shown in Table 1 with corresponding sub-ordinate themes where identified.

Table 1. Super-ordinate and sub-ordinate themes

Super-ordinate Themes	Sub-ordinate themes
Noticing change	<ul style="list-style-type: none"> • Cognitive change • Behavioural change
Managing expectations	<ul style="list-style-type: none"> • What will tomorrow bring? • An uncertain future • Cognitive remediation • Maintaining normality • Planning for the future
Managing personal feelings	<ul style="list-style-type: none"> • Loss • Frustration • It's not their fault • Nobody knows what it's like vs. I don't want them to know what it's like • Sharing responsibility • Beyond friends and family
Commitment	

NOTICING CHANGE

Cognitive change

The quotations below illustrate the insidious onset of their loved ones memory impairment or the caregivers increasing recognition of this over time, which initially goes unnoticed.

"It didn't come until I would say... I didn't even notice it, it was my daughter Lisa that noticed it, like you know, forgetting different things twice or three times "I don't remember where I put the key" and that... we went to see Dr eh, Mason,... he didn't think there was anything seriously wrong with him" (Liz, p1, lines 6-10).

"His memory is the main one, him not having a very good memory and that's deteriorated. Well, it wasn't so,... so obvious at the beginning but as we went on, later on, so that's the main issue" (Katie, p1, line 3-6) and "we were really worried, that's when we started looking into it and asking doctors and they said "oh, didn't you know that, yes, that's a side effect,... obviously he's thinking we already knew that information"(Katie, p2, lines 2-7).

"I mean, he's definitely more forgetful now, and ehm, he has a much shorter fuse, you know? But, at the time, I wasn't aware of that ehm, I suppose" (Paula, p1, line 5-6).

“His memory now is you know,... quite short. It’s just gradually, he would sort of, like if you send him for something, he’ll forget what he’s going for sometimes” (Tina, p1, lines 6-7).

Behavioural change

Although memory difficulties are recognised by caregivers, they also experience noticeable changes in their spouse’s behaviour, as a result of cognitive changes. The reporting of behavioural changes indicates that the memory problem itself is not the only difficulty, or the most salient difficulty for them.

“constantly being told I was wrong and things like that and... ehm, never quite coming up to the,... doing enough” (Ange, p2, lines 3-4) and “he wasn’t as laid back, he was, ehm,... he was kinda of a spiky energy” (Ange, p7, line 4).

“he just switches off a lot, you know, he just shuts down now” (Tina, p1, line 10) and “if there’s problem’s he’ll go and hide, he doesn’t want to know, he cannae deal wae a lot of things or anything anymore, or compared to what he used to” (Tina, p2, line 10).

“he just wisnae interested, wouldn’t go out, wouldn’t do nothing” (Liz, p2, line 2) and “he’s lost a lot of confidence in himself” (Liz, p7, line 15).

These changes affect the caregivers in a variety of ways. They include feelings of uncertainty regarding what the future holds and personal feelings such as a sense of loss and frustration.

MANAGING EXPECTATIONS

What will tomorrow bring?

Participants experienced ambiguity about their immediate future owing to what is perceived as unpredictable behaviour.

“There’s some mornings I’ve got up and I’ll say to myself, I wonder how he’ll be today?” (Liz, p13, line 9).

Although caregivers communicate these changes as unpredictable, from the content of their narrative they appear somewhat aware of the mediators of change. In the

examples below, the caregivers perceive these “unpredictable” changes as mediated by mood or environment.

“it’s unpredictable, there’s no kind of pattern...I find if he’s stressed about something as well, he tends to like,... if he knows he’s got something coming up, maybe an important thing... or if he’s got time limits on him, he gets more stressed, which then, he can’t remember” (Katie, p6, line 9-12).

“When Jake gets up I just wait to see what kinda mood he’s goni be in,... if he’s goni maybe speak, or if he’s just goni sit” (Tina, p4, line 8-9) and “then other times he could be, be good for a couple of weeks and then he’d go back to... it just depends on how he is feeling at the time” (Tina, p2, line 8).

An uncertain future

Participants experienced a fear of uncertainty about their future, with regards to possible deterioration in their spouse’s cognition and behaviour and the impact it may have on their lives.

“it really challenged our relationship” (Ange, p10, line 18) and “I didn’t know if it would survive” (Ange, p11, line 4).

“obviously it was a stressful time and how it affected me was I suddenly sort of thought “oh my god, this is terrible” you know, I’ve got two sons and I thought I’m going to be the breadwinner, I’m going to have to get this sorted out” (Paula, p3, lines 1-3).

“when we first found out about his memory it was quite upsetting, we could hardly speak to each other, both of us were scared, we didn’t know if it was goni have a long term effect, like was he goni deteriorate?” (Katie, p14, lines 13-16) and “it was a worry because we didn’t initially know how bad his memory was goni be, but we know that it’s capped and shouldn’t get any worse” (Katie, p8, lines 21-22).

Repetition regarding deterioration on two separate occasions indicates that possible deterioration was, and perhaps remains a concern. The use of the word “shouldn’t” stresses that Katie is aware that no further deterioration is not guaranteed and attempts to convince herself of this may be a way of coping with an uncertain future.

Caregivers dealt with this uncertainty and fear of deterioration in a number of ways. These include attempts to prevent further deterioration by using practical strategies to maintain cognitive functioning, attempts to maintain normality and planning for the future.

Cognitive remediation

"I surround him with memory things" (Katie, p1, line 21) and "we've tried wee games that he can play for his memory" (Katie, p5, lines 11-12).

"I put post it's up and I write everything down for him" (Liz, p6, line 24).

Maintaining normality

"He didn't want to go out, he wasn't like that either, he loved a night out but he didn't want to go and I says Robert you can't do this we need to go out" (Liz, p1, lines 16-17).

"so we just talk about our future, what we are going to do, where we are going to go, any countries we want to visit, just normal future kind of a conversations. We'd like another house,... ehm just our future goals and how we are goni get them" (Katie, p8, lines 22-24).

Planning for the future

"so I got a full time job because I just knew that we'd have to have a way forward, if the worst happened" (Paula, p3, line 4).

"You've always got to say, if this goes wrong, this is the plan and this is what we are goni do (Katie, p12, lines 22-23) and,...if you plan ahead yea, it's a lot better and less stressful...he knows what to expect from me and I know what to expect from him" (Katie, p13, lines 1-2).

MANAGING PERSONAL FEELINGS

Loss

As a result of the changes in their spouse, caregivers experience a sense of loss. The way repetition is used in the examples below, illustrate the severity of change ("*different*" and "*totally*") and difficulty accepting this change ("*couldnae*"). There is also a sense that guilt accompanies verbalising these feelings and validation by Tina's daughters may allow her to make this point with more of a clear conscience. The fact

that Ange thought her partner had really changed, and therefore asserting a fact, rather than a subjective feeling, may have allowed her to feel less guilty for expressing this point.

"he just... couldn't be bothered with us,... it was, it was total personality, just totally changed, he's like a different different different person. It's hard to explain because I feel as if,... well I've lost the person that I loved, you know what I mean? He's just totally totally changed,... he just totally,... he's not the person... that I married (Tina, p2, lines 21-24).

"I felt like Norman had really changed at that point, because, ehm, I think he had really changed" (Ange, p4, line 22).

"he's still very quiet, he's still very quiet, no the person he was" (Liz, p7, line 14) and "at the start, I couldnae, I couldnae,... fae the person he was to the person he went to be, I kept saying to myself "that's just no Robert", you know" (Liz, p9, line 3-4).

As a result of cognitive impairments, caregivers have also experienced a number of other losses such as social support and aspirations for the future. This appears as a result of spending more time with their loved one in a carer role; the patients social isolation owing to a change in affect and an inability to undertake employment owing to memory difficulties.

"when Jake shut down and didn't want anybody, ehm, to come, I lost all my friends (Tina, p4, lines 22-23) and "obviously because we never went out anywhere and I was in all the time with Jake" (Tina, p5, line 1).

"so it's quite stressful because we want to do things in the future and there's only one income coming in at the moment so it's quite....(tails off)" (Katie, p9, lines 19-20) and "financially it's a bit restricting,... it's a big restriction,...when you are young, you want to go out and work, to get a nice house, the things you aspire for are just capped, because of the financial constraints of Mike not being able to work" (Katie, p13, lines 16-20).

Frustration

Frustration is a common response to the behaviours displayed as a result of their spouse's limitations. This appears in response to maintaining normality, adjusting to their new role and the demands that accompany their spouse's limitations.

"He didn't want to go out and I says Robert, you can't do this, we need to go out" (Liz, p1, lines 17-18) and "I felt like I was doing everything really and Robert wisnae, he wasn't trying to help himself" (Liz, p10, lines 13-14).

"Sometimes you want to shake him and try and tell him, look, you have to pull your socks up because I need help and I'm dealing with everything" (Tina, p3, lines 3-4).

Frustration or anger appears to be more severe when the caregiver has a belief that the limitations or the subsequent behaviours are under their spouse's control.

"I do lose the rag wae him,...and he'll say, "aw Liz, I cannae help it", and I'll say "you can help it, you're only going fae here to our Kate's", "but I just forget" and then he'll say "I'm sorry" and I'll say "I'm no wanting you to be sorry, I'm just wanting you to keep thinking" (Liz, p16, lines 1-4).

"I've said to his face, goni do it for me and the girls, and he just looks and says "I've tried" (Tina, p7, lines 20-21) and "some people can just get up from it and carry on with their life but Jake just isn't one of them" (Tina, p11, lines 1-2).

It's not their fault

Caregivers appear to be denying the expression of their own emotions. They redefine their attitudes and behaviours, reminding/convincing themselves that their loved one did not choose to be in the position they are (i.e. experiencing cognitive changes and in turn, behavioural changes), making their new reality more acceptable.

"I just tell myself I've got to be there for him and I've just to,... to get myself back on track because at the end of the day, it's not Jake's fault" (Tina, p5, lines 7-8).

"You've always got to have in the back of your mind that it's not Mike's fault" (Katie, p7, line 6) and "you've got to hold back and go well, there's reasons behind it" (Katie, p8, lines 4-5).

Nobody knows what it's like vs. I don't want them to know what it's like

There is a sense that caregivers feel unheard and not understood and as a result, that their needs are not being met. This may be partly attributable to them concealing

how they are feeling and therefore others may be unaware of how burdened they feel and are less forthcoming with offers of support.

"Oh I suppose I felt there was a lack of empathy my way, about what I was going through as well as what he had gone through" (Ange, p4, lines 22-23).

"It's alright for you's, that's what I say to them, you no wae him 7 days a week, you know,...you don't understand...they only see wee bits of it, you know" (Liz, p20, line 1-4).

There appears to be a contradiction in terms of perceiving that their own needs weren't getting met and a simultaneous desire not to burden others.

"I've felt, a lot of times I've felt really really down, and I didn't know who to turn to,...I really didn't know who to turn to coz I didn't want to turn to my daughters coz they're daddy daft" (Liz, p22, lines 13-14) and "most of the time they didn't know half of what I was going through, you know, how I felt, because I didn't tell anybody how I felt" (Liz, p22, lines 19-20).

"My girls have been through a lot, I don't want them to see me falling apart because they've had a hard time as well,... so.... I'd rather deal with it myself" (Tina, p12, lines 3-4).

Sharing responsibility

Despite not wanting to burden others with their concerns about their spouse, advantages are noted when support is accessed. In addition, those who shared the burden of responsibility appeared to be less distressed.

"I've got great family,... both sides, they're there for us night and day, I just need to lift the phone and there's someone at my door for Robert at anytime" (Liz, p19, lines 5-6).

"Mike's family, they're great too...when I go up into the house I don't need to think as much because he has his family around him so we can share the wee bits and bobs and look after him so it's quite good" (Katie, p12, lines 5-8).

While those who hold almost all responsibility for their spouse's needs appear overwhelmed.

"Sometimes I feel I could just walk because I feel as if (sighs) I've had enough at times... but then I say to myself och pull yourself together because he needs me... I practically do everything for him, and when I go out, he's standing at the window waiting on me coming back" (Tina, p3, lines 18-21).

Caregivers coped with emotional distress independently and by talking with others. These examples highlight the divergence in the ways caregivers experienced catharsis. The chosen strategy appears to depend on the context and the caregivers' emotional needs at the time.

"I didn't cry in front of Robert, but I used to cry up the stairs you know" (Liz, p8, lines 11-12) and "believe it or not, I'd say a wee prayer" (Liz, p21, line 13).

"at the time I was designing empathy cards and actually I think creating them was a stress release,...all sorts of emotional words that I was illustrating" (Ange, p5, lines 19-20) and "I suppose it was just a distraction" (Ange, p6, line 2).

"just being with my friends was a big thing, I mean, I don't know how I would have coped without them (Ange, p6, line 4) and "it was just having a sounding board on one level and actually, at other times not talking about it at all because you get really,... you kind of need a break from it" (Ange, p6, lines 9-10).

"I mean it's hard sometimes, and it's emotional but yea, we're just truthful with one another, but sometimes, if it gets intensive I'll just go out with my mum or we'll chat about things and she gives support, or I'll go out with my brother" (Katie, p13, lines 6-8).

Beyond friends and family

Although caregivers adopted a number of strategies to cope with their emotional distress, there is a sense that their emotional needs are not fully met by their friends and family. Consistently, caregivers reported a wish for someone to talk from the beginning of the illness and outwith their family. Despite the profession of that person appearing unimportant, there is a sense that they should be a good listener, reassuring and be knowledgeable about potential late effects of treatment.

"it felt as if Norman had amazing care but...there was nobody that was constant for all of us" (Ange, p14, lines 15-16) and "I actually wanted someone to talk to outside, outside my social group and it

wouldn't have mattered who they were, I literally just wanted to kind of say, this is happening, am I going mad? (laughs) or I can't cope" (Ange, p15, lines 4-6).

"just having someone you can go and speak to,...because it's not Mike you're frustrated with, it's the illness he has you're frustrated with,... and (people in the caregivers position) should ask about the effects of treatment definitely and what to expect in years to come because people could start planning" (Katie, p13, lines 15-16).

"see all the medical side for me it was fantastic, but I felt emotionally all the time" (Liz, p8, line 11) and *"I wish I had someone to talk to at times but I wouldn't have took it to my family"* (Liz, p23, lines 1-2) and *"see fae the day he got home to stay home, well I woulda liked a wee group fae then"* (Liz, p27, line 3) and *"a group that took to do wae stress and anxiety and feeling how you felt"* (Liz, p23, lines 7-8).

COMMITMENT

Despite the aforementioned experiences of loss, frustration, uncertainty and whether or not they are experiencing the physical intimacy which may be expected in romantic relationships, there is a sense of enduring responsibility to their loved ones. A commitment which appears lasting and unyielding.

"another side is uhm,... physical intimacy, which kind of doesn't happen with somebody who has gone through bone marrow transplant for quite a long time,...and that's quite hard to re-kindle" (Ange, p11, lines 6-8).

"I just wish he would even give me a cuddle or,... sorry" (Tina, p8, line 2).

"when you are in a relationship you just get on with it, it's just part of who he is" (Katie, p3, lines 11-12).

"when you are faced with these problems you just have to grit your teeth and get on with it" (Paula, p6, line 5).

DISCUSSION

This study sought to explore caregivers' experiences of their spouse's treatment-related cognitive impairment following HSCT. This was achieved by interviewing five participants and analysing their transcripts using IPA. Results revealed a gradual recognition of cognitive and behavioural change in their spouse which once recognised, contributed to feelings of uncertainty, loss and frustration. Caregivers employed appraisal, emotion and problem focussed coping strategies to deal with their feelings. Despite their distress, caregivers demonstrated an unyielding commitment to their spouse.

Although the primary objective of this study was the exploration of treatment-related cognitive impairment, this symptom appeared to go unnoticed by caregivers initially. HSCT is one of the most complex and life threatening cancer treatments. In addition to managing the physical difficulties that may accompany HSCT, caregivers report uncertainty regarding whether or not their spouse will develop life threatening complications and with a 30% mortality rate many years after transplantation, uncertainty regarding whether or not their loved one will survive³⁰. In the context of the distress induced by these difficulties, their role change and increase in caregiving responsibilities, it is unsurprising that this change in cognitive functioning initially goes unnoticed.

Caregivers commented on the behavioural changes following treatment. This suggests that it is not possible to study one aspect of treatment symptomatology in isolation as a result of the far reaching effects of cognitive impairment. It does not appear to be the cognitive impairment per se which impacts upon the caregivers lives, but the consequences of these cognitive and behavioural changes. There was also a sense that caregivers did not know to expect changes which led to feelings of uncertainty about the future and efforts to cope with such uncertainty. Previous research has indicated that both lack of personal control and lack of preparedness increase caregiver distress¹⁸. In congruence with these findings, results from the current study highlighted that caregivers would value being more informed about

potential late effects of treatment, mirroring the result from Jim *et al.*'s.¹² exploration of patients' experiences mentioned previously.

In recent years, more research has focussed on the exploration of the moderating effects of interpersonal resources within a couple, namely the relationship *quality* between caregiver and receiver in addition to the caregiver's individual resources³¹. Schumacher *et al.*³¹ explored whether caregivers' perceptions of *mutuality* in their relationship and *preparedness* for caregiving, moderated the associations between perceived difficulty of caregiving and mood disturbance. Results revealed that a good relationship between caregiver and patient was insufficient to protect caregivers from negative affect. Caregivers also needed to consider themselves well-prepared for their caregiving duties. In addition, when both mutuality and preparedness were high, mood disturbance did not increase with increasing caregiving demand. Results from the current study support these findings. It is clear that participants who seek information in an attempt to be prepared and plan for the future and who report satisfaction with their relationship appear less distressed by the limitations of their spouse, despite high caregiving demands. Conversely, those who infer dissatisfaction with their relationship and display a sense of learned helplessness, demonstrating no efforts to become more prepared, appear more distressed. However, a number of other factors may moderate the relationship between caregiving demand and wellbeing. These may include personality characteristics, length of time as a caregiver, the caregivers current mental health, age and gender.

As recognition of cognitive and behavioural changes increased, caregivers reported frustration at their spouse's lack of willingness to socialise and help themselves and their caregiver, which they found stressful. This illustrates an example of perceived inequity in the relationship in which the caregivers perceive being under benefitted, which as noted before, leads to higher caregiver burden. Equity theory asserts that when in this position, individuals strive to restore equity by altering their inputs, leaving the relationship or cognitively distorting inputs and outcomes¹⁵. There was a consistent sense that caregivers had an enduring commitment to their spouse despite their difficulties and therefore leaving the relationship was not considered a feasible option. One possible reason for this may be the context in which caregivers

find themselves, having observed their loved one endure a complex and life threatening cancer treatment, following which they may feel it is inappropriate to strive to restore equity by this means. Rather, caregivers often put their partner's needs before their own, at the expense of their own social interaction and work commitments. This has been identified in other explorations of caregiver burden in adult cancer populations in which caregivers have reported to modify their lifestyle to accommodate the care recipient's needs, such as reducing their contact with friends and family and restricting their leisure activity³.

In order to resolve inequity in the relationship, caregivers adopt a form of appraisal coping - accepting the situation by externally attributing their spouse's difficulties. In interpersonal relationships, attributions are used to explain, justify or excuse behaviour. Weiner³² asserted that when the cause of requiring help was perceived to be external and uncontrollable, others were more likely to respond with sympathy and provide help. In line with this theory, caregivers consistently reported instances of reminding themselves that the limitations they were frustrated with were not the fault of their spouse, or under their control. When the cause of the behaviour is perceived to be internal and controllable, others are more likely to respond with negative emotions such as anger and less likely to help. In the current study, caregiver distress appeared to be higher when they perceived their spouse's limitations as under their control.

All participants illustrated the use of emotion focussed strategies (emotional discharge) or problem focussed strategies (seeking information and support). However, despite using similar strategies, caregiver outcomes varied considerably. For example, all participants used emotional discharge i.e. venting their feelings to their partner. For some, this reduced distress, for others this appeared to increase distress. In such cases, the outcome appeared not so much dependant on the individual coping strategy employed but on the response, or lack thereof, from their spouse. In keeping with the literature this highlights the effect of 'protective buffering' in increasing caregiver distress. It is also possible that outcomes may have been moderated by factors suggested by Moos and Schaefer (1984)³³. Personal factors such as current level of distress, personality, beliefs and previous experiences

appeared to affect whether or not caregivers made use of the social support available to them. Irrespective of how successful their coping efforts were, there was a consensus that additional support would be desirable.

Strengths and limitations

The use of qualitative methodology is considered a strength as it allowed for an in-depth exploration of caregivers' experiences of late effects of HSCT, which to the authors knowledge is the first study examining this. Study limitations include the small sample size which consisted of all white Scottish female caregivers, three of which were aged between 60-65 (Appendix 2.14). Although it was felt data saturation was reached with the current sample, a more culturally diverse sample across the age range may have yielded additional themes. The sample was relatively homogenous with the exception of one caregiver aged 35. The main limitation was the response rate. Twelve participants were provided with information packs, however, only five participants (42%) consented to take part. There was clear divergence in the experiences of caregivers, therefore it is possible that the caregivers who took part represent those at the extreme of each end of the experience and coping spectrum. Low response rate may also be explained by caregivers having a number of other responsibilities perhaps with limited time for tasks which will not have any immediate benefits for them. There is also a possibility that the patient population involved provided a barrier to accessing caregivers. There was a delay in interviewing two participants as their spouses had forgotten to provide them with the information pack.

Clinical implications and future directions

The current results highlight three potential avenues for clinical application. At present patients are given a "next steps" booklet which was written to increase their understanding of the long-term recovery and effects of stem cell transplantation. However, there is very little information in this booklet about the cognitive late-effects of treatment. Therefore, supplementing this with a discussion about potential cognitive late-effects with patients and their spouses at the pre-discharge stage may be helpful. Being more informed might help to reduce the uncertainty spouses report and increase their ability to plan for the future. Information about the biological causes of such impairment should be included which might help to increase spouses

understanding of the lack of controllability of the impairment. At present, a cognitive rehabilitation group is being developed and piloted at the BWoSICC. This will include a session for carers which the results of this study will inform. Secondly, couples might benefit from education about the value of emotional expression within the relationship. A reduction in protective buffering from both parties may increase mutuality in the relationship which, in addition to preparedness mentioned above, has been demonstrated to moderate the effects of caregiving demand on mood disturbance. Thirdly, spouses reported a desire for someone to provide emotional support outwith their family. This is the role of the Clinical Nurse Specialists. It is important to ensure that both the patient and their family members know who this is, how to contact them and to clarify their role in terms of providing emotional support in addition to physical care. As cancer has been acknowledged as a family disease, and caregivers and care recipients are likely to have different needs, future research should consider exploring the experiences of couples in order to identify any mutual needs, where interventions are likely to create optimum impact. Finally, given the current and future focus on health and social care integration, it will be important to consider how the needs of patients and their spouses can be met by joint working between health, social care and third sector services.

Conclusions

The results of this study highlight that caregivers adopt a variety of appraisal, emotion and problem focussed strategies to deal with feelings of uncertainty, loss and frustration owing to the changes identified in their spouse. In keeping with previous findings exploring patients' experiences, caregivers' highlighted a desire for education about late effects of treatment and emotional support outwith the family. Meeting these needs would help the caregiver to feel more prepared, which may increase their sense of control over their future. Understanding the lack of controllability their spouse has over their cognitive and behavioural changes has been demonstrated to evoke sympathy and in turn, helping behaviour. Education about the role of 'protective buffering' may help improve communication of emotions within the care dyad. All of these above factors have been demonstrated to reduce caregiver burden.

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Appendix 1.1 Guidelines for submission to Journal of Psychosomatic Research



JOURNAL OF PSYCHOSOMATIC RESEARCH

Official Journal of the [European Association of Psychosomatic Medicine](#) and affiliated with the [International College of Psychosomatic Medicine](#)

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DESCRIPTION

The *Journal of Psychosomatic Research* is a multidisciplinary research journal covering all aspects of the relationships between **psychology** and **medicine**. The scope is broad and ranges from basic human biological and psychological research to evaluations of **treatment** and services. Papers will normally be concerned with **illness** or **patients** rather than studies of healthy populations. Studies concerning special populations, such as the elderly and children and adolescents, are welcome. In addition to peer-reviewed original papers, the journal publishes editorials, reviews, and other papers related to the journal's aims.

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PREPARATION

Manuscripts should conform to the uniform requirements known as the 'Vancouver style' (International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. N Engl J Med 1997; 336:309-315). The Editors and Referees attach considerable importance to a succinct and lucid prose style and well organized tables. Authors whose native language is not English are advised to seek help before submission. Statistical procedures should be clearly explained. Manuscripts should conform to the uniform requirements known as the 'Vancouver style' (International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. N Engl J Med 1997; 336:309-315). The Editors and Referees attach considerable importance to a succinct and lucid prose style and well organized tables. Authors whose native language is not English are advised to seek help before submission. Statistical procedures should be clearly explained.

Formatting requirements

There are no strict formatting requirements but all manuscripts must contain the essential elements needed to convey your manuscript, for example Abstract, Keywords, Introduction, Materials and Methods, Results, Conclusions, Artwork and Tables with Captions.

If your article includes any Videos and/or other Supplementary material, this should be included in your initial submission for peer review purposes.

Divide the article into clearly defined sections.

Figures and tables embedded in text

Please ensure the figures and the tables included in the single file are placed next to the relevant text in the manuscript, rather than at the bottom or the top of the file.

Structured Abstract

This should be subdivided under the headings **Objective, Methods, Results, and Conclusion** and should not exceed 250 words.

Keywords

Up to six keywords should be listed in alphabetical order after the abstract. These terms should optimally characterize the paper to facilitate choice of peer reviewers.

Article Structure

The text should be divided into sections with main headings: Introduction, Method, Results and Discussion and, in total, these sections should not normally be greater than 4000 words in length.

Review Articles

Review papers are normally 4000-5000 words (Introduction through Discussion). Authors are advised to consult one of the Editors with an outline before submitting a review.

For full details please visit:

https://www.elsevier.com/wps/find/journaldescription.cws_home/525474?generatepdf=true

Appendix 1.2 Search strategy for Embase

1. Bone marrow transplantation/
2. Hematopoietic stem cell transplantation/
3. (hematopoietic adj2 transplant*).mp [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
4. (haematopoietic adj2 transplant*).mp [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
5. (bone marrow adj2 transplant*).mp [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
6. Adaptation, psychological
7. Emotional adjustment
8. Coping behaviour
9. Mental stress
10. ((emotional or psychological) adj (wellbeing or coping)).mp [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
11. 1 OR 2 OR 3 OR 4 OR 5
12. 6 OR 7 OR 8 OR 9 OR 10
13. 11 AND 12
14. Limit 13 to (human and English language and journal and adult <18 to 64 years>)

Appendix 1.3 Reasons for exclusion at full text level

Reasons for exclusion

- 1 - Psychological adjustment not the outcome variable
- 2 - No transplant procedures (e.g. chemotherapy only)
- 3 - Examining predictors of distress prior to transplant procedure
- 4 – Protective/risk factors for adjustment are not psychological e.g. demographics/personal changes/medical factors/symptom distress/physical limitations)

Study	Reason
Baker F, Marcellus D, Zabora J, Polland A, Jodrey D. Psychological Distress Among Adult Patient Being Evaluated for Bone Marrow Transplantation. <i>Psychosomatics</i> . 1997; 38 (1):10-19.	3
Curbow B, Somerfield MR, Baker F, Wingard JR, Legro MW. Personal Changes, Dispositional Optimism and Psychological Adjustment to Bone Marrow Transplantation. <i>Journal of Behavioural Medicine</i> . 1993; 16 (5):423-443.	4
Frick E, Fegg MJ, Tyroller M, Fischer N, Bumeder I. Patients' health beliefs and coping prior to autologous peripheral stem cell transplantation. <i>European Journal of Cancer Care</i> . 2007; 16:156-163.	3
Miller DL, Manne SL, Taylor K, Keates J, Dougherty J. Psychological Distress and Well-Being in Advanced Cancer: The Effects of Optimism and Coping. <i>Journal of Clinical Psychology in Medical Settings</i> . 1996; 3 (2):115-130.	2
Pillay B, Lee SJ, Katona L, Burney S, Avery S. Psychosocial factors associated with quality of life in allogeneic stem cell transplant patients prior to transplant. <i>Psycho-Oncology</i> . 2014; 23:642-649.	3
Prieto JM, Blanch J, Atala J, Carreras E, Rovira M, Cirera E, Gasto C. Stem cell transplantation: Risk factors for psychiatric morbidity. <i>European Journal of Cancer Care</i> . 2006; 42:514-520.	4
Rodrigue JR, Boggs SR, Weiner RS, Behen JM. Mood, Coping Style and Personality Functioning Among Adult Bone Marrow Transplant Candidates. <i>Psychosomatics</i> . 1993; 34 (2):159-164.	3
Rodrigue JR, Pearman TP, Moreb J. Morbidity and Mortality Following Bone Marrow Transplantation: Predictive Utility of Pre-BMT Affective Functioning, Compliance and Social Support Stability. <i>International Journal of Behavioural Medicine</i> . 1999; 6 (3):241-254.	1

Appendix 1.4 Quality appraisal tool (Downs & Black 1998 Checklist)

All criteria	Description of criteria (with additional explanation if required, determined by consensus of raters)	Possible answers	
1	Is the hypothesis/aim/objective of the study clearly described? Must be explicit.	Yes/No	
2	Are the main outcomes to be measured clearly described in the introduction or Methods section? If the main outcomes are first mentioned in the Results section, the question should be answered no. ALL primary outcomes should be described for YES.	Yes/No	
3	Are the characteristics of the patients in the study clearly described? In cohort studies and trials, inclusion and/or exclusion criteria should be considered. In case-control studies, a case-definition and the source for controls should be given. Single case studies must state a source of patient.	Yes/No	
4	Are the interventions of interest clearly described? Treatments and placebo that are to be compared should be clearly described.	Yes/No	X
5	Are the distributions of principle confounders in each group of subjects to be compared clearly described? A list of principle confounders is provided. YES= age, severity.	Yes/No	
6	Are the main findings of the study clearly described? Simple outcome data (including dominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions.	Yes/No	
7	Does the study provide estimates of the random variability in the data for main outcomes? In normally distributed data, the inter-quartile range of results should be reported. In normally distributed data the standard error, standard deviation or confidence intervals should be reported.	Yes/No	X
8	Have all the important adverse events that may be a consequence of the interventions been reported? This should be answered yes if the study demonstrates that there was a comprehensive attempt to measure adverse events (COMPLICATIONS BUT NOT AN INCREASE IN PAIN).	Yes/No	X
9	Have the characteristics of patients lost to follow-up been described? If not explicit = NO. RETROSPECTIVE – if not described = UTD; if not explicit re: numbers agreeing to participate = NO. Needs to be >85%	Yes/No/ UTD	
10	Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes, except where the probability is less than 0.001?	Yes/No	
11	Were the subjects asked to participate in the study representative of the entire population from which they were recruited? The study must identify the source population for patients and describe how the patients were selected.	Yes/No/ UTD	
12	Were those subjects who were prepared to participate representative of the entire population from which they were recruited? The proportion of those asked who agreed should be stated.	Yes/No/ UTD	
13	Were the staff, places and facilities where the patients were treated, representative of the treatment the majority of patients receive? For the question to be answered yes the study should demonstrate that the intervention was representative of that in use of the source population. Must state type of hospital and country for YES.	Yes/No/ UTD	X
14	Was an attempt made to blind study subjects to the intervention they have received? For studies where the patients would have no way of knowing which intervention they received, this should be answered yes. Retrospective, single group = NO; UTD if >1 group and blinding not explicitly stated.	Yes/No/ UTD	X
15	Was an attempt made to blind those measuring the main outcomes of the intervention? Must be explicit.	Yes/No/ UTD	X

16	If any of the results of the study were based on “data dredging”, was this made clear? Any analyses that had not been planned at the outset of the study should be clearly indicated. Retrospective = NO. Prospective = YES.	Yes/No/ UTD	
17	In trials and cohort studies, do the analyses adjust for different lengths of follow up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls? Where the follow up was the same for all study patients the answer should be yes. Studies where differences in follow up are ignored should be answered no. Acceptable range 1 yr follow up=1 month each way; months....10 years follow up = 10 months.	Yes/No/ UTD	
18	Were the statistical tests used to assess the main outcomes appropriate? The statistical techniques used must be appropriate to the data. If no tests done, but would have been appropriate to do = NO.	Yes/No/ UTD	
19	Was compliance with the intervention/s reliable? Where there was non compliance with the allocated treatment or where there was contamination of one group, the question should be answered no. Surgical studies will be YES unless procedure not completed.	Yes/No/ UTD	X
20	Were the main outcome measures used accurate (valid and reliable)? Where the outcome measures are clearly described, which refer to other work or that demonstrate the outcome measures are accurate = YES. ALL primary outcome measures are valid and reliable for YES.	Yes/No/ UTD	
21	Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls recruited from the same population? Patients for all comparison groups should be selected from the same hospital. The question should be answered UTD for cohort and case control studies where there is no information concerning the source of patients.	Yes/No/ UTD	
22	Were study subjects in different interventions group (trials and cohort studies) or were the cases and controls recruited from the same population? For a study which does not specify the time period over which patients were recruited, the questions should be answered UTD. Surgical studies must be <10 years for YES, if >10 then NO.	Yes/No/ UTD	
23	Were study subjects randomised to intervention groups? Studies which state that subjects were randomised should be answered yes except where method of randomisation would not ensure random allocation.	Yes/No/ UTD	X
24	Was the randomised intervention assignment concealed from both parties and health care staff until recruitment was complete? All randomised studies should be answered no. If assignment was concealed from patients but not from staff, it should be answered no.	Yes/No/ UTD	X
25	Was there adequate adjustment for confounding in the analyses from which the main findings were drawn? In non-randomised studies if the effect of the main confounders was not investigated or no adjustment was in the final analysis was made the question should be answered no. If no significant difference between groups then YES.	Yes/No/ UTD	
26	Were losses of patients to follow up taken into account? If the numbers of patients lost to follow up are not reported = UTD.	Yes/No/ UTD	
27	Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance <5%. Sample sizes have been calculated to detect a difference of x% and y%.	1-5	

‘X’ indicates the items which were removed for the current systematic review.

Appendix 1.5 Quality ratings of included studies

	Reporting /7	External validity /2	Internal validity bias /4	Internal validity confounding /4	Power /1	Overall score /18
Fife et al (2000)	5/7	1/2	4/4	2/4	1/1	13/18
Goetzman et al (2007)	5/7	1/2	4/4	4/4	1/1	15/18
Hochhausen et al (2007)	4/7	1/2	4/4	4/4	1/1	14/18
Jacobson et al (2002)	7/7	1/2	3/4	2/4	1/1	14/18
Johnson-Vickberg et al (2001)	6/7	2/2	4/4	4/4	1/1	17/18
Lee et al (2005)	6/7	2/2	2/4	4/4	1/1	15/18
Rosenberg et al (2015)	5/7	2/2	4/4	4/4	1/1	16/18
Schumacher et al (2014)	6/7	2/2	4/4	4/4	1/1	17/18
Warchala et al (2015)	6/7	1/2	3/4	2/4	1/1	13/18
Wells et al (2009)	7/7	2/2	3/4	3/4	1/1	16/18
Widows et al (2000)	7/7	2/2	4/4	4/4	1/1	18/18

Appendix 1.6 Psychological adjustment outcome measures and associative factors measures

Outcome measures

- Bi-polar Profile of Mood States (POMS)
- SF-36 Health Survey (SF-36)
- Questions on Life Satisfaction Questionnaire
- The Centre for Epidemiological Studies of Depression (CES-D)
- Functional Assessment of Cancer Therapy General (FACT-G)
- PTSD Checklist – Civilian Version (PCL-C)
- Brief Symptom Inventory – Global Severity Index (BSI-GSI)
- Beck Depression Inventory 2nd Edition (BDI-II)
- Hospital Anxiety and Depression Scale (HADS)
- Cancer and Treatment Distress measure (CTD)
- EORTC Quality of Life Questionnaire (EORTC QLQ-C30)
- General Self-efficacy Scale (GSES)
- State Trait Anxiety Inventory-State Anxiety Subscale (STAI)
- Structured Clinical Interview for DSM-IV Axis 1 Disorders:non patient edition (SCID-I/NP)

Associative factors measures

- Perceived Family and Perceived Friends Social Support Scale (PFPFSSS)
- Perceived Health Care Provider Support Scale (PHCPSS)
- Ways of Coping Checklist (WCC)
- Mastery Scale
- Meaning of Illness Scale (MIS)
- Sense of Coherence Scale Short Version (SOC-13)
- Life Orientation Test (LOT)
- Hospital Anxiety and Depression Scale (HADS)
- Social Support Questionnaire (F-SozU)
- Rand Medical Outcomes Study Social Support Survey (MOS)
- Cancer Behaviour Inventory Long Form (CBI-L)
- Coping Responses Inventory (CRI)
- Profile of Mood States (POMS)
- Interpersonal Support Evaluation List Short Form (ISEL-SF)
- Life Attitude Profile Revised (LAP-R)
- Beck Depression Inventory 2nd Edition (BDI-II)
- Hospital Anxiety and Depression Scale (HADS)
- PTSD Checklist – Civilian Version (PCL-C)
- Conner Davidson Resilience Scale (CDRS)
- Acceptance of Illness Scale (AIS)
- Coutald Emotional Control Scale (CECS)
- Mental Adjustment to Cancer (MAC)
- Brief COPE
- Social Constraint Scale (SCS)
- Trauma Experience Questionnaire

Appendix 2.1 Major research project proposal

ABSTRACT

Background: For many cancers the treatments involved, such as chemotherapy can be physically and psychologically challenging and be associated with lasting adverse secondary effects, one of which is cognitive impairment. Common changes occur primarily in the domains of executive functioning, processing speed, memory and attention. The incidence and severity of this symptom varies widely, however it can significantly impact quality of life by interfering with patients' activities of daily living, relationships and future plans. This symptom can also pose challenges for the patients' caregiver, an area which has received comparatively less attention.

Aims: The aim of this study is to investigate caregivers' experiences of treatment related cognitive impairment in patients who have undergone Haematopoietic Stem Cell Transplant (HSCT), how they coped both practically and emotionally and what supports they believe could help them

Methods: Four to ten participants who are a caregiver to an individual who has undergone a HSCT in the last 20 years will be recruited via the Beatson West of Scotland Cancer Centre (BWoSCC). Each participant will complete an in depth interview exploring their experiences which will be analysed using Interpretative Phenomenological Analysis (IPA).

Applications: Given that cognitive compensatory interventions are often enhanced when supported by carers, a greater understanding of caregivers' experiences may provide a rationale for the development of a service to meet their needs both psychologically and practically and in turn, improve the outcomes of patients undergoing cognitive remediation.

INTRODUCTION

More than one in three people in the UK will develop some form of cancer during their lifetime, of which there are more than 200 types, each with different causes, symptoms and treatments (Cancer Research UK, 2014). For many cancers, the treatments involved can be physically and psychologically challenging and associated with lasting adverse secondary effects, such as cognitive impairment (MacMillan Cancer Support, 2013).

Although the existence and causes of treatment-related cognitive impairment or 'chemo brain' have been a subject of debate, many studies have confirmed that it is a real, measurable side effect of chemotherapy (Evans & Eschiti, 2009). This was first identified in the 1980's when breast cancer patients reported difficulties with cognition during and after chemotherapy (van Dam et al. 1998). Most of the research investigating treatment-related cognitive impairment has been carried out with breast cancer patients, however the exact incidence of its occurrence is unknown owing to the different methods employed in the studies such a lack of control group of cancer patients not treated with chemotherapy and a lack of baseline measures (van Dam et al. 1998). At present, it is estimated that treatment-related cognitive impairment affects between 17-78% (Schagen & Wefel, 2013).

While physical difficulties may be experienced as transient side effects of cancer treatment, for example, increased infection owing to a lowered immunity or day time tiredness owing to sleep problems, some patients continue to experience cognitive

difficulties long after their treatment has ended. For some patients, cognitive impairment is present up to twenty years following chemotherapy (Schagen & Wefel, 2013). Common changes occur primarily in the domains of executive functioning, processing speed, memory and attention (Ahles & Saykin, 2001). This is most often seen in patients treated for breast, ovarian and prostate cancer in addition to other types of cancers requiring high dose chemotherapy such as cancers of the blood or bone marrow.

Although blood cancers account for only up to 3% of cancer cases, around 26,700 cases of the three most common blood cancers (leukemia, lymphoma, and myeloma) are diagnosed in the UK every year, 94% of which occur in adults (Cancer Research UK, 2014). Haematopoietic Stem Cell Transplant (HSCT) has become the standard treatment for certain types of blood or bone marrow cancer and offers the possibility of a cure for illness such as multiple myeloma, lymphoma or leukaemia, amongst others. HSCT involves the destruction of the recipient's immune system with high-dose chemotherapy and occasionally total body irradiation (tbi), together with immunosuppressant medication supported by steroids and anti-rejection drugs in order to eradicate the disease prior to the infusion of new stem cells and also to suppress immune reactions i.e. graft versus host disease (GvHD), thereby preventing the donor stem cells from rejecting the recipients' body (Cancer Research UK, 2014).

Bosworth et al., (2013) carried out a 2 year prospective study of cognitive function conducted on 242 HSCT recipients and 98 healthy controls. Participants were asked to undergo a two hour battery of standardized neurocognitive tests measuring executive function, processing speed, verbal fluency and fine motor dexterity. Participants took this test at six, 12 and 24 months after transplant. Owing to a high attrition rate only half of the participants remained at the end of the study. Despite the reduction in sample size, the researchers found that all four measures of cognitive function were significantly worse in HSCT participants. With regards to the duration of symptoms, Syrjala et al., (2004) observed significant reductions in neuropsychological test performance between their first and second time points, pre HSCT and 80 days respectively, and a general recuperation at 1 year post HSCT. Booth-Jones et al., (2005) examined patients 6 months after HSCT finding at least mild cognitive deficits in 51% and moderate to severe impairment in 28%.

It is difficult to predict which patients will develop treatment-related cognitive impairment and for those who do, as evident in the aforementioned studies, duration and severity are highly variable. In addition, changes can occur as early as the first chemotherapy session and/or accumulate and develop over subsequent treatments. Even mild cognitive difficulties can have practical and psychological consequences, particularly when persistent or left untreated (Schagen et al., 2014). What is certain is that treatment related cognitive dysfunction can significantly impact quality of life by interfering with patients' activities of daily living, interpersonal relationships and future plans, this is in addition to a life altering cancer diagnosis.

Advances in medicine have improved patient outcomes after transplantation, with more than 54% of patients now alive one year after unrelated donor stem cell transplantation compared to 42% ten years ago. Moreover, the increasing ability to transplant older patients continues to drive the growing number of transplants in the UK (UK Stem Cell Strategic Forum, 2010). Given the increasing number of cancer survivors who have undergone HSCT, the clinical relevance of treatment-related cognitive impairment is significant.

A few qualitative studies have explored the subjective experiences of treatment-related cognitive impairment in cancer patients, however, this is most often amongst breast cancer survivors, the most studied group with regards to this symptom. These studies have explored quality of life and social reintegration following treatment and have attempted to address the needs of patients living with these difficulties. This has included increasing education regarding the potential for cognitive changes associated with treatment.

Cancer not only affects the patient but also has a large impact on family members and carers and partners who may find that their roles, responsibilities and priorities change after their loved one's cancer diagnosis and throughout treatment and recovery (Schubart et al., 2008). Owing to the recognition of this fact, there have been a number of studies investigating carers' experiences of diagnosis, prognosis and the burden of care when caring for a loved one with cancer (Doorenbos et al., 2007, XinGao et al., 2013). Some of the challenges faced include carer sacrifices, monetary losses and poor physical and emotional health (Schubart et al., 2008). Comparatively less research has investigated caregivers' experiences specifically of their partner's cognitive impairment and how they coped with their experience. Following their partners treatment, ongoing limitations in cognitive functioning and therefore, quality of life pose additional challenges for caregivers than those mentioned above, in particular, neurocognitive changes that can be difficult to manage (Schubart et al., 2008).

1. AIMS

The aims of this study are to investigate:

- Caregivers' experiences of treatment-related cognitive impairment in patients (i.e. their loved ones) who have undergone a HSCT.
- How caregivers coped practically and emotionally.
- What supports they believe could help them.

2. PLAN OF INVESTIGATION

2.1 Participants

Purposive sampling will be used to recruit individuals via the Beatson West of Scotland Cancer Centre (BWoSCC). Consultant Haemato-oncologists will identify individuals who are a caregiver to somebody who:

- Reports experiencing a degree of cognitive impairment which they associate with their Bone Marrow Transplant. These difficulties are identified using the NHS GG&C Haematopoietic Stem Cell Transplantation Service 'Patient Distress Thermometer'. The Patient Distress Thermometer is already used as part of the routine assessment at the Late Effects Clinic and is therefore within the normal working remit of the staff.
- Has undergone total body irradiation, high dose chemotherapy or a combination of these within the last 20 years.
- Has no known psychiatric or neurological problems likely to lead to cognitive impairments e.g. schizophrenia, previous head injury, organic cognitive decline.
- Has no current use of psychotropic medication.
- Has no known learning disability.

Participants will be excluded from the study if:

- They do not speak fluent English as the interviews will be conducted in English.
- Their partner has received total body irradiation, high dose chemotherapy or a combination of these within the last year.
- Their loved one lacks the capacity to consent for the caregiver to take part.

2.2 Recruitment Procedures

Subject to ethical approval and agreement from Consultant Haemato-oncologists and Senior Nurses, individuals who are identified as meeting the inclusion criteria and not meeting exclusion criteria will be identified by these staff at the Bone Marrow Transplant Late Effects outpatient clinic at the BWoSCC. Patients who have undergone a Bone Marrow Transplant attend this clinic annually to identify any difficulties they may be experiencing following cancer treatment. These include physical, emotional, practical, spiritual and relationship difficulties. These difficulties are identified using the NHS Greater Glasgow & Clyde Haematopoietic Stem Cell Transplantation Services 'Patient Distress Thermometer'.

If the patient identifies a difficulty with their memory/concentration, an information pack will be provided to patients. This will contain a cover letter detailing the rationale and aim of the study, an information sheet detailing what the study involves and the primary researcher's contact details, should the patient wish to ask any questions prior to providing written informed consent and a consent form to allow the patient to consent for their caregiver to take part, if they wish to. The patient consent form will request confirmation that the patient has had the opportunity to ask any questions about the study and is happy for their caregiver to participate.

The information pack will also contain an information sheet and two consent forms for the potential participant. One which requests their permission for the primary researcher to contact them to discuss the research further and allow them to ask any questions and one which allows them to consent to take part in the study. When patient consent and permission to contact the participant consent forms have both been received, the primary researcher will contact the caregiver to allow them to ask any questions about the study before they decide if they wish to participate, and if so, allow an appointment to be made. Written informed consent will be obtained from the participant before the interview begins. The patient themselves will also be informed about the currently developing Cognitive Rehabilitation Service at the BWoSCC and referred to this service if they wish to be. This service aims to provide patients with cognitive rehabilitation techniques to help manage their cancer related cognitive impairment.

2.3 Measures

A topic guide will be developed through discussion with the primary researcher and supervisors of the project and based on the previous literature. Given the scarcity of reports of caregivers' experiences of cognitive impairment specifically, the topic guide will be based on the findings of previous research of caregivers' experiences of cancer symptoms more generally. The aim of the interview is to explore what the participant feels is important about their experience, therefore, the topic guide will not constrict this exploration of experience, rather the interview will follow the concerns of the participant (Smith, Flowers & Larkin, 2009; p.58).

2.4 Design

Interpretative Phenomenological Analysis has been informed by three key philosophies: 1. phenomenology, a philosophical approach to the study of experience; 2. hermeneutics, a method of interpretation; and 3. idiography, a focus on the particular. Therefore, the aim of IPA is to explore what personal and social experiences mean to the people who experience them and to make sense of what the person is telling us i.e. to make interpretations about those experiences (Smith, Flowers & Larkin, 2009; pp.11-39). IPA was therefore considered to be the approach most able to address the aim of this study.

2.5 Research procedures

Pilot interviews will be carried out with a subset of the sample (n=2) prior to data collection in order to identify if the topic guide is successful at eliciting data consonant with the aims of the study. If not, the topic guide will be modified and a second test of the topic guide will be conducted. If no changes are made to the topic guide following the pilot interviews, these interviews will be included in the analysis. The primary researcher will conduct interviews for approximately 45-90 minutes with each participant using the aforementioned topic guide to guide the interview. All interviews will be recorded using a digital voice recorder or for telephone interviews (when a face to face interview is not possible), via a device which enables the recording of the telephone conversation onto the digital voice recorder. They will then be transcribed verbatim by the primary researcher and any identifiers of people or places will be removed and replaced by a pseudonym prior to the second researcher analysing a subsample of interviews to ensure that the patient's identity is concealed. This recording will be stored on a University of Glasgow laptop encrypted with a security application accredited to NHS standards. When transcription is completed and checked for accuracy, the interview will be transferred onto a compact disc (CD) and retained with other source data. Paper documents, such as consent forms and transcribed interviews will be stored in a locked filing cabinet in the office of the Chief Investigator of this project, Dr Sarah Wilson (Senior Lecturer in Health Psychology, University of Glasgow). The transcripts will be analysed using IPA.

2.6 Data Analysis

In order to analyse the data, the six step process described by Smith, Flowers and Larkin, (2009; pp.82-106) will be followed. Following verbatim transcription of the interviews, analysis will involve immersing oneself in the data and noting any recollections of the interview experience and initial or striking observations of the transcript. Descriptive, linguistic and conceptual noting then begins which allows the researcher to engage with the text in detail and begin to analyse the text at an interpretive level. Analysing the descriptive, linguistic and conceptual notes will allow the researcher to identify emergent themes and when these have been established, consider how these themes are connected. This process is then repeated with subsequent transcripts while allowing new themes to emerge. The final stage involves identifying themes across cases.

In the process of IPA, the researcher plays an active role in interpreting the data. It has been acknowledged that "inevitably the analysis is a joint product of the participants and analyst, the end result is always an account of how the analyst thinks the participant is thinking, thus the truth claims of IPA analysis are always tentative and analysis is subjective" (Smith, Flowers and Larkin, 2009; p.80). Prior to analysis, the primary researcher will practice reflexivity to ensure her perspectives are transparent from the outset. In order to reduce any bias in analysis owing to the primary researchers beliefs,

a second researcher will analyse a subsample of interviews (n=2) to ensure validity of the analysis.

2.7 Justification of sample size

IPA is an ideographic approach and therefore has a commitment to detail and depth of analysis when attempting to understand a particular phenomena in a particular context. Consequently, the use of small sample sizes when employing IPA is recommended. This allows the researcher to gain an in-depth understanding of the individual experiences of the participants (Smith, Flowers & Larkin, 2009; p.51). In professional doctorates, numbers of interviews (rather than number of participants) are typically between four and ten. The current study will aim to recruit ten participants, each of whom will be interviewed once (Smith, Flowers & Larkin, 2009; p.52). The approximate number of patients presenting with cognitive impairment at the Late Effects Clinic each month is likely to be between 6 and 27. This calculation is based on an average of 35 patients attending the clinic per month, of which between 17 and 78% may present with cognitive impairment (Schagen et al. 2014).

2.8 Settings and Equipment

Interviews will be conducted by the primary researcher in a private room at the BWoSCC. If this is not convenient for the participant a telephone interview will be arranged. Telephone interviews will also be carried out from a private room at the BWoSCC. After receiving permission to contact the participant to discuss the research further, if they wish to participate and also wish to be interviewed over the telephone, the participant will be asked to sign the consent form from the information pack and return this in the freepost envelope provided. When this has been received, the primary researcher will contact the participant to arrange a suitable time to meet.

3. HEALTH AND SAFETY ISSUES

3.1 Researcher safety issues

As the interviews will be conducted on an individual basis, the safety of the primary researcher who will be conducting the interview will be ensured by carrying out interviews within normal working hours (9am-5pm) at the BWoSCC. This will help ensure that staff are nearby should any safety issues arise. No interviews will take place at the participants' home address.

3.2 Participant safety issues

Caring for an individual undergoing intensive surgery and consequently suffering from a degree of cognitive impairment is likely to be a highly emotive and stressful experience. Therefore, before the interview begins, the participant will be informed that they may stop the interview at any time.

If during the interview, the primary researcher identifies any signs of distress or psychological difficulties, the interview will be suspended, the participant will be offered emotional support and reminded that they can end the interview if they do not wish to continue. If it becomes apparent that there are significant mental health problems, the primary researcher will offer a referral to cancer support agencies such as Maggie's Cancer Support Scotland, MacMillan's support line or the counsellor at the BWoSCC. They will also be advised to visit their own GP for assessment and support.

4. ETHICAL ISSUES (including where submissions will be made)

Ethical approval will be sought from the Research Ethics Committee at the BWoSCC and NHS Greater Glasgow and Clyde. Although this study aims to gain an understanding of caregivers' experiences of their loved one's cognitive impairment, consent will require to be sought from the patient themselves to allow their caregiver to discuss the patients' difficulties and how they are being affected by them. Therefore, when Consultant Haemato-oncologists and/or Senior Nurses inform the patient of the study, the information sheet provided will detail what areas of discussion will be and if they are happy to be discussed, invite the patient to invite their caregiver to participate in the study. By doing this, the patient themselves will be consenting to allow their caregiver to discuss the patients difficulties. This will be demonstrated by ensuring the patient has provided written informed consent before any communication is made with their caregiver. Please see Section 2.2 - Recruitment procedures.

5. FINANCIAL ISSUES

Recording and transcribing equipment will be borrowed from the Mental Health and Wellbeing department at the University of Glasgow. Envelopes and postage costs may be incurred if the posting of information sheets is not carried out via the BWoSCC. Costs will include printing information sheets and consent forms and one telephone pick up hands free cable which will be used for telephone interviews.

6. TIMETABLE

March 2015	Submit proposal to university
June/July 2015	Proposal (including all appendices and ethics application) assessed
August/September 2015	Apply for ethical approval from the from the Research Ethics Committee at the BWoSCC and NHSGG&C
October 2015-December 2015	Recruitment
January- February 2016	Transcription of interviews (approximately 80 hours of transcription)
February-March 2016	Analysis
April – June 2016	Write up of research
July 2016	Submit research

7. PRACTICAL APPLICATIONS

At the BWoSCC a current service development is the support of patients who have treatment related cognitive impairment. Given that cognitive compensatory interventions are often enhanced when supported by carers, the current study may provide a rationale for the development of a service to meet their needs both psychologically and practically and in turn, improve the outcomes for patients who are undergoing cognitive remediation.

8. DISSEMINATION OF FINDINGS

With the patient and participant's permission, quotations from the interview will be used in the final report which will be written up and submitted as partial fulfilment in the degree of Doctorate in Clinical Psychology. After completion, the thesis will be held within the Glasgow Theses Service which is freely available electronically. Quotations and a summary of the findings may also be presented at conferences and published in an academic journal. Patients and participants will be offered to receive a summary of the study results.

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Appendix 2.2 Guidelines for submission to Bone Marrow Transplantation

	
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[ABOUT THE JOURNAL](#)

[Aims and Scope](#)

Bone Marrow Transplantation publishes high quality, peer reviewed original research and review articles that address all aspects of the basic biology and clinical use of haemopoietic cell transplantation. The journal also covers all aspects of the research and treatment of transplant-related complications and consequences including quality of life and psychological issues. Basic research studies on topics of relevance are also covered.

The broad scope of the journal encompasses topics such as stem cell biology, transplantation immunology (including animal models), translational research, biomarkers, cellular therapy, and clinical results of specific protocols.

[Journal Details](#)

Editors-in-Chief:

Hillard Lazarus, University Hospitals Case Medical Center,
Cleveland, USA

Mohamad Mohy, Saint-Antoine Hospital and University Pierre &
Marie Curie, Paris, France

Editorial office:

Nature Publishing Group, The Macmillan Building, 4 Crinan Street,
London UK

bmt@nature.com

Impact factor: 3.570 (2014 *Journal Citation Reports*, Thomson Reuters, 2015)

Frequency: 12 issues a year

Abstracted in:

MEDLINE/ Index Medicus

EMBASE/Excerpta Medica

Current Contents/Clinical Medicine

Elsevier BIOBASE/Current Awareness in Biological Sciences

Reference Update

SciSearch

Biosis

PREPARATION OF ARTICLES

Please note that original articles must contain the following components. Please see below for further details.

- Cover letter
- Title page (excluding acknowledgements)
- Abstract
- Introduction
- Materials (or Subjects) and Methods
- Results
- Discussion
- Acknowledgements
- Conflict of Interest
- References
- Figure legends
- Tables
- Figures

Reports of clinical trials must adhere to the registration and reporting requirements listed in the [Editorial Policies](#).

Cover Letter: The uploaded covering letter must state the material is original research, has not been previously published and has not been submitted for publication elsewhere while under consideration. If the manuscript has been previously considered for publication in another journal, please include the previous reviewer comments, to help expedite the decision by the Editorial team. Add note about including conflict of interest statement.

Title Page: The title page should bear the title of the paper, the full names of all the authors and their affiliations, together with the name, full postal address, telephone and fax numbers and e-mail address of the author to whom correspondence and offprint requests are to be sent (this information is also asked for on the electronic submission form). The title page must also contain a Conflict of Interest statement (see [Editorial Policy](#) section).

- The title should be brief, informative, of 150 characters or less and should not make a statement or conclusion.
- The running title should consist of no more than 50 letters and spaces. It should be as brief as possible, convey the essential message of the paper and contain no abbreviations.
- Authors should disclose the sources of any support for the work, received in the form of grants and/or equipment and drugs.
- If authors regard it as essential to indicate that two or more co-authors are equal in status, they may be identified by an asterisk symbol with the caption 'These authors contributed equally to this work' immediately under the address list.

Abstract: Original Articles must be prepared with an unstructured abstract designed to summarise the essential features of the paper in a logical and concise sequence.

Materials/Subjects and Methods: This section should contain sufficient detail, so that all experimental procedures can be reproduced, and include references. Methods, however, that have been published in detail elsewhere should not be described in detail. Authors should provide the name of the manufacturer and their location for any specifically named medical equipment and instruments, and all drugs should be identified by their pharmaceutical names, and by their trade name if relevant.

Results and Discussion: The Results section should briefly present the experimental data in text, tables or figures. Tables and figures should not be described extensively in the text, either. The discussion should focus on the interpretation and the significance of the findings with concise objective comments that describe their

relation to other work in the area. It should not repeat information in the results. The final paragraph should highlight the main conclusion(s), and provide some indication of the direction future research should take.

Acknowledgements: These should be brief, and should include sources of support including sponsorship (e.g. university, charity, commercial organisation) and sources of material (e.g. novel drugs) not available commercially.

Conflict of Interest: Authors must declare whether or not there are any competing financial interests in relation to the work described. This information must be included at this stage and will be published as part of the paper. Conflict of interest should be noted in the cover letter and also on the title page. Please see the Conflict of Interest documentation in the [Editorial Policy](#) section for detailed information.

References: Only papers directly related to the article should be cited. Exhaustive lists should be avoided. References should follow the Vancouver format. In the text they should appear as numbers starting at one and at the end of the paper they should be listed (double-spaced) in numerical order corresponding to the order of citation in the text. Where a reference is to appear next to a number in the text, for example following an equation, chemical formula or biological acronym, citations should be written as (ref. X) and not as superscript.

Example: "detectable levels of endogenous Bcl-2 (ref. 3), as confirmed by western blot"

All authors should be listed for papers with up to six authors; for papers with more than six authors, the first six only should be listed, followed by *et al.* Abbreviations for titles of medical periodicals should conform to those used in the latest edition of Index Medicus. The first and last page numbers for each reference should be provided. Abstracts and letters must be identified as such. Papers in press may be included in the list of references.

Personal communications must be allocated a number and included in the list of references in the usual way or simply referred to in the text; the authors may choose which method to use. In either case authors must obtain permission from the individual concerned to quote his/her unpublished work.

Examples:

Journal article, up to six authors:

Belkaid Y, Rouse BT. Natural regulatory T cells in infectious disease. *Nat Immunol* 2005; 6: 353–360.

Journal article, e-pub ahead of print:

Bonin M, Pursche S, Bergeman T, Leopold T, Illmer T, Ehninger G *et al.* F-ara-A pharmacokinetics during reduced-intensity conditioning therapy with fludarabine and busulfan. *Bone Marrow Transplant* 2007; e-pub ahead of print 8 January 2007; doi:10.1038/sj.bmt.1705565

Journal article, in press:

Gallardo RL, Juneja HS, Gardner FH. Normal human marrow stromal cells induce clonal growth of human malignant T-lymphoblasts. *Int J Cell Cloning* (in press).


Complete book:

Atkinson K, Champlin R, Ritz J, Fibbe W, Ljungman P, Brenner MK (eds). *Clinical Bone Marrow and Blood Stem Cell Transplantation*, 3rd edn. Cambridge University Press: Cambridge, UK, 2004.

Chapter in book:

Coccia PF. Hematopoietic cell transplantation for osteopetrosis. In:

Revised 06/07/2016

nature publishing group 

3

For full details please visit:

http://www.nature.com/bmt/bmt_new_gta.pdf

Appendix 2.3 NHS West of Scotland Research Ethics Service (WoSRES) approval

WoSRES
West of Scotland Research Ethics Service

Dr Sarah Wilson
Senior Lecturer, Associate Academic
University of Glasgow
Gartnavel Royal Hospital
Administration Building, 1st Floor
1055 Great Western Road
Glasgow
G12 0XH

West of Scotland REC 4
West Ambulatory Care Hospital
Dalnair Street
Yorkhill
Glasgow
www.nhs.uk/ggc

Date 13 July 2016
Direct line 0141-232-1806
e-mail Wosrec4@ggc.scot.nhs.uk



Version 3 Originally issued 04 February 2016; reissued due to incorrect study title

Dear Dr Wilson

Study title:	Caregivers experiences and coping strategies relating to patients subjective treatment related cognitive impairment following Haematopoietic Stem Cell Transplant (HSCT)
REC reference:	16/WS/0003
IRAS project ID:	187898

Thank you for your email of 3 February 2016. I can confirm the REC has received the documents listed below and that these comply with the approval conditions detailed in our letter dated 29 January 2016

Documents received

The documents received were as follows:

Document	Version	Date
Participant information sheet (PIS) [Patient]	4	03 February 2016
Participant information sheet (PIS) [Participant]	4	03 February 2016

Approved documents

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

Document	Version	Date
Covering letter on headed paper [Final cover letter]	2	15 January 2016
Interview schedules or topic guides for participants	1	10 August 2015
Other [Final letter to recruiters (Beatson staff)]	2	15 January 2016
Other [Joint Patient AND Participant consent form]	3	15 January 2016

<i>Document</i>	<i>Version</i>	<i>Date</i>
Participant consent form [Final PATIENT consent form]	2	23 October 2015
Participant consent form [Final permission to contact participant]	1	24 August 2015
Participant consent form [Final participant consent form]	2	23 October 2015
Participant information sheet (PIS) [Patient]	4	03 February 2016
Participant information sheet (PIS) [Participant]	4	03 February 2016
REC Application Form [REC_Form_04122015]		04 December 2015
Research protocol or project proposal [Final research proposal]	4	23 October 2015
Research protocol or project proposal [Final research proposal]	5	15 January 2016
Summary CV for Chief Investigator (CI) [Sarah Wilson (CI) CV]	1	24 July 2015
Summary CV for student [Gemma McGill (Primary Researcher) CV]	1	16 September 2015

You should ensure that the sponsor has a copy of the final documentation for the study. It is the sponsor's responsibility to ensure that the documentation is made available to R&D offices at all participating sites.

16/WS/0003

Please quote this number on all correspondence

Yours sincerely



Miss Sophie Bagnall
Assistant Coordinator

Copy to: Ms Emma-Jane Gault
Ms Elaine O'Neill, NHS Greater Glasgow and Clyde

Appendix 2.4 Beatson West of Scotland Cancer Centre (BWoSCC) approval

CTEC approval

Avril Trevethan

Sent: 09 October 2015 15:18
To: [Gemma McGill](#)

Hi Gemma,

I would like to confirm that your trial below received 'A' approval at today's CTEC meeting. Can I clarify your supervisor Chris surname for the minutes.

**Title: GMG – Transplant-Caregivers
Treatment-related cognitive impairment following Haematopoietic Stem Cell
Transplant:
Caregivers' experiences and coping strategies**

Good luck with your research.

Kind regards
Avril

Avril Trevethan
Regulatory Administrator
Cancer Research UK Clinical Trials Unit
(partner in CaCTUS - Cancer Clinical Trials Unit Scotland) West of Scotland
Beatson Cancer Centre,
Level 0
1053 Great Western Road
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Tel. No: 0141 301 7176

E-mail address: Avril.Trevethan@glasgow.ac.uk
Visit our web site at: <http://www.crukctuglasgow.org>
The University of Glasgow, charity number SC004401

Appendix 2.5 NHS Greater Glasgow and Clyde Research and Development approval



Administrator: Mrs Elaine O'Neill
Telephone Number: 0141 232 1815
E-Mail: elaine.o'neill2@ggc.scot.nhs.uk
Website: www.nhsggc.org.uk/r&d

R&D Management Office
West Glasgow ACH
Dalnair Street
Glasgow G3 8SW

8 February 2016 – Re-issue

Miss Gemma McGill
Trainee Clinical Psychologist
Gartnavel Royal Hospital
1055 Great Western Road
Glasgow G12 0XH

NHS GG&C Board Approval

Dear Miss McGill,

Study Title:	Caregivers experiences and coping strategies relating to patients subjective treatment related cognitive impairment following Haematopoietic Stem Cell Transplant
Principal Investigator:	Miss Gemma McGill
GG&C HB site	The Beatson West of Scotland Cancer Centre
Sponsor	NHS Greater Glasgow and Clyde
R&D reference:	GN15HA386
REC reference:	16/WS/0003
Protocol no:	V5; 15/01/16

I am pleased to confirm that Greater Glasgow & Clyde Health Board is now able to grant **Approval** for the above study.

Conditions of Approval

1. **For Clinical Trials** as defined by the Medicines for Human Use Clinical Trial Regulations, 2004
 - a. During the life span of the study GGHB requires the following information relating to this site
 - i. Notification of any potential serious breaches.
 - ii. Notification of any regulatory inspections.

It is your responsibility to ensure that all staff involved in the study at this site have the appropriate GCP training according to the GGHB GCP policy (www.nhsggc.org.uk/content/default.asp?page=s1411), evidence of such training to be filed in the site file.

Appendix 2.6 NHS West of Scotland Research Ethics Service (WoSRES) minor amendment approval

WoSRES

West of Scotland Research Ethics Service

Miss Gemma McGill
Gartnavel Royal Hospital
Administration Building, 1st Floor, 1055 Great
Western Road
Glasgow
G12 0XH

West of Scotland REC 4
West Ambulatory Care Hospital
Dalnair Street
Yorkhill
Glasgow
www.nhsggc.org.uk

Date 13 July 2016
Direct line 0141-232-1807
e-mail Wosrec4@ggc.scot.nhs.uk



Version 3 Originally issued 06 May 2016; Reissued due to incorrect study title

Dear Miss McGill

Study title: Caregivers experiences and coping strategies relating to patients subjective treatment related cognitive impairment following Haematopoietic Stem Cell Transplant (HSCT)
REC reference: 16/WS/0003
Amendment number: AM01 (REC Ref AM02)
Amendment date: 04 May 2016
IRAS project ID: 187898

Summary of Amendment;

This substantial amendment refers to the recruitment process. In the original application the recruitment was done at the patient's annual review, the PIS will now be sent out to the homes of patients that are deemed eligible by the Clinical Team.

Thank you for your email of 04 May 2016, notifying the Committee of the above amendment.

The Committee does not consider this to be a "substantial amendment" as defined in the Standard Operating Procedures for Research Ethics Committees. The amendment does not therefore require an ethical opinion from the Committee and may be implemented immediately, provided that it does not affect the approval for the research given by the R&D office for the relevant NHS care organisation.

Documents received

The documents received were as follows:

Document	Version	Date
Notice of Minor Amendment [Email from student]	AM01 (REC Ref AM02)	04 May 2016

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for

Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

16/WS/0003:

Please quote this number on all correspondence

Yours sincerely



Sophie Bagnall
Assistant Coordinator

Copy to:

Ms Elaine O'Neill, NHS Greater Glasgow and Clyde
Dr Sarah Wilson, University of Glasgow
Ms Emma-Jane Gault

Appendix 2.7 NHS Greater Glasgow and Clyde Research and Development minor amendment approval

Non-substantial Amendment – R&D Ref GN15HA386 Protocol V5 Non-substantial Amendment AM01 (22/04/16)

O'Neill, Elaine [Elaine.O'Neill2@ggc.scot.nhs.uk]

Sent: 18 May 2016 15:04

To: Gemma McGill

Dear Miss G McGill,

R&D Ref: GN15HA386 **Ethics Ref:** 16/WS/0003

Investigator: Miss Gemma McGill

Project Title: 'Caregivers experiences and coping strategies relating to patients subjective treatment related cognitive impairment following Haematopoietic Stem Cell Transplant'

Protocol Number: V5; 15/01/16

Amendment: Non-substantial Amendment AM01 (22/04/16)

Sponsor: NHS Greater Glasgow and Clyde

I am pleased to inform you that R&D have reviewed the above study's Amendment AM01 (22/04/16) and can confirm that Management Approval is still valid for this study.

Reviewed Documents:	Version	Dated
Ethics acknowledgement		06/05/16
Notice of minor amendment – email		22/04/16

I wish you every success with this research project.

Kind regards
NHS GG&C R&D
West Glasgow Ambulatory Care Hospital
Dalnair Street
Glasgow G3 8SW

Tel: +44 (0)141 232 1815

Generic email for PR team: RandD.PRTeam@ggc.scot.nhs.uk

Web: www.nhsggc.org.uk/r&d

Please note that R&D operates a paperlite electronic record system. Please submit study documents via email

Appendix 2.8 Letter to recruiters



Dear Colleague,

Re: “Caregivers Experiences and Coping Strategies Relating to Patients Subjective Treatment-Related Cognitive Impairment following Haematopoietic Stem Cell Transplant”

Thank you for taking the time to read this information sheet. My name is Gemma McGill and I am a Trainee Clinical Psychologist at the University of Glasgow. I am currently in the initial planning stages of a qualitative research project which aims to investigate caregivers’ experiences of treatment related cognitive impairment in patients who have undergone Haematopoietic Stem Cell Transplant (HSCT). Given that cognitive compensatory interventions are often enhanced when supported by carers, a greater understanding of caregivers’ experiences of these challenges will help us to better understand their needs and provide appropriate support. This in turn could improve the outcomes of patients undergoing cognitive rehabilitation.

I aim to recruit 10 participants to this research. These would be the caregivers of patients who have received an allogeneic stem cell transplant in NHS GG&C. The following inclusion criteria will apply.

I would be grateful if you could identify individuals who are a caregiver to somebody who:

- Reports experiencing a degree of cognitive impairment which they associate with their Bone Marrow Transplant. These difficulties are identified using the NHS GG&C Haematopoietic Stem Cell Transplantation Service ‘Patient Distress Thermometer’.
- Has undergone total body irradiation, high dose chemotherapy or a combination of these within the last 20 years.
- Has no known psychiatric or neurological problems likely to lead to cognitive impairments e.g. schizophrenia, previous head injury, organic cognitive decline.
- Has no current use of psychotropic medication.
- Has no known learning disability.

Participants will be excluded from the study if:

- They do not speak fluent English as the interviews will be conducted in English.
- Their loved one has received total body irradiation, high dose chemotherapy or a combination of these within the last year.

- Their loved one lacks capacity to consent for their caregiver to take part.

Subject to your agreement, I will ask you to identify individuals who meet the inclusion criteria and who do not meet the exclusion criteria at the Bone Marrow Transplant Late Effects Clinic at the BWoSCC. If the patient identifies a difficulty with their memory/concentration, I will ask you to provide the patient with an information pack. This will include a covering letter, information sheets for the patient and their caregiver detailing the rationale, the aim of the study and what would be required of the caregiver e.g. areas of discussion should the patient consent and invite their caregiver to participate, and a consent form.

Please find enclosed the documents referred to above. I would be grateful if you could let me know if this recruitment procedure sounds feasible and if you are able to help. Thank you in advance for your time.

Please do not hesitate to contact me at g.mcgill.1@research.gla.ac.uk or Dr Christopher Hewitt at christopher.hewitt@ggc.scot.nhs.uk if you have any questions about this research.

Yours sincerely,

Gemma McGill
Trainee Clinical Psychologist

Under supervision of

Dr Christopher Hewitt (Consultant Clinical Psychologist, BWoSCC)
Dr Sarah Wilson (Senior Lecturer in Health Psychology, University of Glasgow)



“Caregivers Experiences and Coping Strategies Relating to Patients Subjective Treatment-Related Cognitive Impairment following Haematopoietic Stem Cell Transplant”

Dear.....

Thank you for taking the time to read this letter. My name is Gemma McGill and I am a Trainee Clinical Psychologist studying at the University of Glasgow. I understand that the symptoms you might experience following cancer treatment (such as difficulties with your memory and concentration) can impact upon your day to day activities and quality of life. In addition, I understand that these symptoms may not only affect the individual who has had the illness, but also family members and caregivers, amongst others. I am interested in finding out more about caregivers' experiences of the symptoms you may be experiencing following your cancer treatment, and how they have coped with these experiences.

Please find enclosed an information sheet which tells you more about this research project. If you are happy for your caregiver to be offered the opportunity to take part in this research, please provide them with the information sheet titled “Participant information sheet.” If your caregiver is interested in taking part in this project, I would be grateful if you both could complete the “Patient and Participant” consent form, and return this to me at your earliest convenience, in the stamped addressed envelope provided.

If you would like more information beyond what is provided in the enclosed information sheets, please do not hesitate to contact me on 07854 454 691 or at g.mcgill.1@research.gla.ac.uk

Thank you for your time.

Yours sincerely,

Gemma McGill
(Trainee Clinical Psychologist)

Under supervision of
Dr Christopher Hewitt
(Consultant Clinical Psychologist, Beatson West of Scotland Cancer Centre)

Dr Sarah Wilson
(Senior Lecturer in Health Psychology, University of Glasgow)



Patient Information sheet

“Caregivers Experiences and Coping Strategies Relating to Patients Subjective Treatment-Related Cognitive Impairment following Haematopoietic Stem Cell Transplant”

Thank you for taking the time to read this information sheet. Being provided with this information sheet means that your caregiver is eligible to take part in this research. Before you decide if you would like to invite your caregiver to take part, it is important that you understand why this study is being carried out and what it will involve.

Why is my caregiver being asked to participate?

My name is Gemma McGill and I am a Trainee Clinical Psychologist studying at the University of Glasgow. I am interested in finding out more about caregivers' experiences of their loved one's cognitive difficulties, such as difficulties with memory, concentration and planning, amongst others, following cancer treatment. This is because we know that cancer and its treatment not only affects the individual who has had the illness, but also family members and caregivers. Ongoing difficulties in cognitive functioning can pose challenges for caregivers and I am interested in learning more about these experiences.

Does my caregiver have to take part?

No, your caregiver's participation is voluntary and would require your consent.

What would the interview involve?

Following receipt of both your, and your caregivers consent, I would arrange a time that is convenient to talk to your caregiver. This would take place at the Beatson West of Scotland Cancer Centre (BWOSCC) or if that was not convenient, over the telephone. The interview would last between 45-90 minutes. The aim of the interview is to explore your caregiver's experiences with regard to any cognitive symptoms you have experienced following your cancer treatment; how they have coped with these both practically and emotionally and what supports they think may be helpful to them. The interview would be recorded which would allow me to have an accurate record of our discussion.

What are the advantages of taking part?

There are no direct or immediate benefits for you if you decide to consent for your caregiver to take part. However, what we learn from your caregivers' experiences would help to inform how services might better meet the needs of caregivers in the future. In addition, strategies which are sometimes given to patients to help with cognitive difficulties are often enhanced when supported by input from caregivers. Therefore, a better understanding of caregivers' needs in relation to the cognitive difficulties you are experiencing may improve the outcomes for other individuals with similar difficulties.

Will I or my caregiver be paid for taking part?

No payment will be made for taking part.

What are the disadvantages of taking part?

There are no direct disadvantages for you if you decide to consent for your caregiver to take part. However, it is possible that the interview may cover topics that your caregiver may find difficult to talk about, depending on their experiences. They will be informed that they may end the interview at any time. If they wish to continue, regular breaks will be offered. They will also be signposted to appropriate sources of support if they think they would benefit from this, or be advised to contact their own GP.

Who will know my caregiver is taking part?

The staff at the Bone Marrow Transplant Late Effects Clinic will know that your caregiver is eligible to take part in the study and therefore, will have provided you with this information sheet. However, they will not know if you provided consent for your caregiver to take part. Therefore, nobody involved in your care will know your caregiver is taking part. The information your caregiver provides will be confidential, unless something is revealed during the discussion which indicated that you, your caregiver, or someone else is at risk of harm. In that situation, I have a duty of care to share this information with the appropriate professionals, but I would tell your caregiver before I did this.

What will happen to the information my caregiver and I provide?

The interview will be recorded which will allow me to have an accurate record of the discussion between your caregiver and I. The recording will be stored on a password protected computer which only I have access to. Following the interview, the recording will be typed up and any information that identifies people or places will be removed and replaced so that neither you nor your caregiver can be identified. A sample of typed up interviews will be read by my supervisors; however, this will be following the removal of any identifiable information, so they will not be able to identify you or your caregiver. The recorded interview will be transferred onto a compact disc (CD) and stored securely along with your signed consent form, in a locked filing cabinet in the office of the Chief Investigator of this project, Dr Sarah Wilson (Senior Lecturer in Health Psychology, University of Glasgow). The recording will then be deleted from the computer. Representatives of the study Sponsor, NHS GG&C may look at your personal information to make sure that the study is being conducted properly.

What will happen to the results of the study?

With your permission, we may want to use quotations from your caregiver's interview in the final report which will be written up and submitted as part of my academic work for my degree in Doctorate in Clinical Psychology. The quotations may also be presented at conferences and published in academic journals. As mentioned previously, all information that could identify you or your caregiver will have been removed. You will be provided with a summary of the results if you wish, and access to the full report will be available electronically via the University of Glasgow Theses Service.

Who has reviewed this study?

This study has been reviewed by academic staff from the Doctorate in Clinical Psychology at the University of Glasgow. It has also been reviewed by a Research Ethics Committee

which exists to protect your interests, and the Research and Development department of NHS Greater Glasgow and Clyde.

Independent Advisor for further information

If you are undecided about inviting your caregiver to take part and would like to speak to someone who is not directly involved in this study but who is aware of what the study involves, please contact Dr Hamish McLeod, (Programme Director for Doctorate in Clinical Psychology and Senior Lecturer at the Institute of Mental Health and Wellbeing). You can contact Dr McLeod on 0141 211 3920 or email him at Hamish.McLeod@glasgow.ac.uk

I am happy for my caregiver to participate, what should I do?

I would kindly ask that you give them the enclosed information sheet titled "Participant information sheet." If your caregiver is interested in taking part in this project, I would be grateful if you could both complete the "Patient and Participant" consent form, and return this to me at your earliest convenience, in the stamped addressed envelope provided. This confirms that you have both read and understood the information provided to you, that you have had the opportunity to ask any questions about the study, and that you are happy for your caregiver to participate. Due to the design of the study, a maximum of 10 caregivers will be interviewed, and therefore, recruitment will be on a first-come, first-served basis.

If you would like more information beyond what is provided in the enclosed information sheet or to discuss this project further, please do not hesitate to contact me on 07854 454 691 or at g.mcgill.1@research.gla.ac.uk

Thank you for your time.

Sincerely,

Gemma McGill
(Trainee Clinical Psychologist)

Under supervision of

Dr Christopher Hewitt (Consultant Clinical Psychologist, BWoSCC)
Dr Sarah Wilson (Senior Lecturer in Health Psychology, University of Glasgow)



Participant Information sheet

“Caregivers Experiences and Coping Strategies Relating to Patients Subjective Treatment-Related Cognitive Impairment following Haematopoietic Stem Cell Transplant”

Thank you for taking the time to read this information sheet. Being provided with this information sheet means that you are eligible to take part in this research if your loved one provides their consent. Before you decide if you would like participate it is important that you understand why this study is being carried out and what it will involve.

Why am I being asked to participate?

My name is Gemma McGill and I am a Trainee Clinical Psychologist studying at the University of Glasgow. I am interested in finding out more about caregivers' experiences of their loved one's cognitive difficulties. These include poor memory, concentration and planning, amongst others, following cancer treatment. We know that cancer and its treatment not only affects the individual who has had the illness, but also family members and caregivers. Ongoing cognitive difficulties can pose challenges for caregivers and I am interested in learning more about these experiences.

Do I have to take part?

No, participation is voluntary. If you did decide to take part, you are free to withdraw from the study at any time. It will not affect the medical care your loved one receives if you decide not to take part or if you withdraw from the study after you have agreed to take part.

What would the interview involve?

Following receipt of both your, and your loved one's consent, I would arrange a time that is convenient to talk to you. This would take place at the Beatson West of Scotland Cancer Centre (BWOSCC) or if that was not convenient, over the telephone. The interview would last between 45-90 minutes. The aim of the interview is to explore your experiences with regard to any cognitive symptoms your loved one has experienced following their cancer treatment; how you have coped with these experiences both practically and emotionally and what supports you think would help you. The interview would be recorded which would allow me to have an accurate record of our discussion.

What are the advantages of taking part?

There are no direct or immediate benefits for you if you decide to take part. However, what we learn from your experiences will help us to understand how services might better meet the needs of caregivers in the future. In addition, strategies which can be

given to patients to help with cognitive difficulties are often enhanced when supported by caregivers. Therefore, a service which helps caregivers to better understand or cope with the cognitive difficulties their loved ones are experiencing may, in turn, improve the outcomes for the individuals engaged in rehabilitation for these difficulties.

Will I or my loved one be paid for taking part?

No payment will be made for taking part.

What are the disadvantages of taking part?

You may have found that caring for an individual with cognitive difficulties is a challenging experience. It is possible that the interview may cover topics that you may find difficult to talk about. If this is the case, you may stop the interview at any time. If you wish to continue, regular breaks will be offered. You will also be directed to sources of support if you think you would benefit from this.

Who will know I am taking part?

The staff at the Bone Marrow Transplant Late Effects Clinic will know that you are eligible to take part in the study and will have provided your loved one with an information pack. However, they will not know if your loved one provided their consent for you to be invited to participate and therefore will not know if you are taking part. The information you provide will be confidential, unless something is revealed during the discussion which indicated that you, your loved one or someone else is at risk of harm. In that situation, I have a duty of care to share this information with the appropriate professionals, but I would tell you before I did this.

What will happen to the information I provide?

The interview will be recorded which will allow me to have an accurate record of our discussion. The recording will be stored on a password protected computer which only I have access to. Following the interview, the recording will be typed up and any information that identifies people or places will be removed and replaced so that neither you nor your loved one can be identified. A sample of typed up interviews will be read by my supervisors; however, this will be following the removal of any identifiable information, so they will not be able to identify you or your loved one. The recorded interview will be transferred onto a compact disc (CD) and stored securely along with your signed consent form, in a locked filing cabinet in the office of the Chief Investigator of this project, Dr Sarah Wilson (Senior Lecturer in Health Psychology, University of Glasgow). The recording will then be deleted from the computer. Representatives of the study Sponsor, NHS GG&C may look at your personal information to make sure that the study is being conducted properly.

What will happen to the results of the study?

With your permission, we may want to use quotations from your interview in the final report which will be written up and submitted as part of my academic work for my degree in Doctorate in Clinical Psychology. The quotations may also be presented at conferences and published in academic journals. As mentioned previously, all information that could identify you or your loved one will have been removed. You will be provided with a summary of the results if you wish, and access to the full report will be available electronically via the University of Glasgow Theses Service.

Who has reviewed this study?

This study has been reviewed by academic staff from the Doctorate in Clinical Psychology at the University of Glasgow. It has also been reviewed by a Research Ethics Committee which exists to protect your interests, and the Research and Development department of NHS Greater Glasgow and Clyde.

Independent Advisor for further information

If you are undecided about taking part and would like to speak to someone who is not directly involved in this study but who is aware of what the study involves, please contact Dr Hamish McLeod, (Programme Director for Doctorate in Clinical Psychology and Senior Lecturer at the Institute of Mental Health and Wellbeing). You can contact Dr McLeod on 0141 211 3920 or email him at Hamish.McLeod@glasgow.ac.uk

I think I would like to participate, what should I do?

If you would like to participate I would ask that you kindly complete the “Patient and Participant Consent Form”, and return this to me at your earliest convenience, in the stamped addressed envelope provided. This confirms that you have both read and understood the information provided to you, that you have had the opportunity to ask any questions and that you are willing to take part.

I would be grateful if you could provide your contact details on page 3 of the “Patient and Participant Consent Form.” This will allow me to contact you to arrange a suitable time for the interview.

Due to the design of the study, a maximum of 10 caregivers will be interviewed, and therefore, recruitment will be on a first-come, first-served basis. If 10 other caregivers have already expressed an interest when I receive your consent form, I will contact you to let you know. If you still wish to take part, you will be invited to join a waiting list in case any other caregivers decide that they no longer wish to take part.

If you would like more information beyond what is provided in the enclosed information sheet or to discuss this project further, please do not hesitate to contact me on 07854 454 691 or at g.mcgill.1@research.gla.ac.uk

Thank you for your time.

Sincerely,

Gemma McGill
(Trainee Clinical Psychologist)

Under supervision of

Dr Christopher Hewitt (Consultant Clinical Psychologist, BWoSCC)
Dr Sarah Wilson (Senior Lecturer in Health Psychology, University of Glasgow)



Patient and Participant Consent form

“Caregivers Experiences and Coping Strategies Relating to Patients Subjective Treatment-Related Cognitive Impairment following Haematopoietic Stem Cell Transplant”

I would be grateful if the **patient** who attends the Bone Marrow Transplant Late Effects Clinic could please complete page 1 and 2 of this consent form.

Please initial box

I confirm that I have read and understood the information provided in the patient information sheet (Version 4, 3.2.16) for the above study.

☐

I confirm that I have had the opportunity to ask questions before inviting my caregiver to participate in the above study.

☐

I understand that my caregiver’s participation is voluntary and their decision to withdraw from the study at any time will not affect my medical treatment in any way.

☐

I understand that the interview will be recorded, kept confidential and stored securely within the University of Glasgow until it is destroyed in line with University of Glasgow and NHS Greater Glasgow and Clyde procedures.

☐

I understand that anonymised quotations from my caregiver’s interview may be used in the final report written as part of the researcher’s academic work for the degree in Doctorate in Clinical Psychology and presented at conferences, published in academic journals and be accessed via the University of Glasgow Theses Service.

☐

I consent for my caregiver to take part in this study if they wish to.

☐

I consent for my caregiver to disclose my age and gender if they feel it is necessary for the explanation of issues.

☐

I would like to receive a written summary of the results when the study has been completed (Please provide your contact details overleaf.)

☐

Please insert posting address:

.....
.....

Or emailed to me at the following email address, (please insert email address).

.....

Name of patient

Signature

Date

Name of researcher

Signature

Date

(To be completed by primary researcher following receipt of patient and participant consent.)

I would be grateful if the **caregiver** could please complete page 3 and 4 of this consent form.

Please initial box

I confirm that I have read and understood the information provided in the participant information sheet (Version 4, 3.2.16) for the above study.

☐

I confirm that I have had the opportunity to ask questions about the above study before providing my consent to participate.

☐

I understand that my participation is voluntary and that my decision to withdraw from the study at any time will not affect my loved one's medical treatment in any way.

☐

I understand that the interview will be recorded, kept confidential and stored securely within the University of Glasgow until it is destroyed in line with University of Glasgow and NHS Greater Glasgow and Clyde procedures.

☐

I understand that anonymised quotations from my interview may be used in the final report written as part of the researcher's academic work for the degree in Doctorate in Clinical Psychology and presented at conferences, published in academic journals and be accessed via the University of Glasgow Theses Service.

☐

I consent to take part in this study.

☐

I would like to receive a written summary of the results when the study has been Completed. Please provide your contact details below.

☐

Please insert posting address:

.....
.....

Or emailed to me at the following email address, (please insert email address).

.....

Home phone number:

Mobile phone number:

Name of participant (caregiver)

Signature

Date

Name of researcher

Signature

Date

(To be completed by primary researcher following receipt of patient and participant consent).

Appendix 2.13 Topic guide for interview

1	What do you and your partner/loved one call the difficulties they are experiencing?
2	Can you tell me about when you first realised/noticed your (partner/loved one) was having some difficulties with their (insert their choice of term, e.g. memory) Prompts: - When was this? (try to determine how recently after treatment) -What was happening around that time for you and your loved one (to determine levels of stress) -How were you feeling at that time?
3	Can you describe the difficulties they had/have? Prompts: What difficulties did you/partner notice: Memory Attention Concentration Planning Multi-tasking
4	What did you think was causing this? Prompts: Did you know to expect this? How did you know to expect this? (who told you?) How did that make you feel?
5	What were/are the implications of these difficulties? Prompts: Has there been any effect on your relationship? Roles/responsibilities Stress levels / your own health Work Leisure time / home life Future plans What has been the best/worst aspect of your situation?
6	How do you cope/manage these difficulties emotionally? How have you coped/managed? Prompts: What helps/doesn't help?
7	How do you/have you coped/managed these difficulties practically? Prompts: What helps / doesn't help?
8	Has there been any change in the symptoms or symptom severity over time? Prompts: Improved/declined – what effect has that had on you? Do you expect a change? How do you feel about that?
9	Is there anything you wish you had known about the cognitive impairment before your experiences? Prompt: Would that have made a difference to: Relationships Stress Health Work etc (as in question 5)
10	Would anything have made your experience easier to cope with? Prompt: Do you feel there are services available to support you? Yes: What are they? In what ways are they helpful/unhelpful? No: Has anyone informed you of them?
11	When would this support have been most helpful?
12	What advice would you give to someone in a similar situation to yourself?

Appendix 2.14 Participant demographics

Participant no.	Participant gender	Participant age	Patient gender	Patient age
1 Liz	Female	65	Male	64
2 Ange	Female	51	Male	54
3 Katie	Female	35	Male	34
4 Paula	Female	64	Male	70
5 Tina	Female	60	Male	61

Appendix 2.15 Excerpts from interviews 3 and 5

Emergent themes	Original transcript - Katie	Exploratory comments
<p>His needs first.</p> <p>Limitations cause frustration.</p> <p>Compensating for his limitations.</p> <p>Commitment to partner.</p> <p>Acceptance, (easier to accept as he hasn't caused this problem)</p>	<p>P: yea, its,... its stressful,... it can be stressful because when I'm at work and I'm in the middle of, my work can be really intensive and I'm maybe in the middle of a situation and I know that Mike has a hospital appointment or he has the dog, the dog has an appointment or something,... I've got to ensure that I've either set my alarm or set his alarm for him to take his medication or for him to take it on time because he forgets quite easily. He forgets they things and then he forgets he's got to go and do something or he's got to go to his mums for something or whatever it may be so I find that yea, when I'm in the middle of doing something at my work I've got to take time out to remember or on Mike's behalf to contact him to let him know, but ehm,... we work really well, we work well together. It's not something that I've actually sat down and thought about until ehm, you've asked me the questions, because I think you just,... when you're in a relationship you just get on with it, it's just part of who he is and who I am, so together as a team</p> <p>I: aw how lucky for Mike that he's got someone so supportive. I mean it sounds like it does really affect you but you've got a sense of well, that's him, we're a team, I just need to sort of get on with things?</p> <p>P: yep, make it as easy for him as I can, because it's not something that he would have wanted or something that he's wished for but it's something that we need to work through, that's just, yea.</p>	<p>Out of the blue that work is intensive, suggests Mike's limitations make an already stressful situation more stressful. Can't simply focus on work at work times. Always thinking of Mike.</p> <p><i>Repetition of forgets suggests this is the main problem.</i></p> <p><i>"whatever it might be" suggests he is forgetting a variety of things.</i></p> <p><i>Repetition, confirming they work well together OR <u>attempts to convince self they work well together?</u></i></p> <p>Helping is obvious/second nature.</p> <p>Belief that if you have committed to someone you deal with their difficulties regardless of the stress it creates.</p> <p>He didn't ask for this limitation</p> <p>Sympathy for Mike causes her to put his needs before her own, despite the stress it causes</p>

Emergent themes	Original transcript - Tina	Exploratory comments
<p>Hopeless, nothing can improve the situation.</p> <p>Learned helplessness.</p> <p>Commitment despite distress.</p>	<p>some people can get up from it and then just carry on with their life, but Jake is just not one of them that can deal with anything</p> <p>I: so the fact that he sort of struggles to cope, that sort of really impacts on you by the sounds of it because you then have to pick up everything</p> <p>P: yep, yep</p> <p>I: and, has there been anything that you think might have made these experiences easier to cope with? Have you received any support?</p> <p>P: no, no.</p> <p>I: is there anything you think might have been helpful? Say you went to someone now, and said these are all the problems I'm having and have had for the past 10/15 years, what sort of support would you think might be helpful, what would make a difference?</p> <p>I: just for my life to go back to where it was at the beginning, (pause), I mean that is the only thing because, as much as I say I'd love to get up and walk away, I love him and I could never leave him</p>	<p><u>Resent that they are the unlucky ones</u> who can't deal with anything, that can't carry on as normal despite difficulties.</p> <p><i>'anything' highlights the severity of lack of coping</i></p> <p><i>Repetition suggest a strong sense of agreement with summary given by interviewer</i></p> <p>Shut down to idea of possible support/help. Perhaps as a result of feeling this way for so long. Does not believe anything will help. <i>Repetition suggest this is a strongly held belief</i></p> <p>Loyalty over-rides difficulties.</p> <p><u>No life other than pre-transplant will do. Sense of conflict between meeting her needs and meeting partners.</u> <i>Pause highlights contemplation, a there is a sense she is remembering the past.</i> Love and commitment prevents her from leaving</p>

Appendix 2.16 Process of Analysis

Smith et al's (2009) six step process of analysis	Process engaged in by researcher
Reading and re-reading	Transcripts were read and re-read, allowing the researcher to become immersed in, and actively engaged with the data.
Initial noting	Original transcript data was copied into a 3 column table. Initial noting of anything of interest was completed in 1 column. This included anything that appeared emotive for the participant, anything that was repeated, use of language such as laughter, pauses, any contradictions, etc.
Developing emergent themes	Using the initial notes, provisional emerging themes were noted in another column which sought to combine the participants original words and thoughts and the researchers interpretation of the words and thoughts.
Searching for connections across emergent themes	Emerging themes were written on post-its and placed on a large table to allow the researcher to explore spatial representations of how the emerging themes best fitted together.
Moving on to the next case	The above process was repeated for the remaining four transcripts.
Looking for patterns across cases	Finally, the researcher looked for connections and patterns across transcripts which allowed for the development of super-ordinate themes.

Appendix 2.17 Quality Assurance

Owing to the subjective nature of qualitative research, it is essential to demonstrate factors that are characteristic of high quality qualitative research. These include *sensitivity to context; commitment and rigour, transparency and coherence, and impact and importance* (Yardley, 2000).

Sensitivity to context	Demonstrated by offering telephone interviews based on knowledge of literature that illustrates that caregivers' have competing demands and little time for their own activities. Similarly, in recognition of the physical uncertainty that surrounds HSCT, it was made clear that participation would have no bearing on their loved one's medical care in any way.
Commitment	Demonstrated by the researcher immersing herself both in the theoretical literature of the topic area and in the raw data. Rigour was demonstrated by reaching data saturation and in turn, illustrating the prevalence of themes across participants. Smith et al., (2009) suggests a sample between four and eight should provide extracts from at least three participants for each theme (See Appendix 2.18 for illustration of theme recurrence). Triangulation of the data was also used to ensure the researchers understanding of the participant's experiences was not based solely on her own perspective, increasing the validity of the results.
Transparency and coherence	Demonstrated by detailing the data collection process and presenting an excerpt of the data from which readers can begin to understand how the researcher interpreted the data and arrived at the chosen themes. In addition, in the process of IPA, the researcher plays an active role in interpreting the data (Smith et al., 2009). It has been acknowledged that "inevitably the analysis is a joint product of the participants and analyst, the end result is always an account of how the analyst thinks the participant is thinking". (Smith et al., 2009; p.80). Therefore the researcher practiced reflexivity when considering her role in the study to ensure her perspectives were transparent from the outset. These were discussed with the academic and field supervisor when the project was in development stages. In addition, following each interview and prior to data analysis the researcher kept a diary of personal feelings in order to become aware of these with the aim of reducing potential bias during interpretation of the data.
Impact and importance	Demonstrated by suggesting an avenue for future research based on a combination of previous literature and current findings and suggesting how, based on the current findings, caregivers' needs can be better met.

Appendix 2.18 Table of recurrence of super-ordinate themes

Super-ordinate themes	Participant 1 - Liz	Participant 2 - Ange	Participant 3 - Katie	Participant 4 -Paula	Participant 5 - Tina
Noticing change	YES	YES	YES	YES	YES
Managing expectations	YES	YES	YES	YES	YES
Managing personal feelings	YES	YES	YES	NO	YES
Commitment	YES	YES	YES	YES	YES

