

**A randomised controlled trial of a  
rehabilitation programme to assist physical  
and psychosocial recovery after stem cell  
transplantation**

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**Lydia Bird BN (Hons)**

**Thesis submitted to the University of Nottingham for the  
degree of Doctor of Philosophy**

**May 2008**

# **Abstract**

## **Background**

Stem cell transplantation is routinely used in the treatment of haematological malignancy. However, it is an intensive treatment frequently associated with a considerable deterioration in patients' wellbeing and prolonged recovery. Research into the amelioration of the negative biopsychosocial factors associated with stem cell transplantation is essential, facilitating nurses and other health professionals to provide the best possible care to individuals who have been treated with a stem cell transplant.

## **Study Design**

58 patients who had been treated with a stem cell transplant were recruited and randomly allocated to either a health profession led rehabilitation programme or a self managed rehabilitation programme. Follow-up measures (SF-36, QHQ, Graham and Longman QoL Scale and SWT) were taken at three and six months. Qualitative interviews were conducted with 15 of the 58 participants and with five members of staff.

## **Results**

In all dimensions of the SF-36 the scores of patients recovering after stem cell transplantation indicated poorer health status in comparison to UK population norms supporting the need for rehabilitation services for this patient group. No evidence of a difference between the two modes of rehabilitation was observed for any of the trial outcomes.

The qualitative interview data indicated that from patients' and staff's perspectives there was scope for improvement in the rehabilitation

programmes. The interview data also highlighted that staff were concerned that the trial conditions had negatively impacted the provision of rehabilitation, drawing attention to the difficulties inherent in the evaluation of complex interventions.

## **Conclusions**

Existing literature, the SF-36 data collected in this study and the experiences of both patients and health professionals expressed in the qualitative component of this study all indicate that rehabilitation is an important component of health care following stem cell transplantation. However, the rehabilitation needs and desires of this patient group are complex and therefore any rehabilitation programme must reflect this complexity. Enabling patients to work collaboratively with health professionals in determining the most appropriate provision of rehabilitation may result in enhanced levels of patient satisfaction with rehabilitation services. However, the efficacy of rehabilitation following stem cell transplantation remains unproven and the provision and evaluation of patient centred rehabilitation raises numerous practical and methodological challenges.

## **Acknowledgements**

I would like to thank my supervisors, Karen Cox and Tony Arthur, for their enthusiasm and unwavering encouragement throughout this project.

Without fail I left our meetings with renewed clarity and purpose. I would also like to thank Tara Niblock, Rebecca Stone and Lynn Watson along with all the staff from the Haematology department at Nottingham City Hospital. Without them this project would never have happened. I would also like to thank the University of Nottingham for the financial support provided to me through the School of Nursing studentship.

I am very grateful to all the patients who gave up their time to participate in the study. In particular I would like to thank the patients and members of staff who gave up their time to be interviewed and who shared their experiences with me.

Finally I want to thank my family and friends for their support, patience and understanding. In particular my thanks go to Martin for his encouragement and belief in me and to Phoebe for giving me perspective when I needed it.

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## **List of Abbreviations**

BMT	Bone Marrow Transplant
CI	Confidence Interval
CMV	Cytomegalovirus
GHQ	General Health Questionnaire
GP	General Practitioner
GVHD	Graft Versus Host Disease
HADS	Hospital Anxiety and Depression Scale
HLA	Human Leukocyte Antigen
HPL	Health Profession Led
NOK	Next Of Kin
QoL	Quality of Life
SCT	Stem Cell Transplant
SD	Standard Deviation
SF-36	Short Form 36 Health Status Questionnaire
SM	Self Managed
SWT	Shuttle Walk Test
UK	United Kingdom

# **Chapter 1 - Introduction**

## **1.1 Stem cell transplantation**

Stem cell transplantation is a routine treatment for many patients diagnosed with a haematological malignancy (Duncombe 2003). However the impact that diagnosis and subsequent treatment with stem cell transplantation has on an individual should not be underestimated. Individuals with haematological malignancies can present with a very short clinical history of weeks or even days. Alternatively patients may have spent months feeling vaguely unwell without seeking medical advice since they had no specific symptoms. Newly diagnosed patients are often encouraged to rapidly progress to active treatment. Treatment usually consists of chemotherapy often combined with total body irradiation. This process causes the destruction of the patient's own bone marrow cells. These cells are then replaced with bone marrow or peripheral blood stem cells that have been collected, either from a donor or from the patient during a period of disease remission. Whilst these treatments do now offer the chance of cure from previously fatal diseases, stem cell transplantation is still a high risk treatment which is associated with significant short and long term side effects that have a considerable impact on every aspect of an individual's life.

## **1.2 The study**

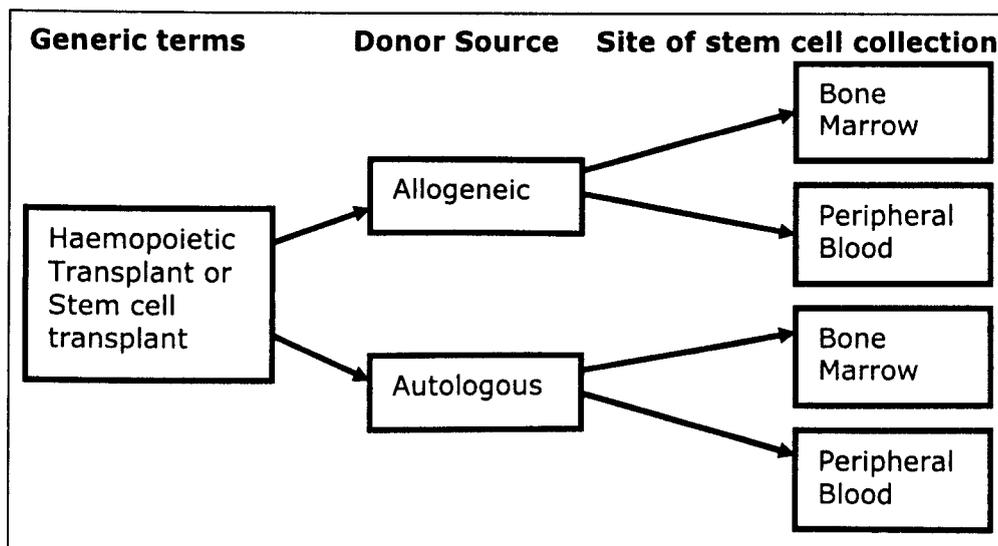
A randomised controlled trial was used to evaluate a health profession led rehabilitation programme following stem cell transplantation for the treatment of haematological malignancies. The health profession led rehabilitation programme consisted of a ten week programme of exercise, relaxation and information. In order to provide a suitable comparator a self managed rehabilitation programme was devised. The self managed

programme consisted of a series of information leaflets. The primary aim of this study was to evaluate the effectiveness of the health profession led rehabilitation programme in promoting recovery six months after stem cell transplantation.

### **1.3 Clarification of terms**

The terms that are commonly used in relation to stem cell transplantation are set out in figure 1.1. The terms 'haemopoietic transplant' and 'stem cell transplant' are synonymous and refer to the transplantation of any stem cells regardless of their source or site of collection. Throughout this study the term stem cell transplant will be used. The term 'allogeneic transplant' refers to a transplant using donated stem cells. The term 'autologous' refers to transplants using stem cells that have been collected from an individual and stored whilst they undergo treatment and then returned to the same individual. Stem cells for use in autologous or allogeneic transplants can be harvested either directly from the bone marrow where they are produced or from the peripheral blood. In order to ensure sufficient numbers of cells are present in peripheral blood prior to collection the individual is treated with chemotherapy and/or growth stimulating factors to increase stem cell production. This study included individuals who had undergone any type of stem cell transplant.

**Figure 1.1: Transplant terminology (adapted from Duncombe 2003)**



### **1.4 Epistemological, ontological and methodological foundations**

This research is based upon a post-positivist epistemology and a critical realist ontological position recognising that we can never verify that we have achieved absolute knowledge, but asserting that it is possible to establish rules of causation that allow general principles to be drawn from specific examples. Traditionally different research methods have been inextricably linked to different ontological positions, quantitative techniques to realism and qualitative techniques to relativism. Post-positivism’s acknowledgement that different research methodologies lead to different types of knowledge is crucial to this research project. Both quantitative and qualitative approaches have been employed in order to explore different aspects of recovery after stem cell transplantation and in so doing to conduct research that is reflective of the experience of patients, and that can be used to influence policy decisions relating to service provision.

## **1.5 Theoretical foundations**

This study is situated within a biopsychosocial framework. At the core of this framework is the conviction that not just biological but also social, psychological and behavioural dimensions are crucial in the assessment of health. The biopsychosocial framework recognises that the boundaries between health and disease, between well and sick, are far from clear and that these concepts are diffused by cultural, social and psychological considerations (Engel, 1977). Further consideration of this theory can be found in section 2.6 of chapter two.

## **1.6 Clinical relevance of the study**

The code for professional conduct for nurses and midwives in the UK states that nurses must deliver care based on the best available evidence (Nursing & Midwifery Council, 2008). However, the guidelines do not provide advice on the appropriate course of action to take when the best available evidence is inconclusive, incomplete or contradictory. This was the situation encountered by the team at a busy haematology centre. The team had identified a need for further support, both physical and psychosocial, to individuals following stem cell transplantation. However, the existing evidence failed to demonstrate how best to proceed with meeting this need. The clinical team approached the University of Nottingham to ask for assistance in the evaluation of a rehabilitation service that they had designed to meet the identified need. Therefore the research on which this thesis is based was initiated in the clinical environment in response to an acknowledged need. It set out to answer a question raised by those actively involved in the delivery of care to those undergoing stem cell transplantation. As such, the study is rooted at the heart of clinical practice.

## **1.7 Overview of the thesis**

Chapter two discusses the use of stem cell transplantation as a treatment for haematological malignancies. The positive and negative sequelae associated with haematological malignancy and stem cell transplantation are considered in order to explore the long-term consequences of this diagnosis and its treatment. Consideration is also given to the research concerning the amelioration of these long-term effects and also to the wider body of work exploring the concept of cancer rehabilitation in general. It is shown that patients who have been diagnosed with a haematological malignancy and undergone treatment with a stem cell transplant have a range of physical, psychological and social rehabilitation needs and that there is some evidence that a combination of exercise, emotional and information may be effective in meeting this need. It is established that further research in this area is required.

In chapter three the methods employed in this study are described. Consideration is first given to the structure and content of the rehabilitation programme. This programme was originally proposed by a clinical team in response to an unmet need that they had perceived in patient care. Details are provided of a preliminary study that was carried out by this clinical team to assess the acceptability and feasibility of the programme. The aim and objectives for the current study are set out, followed by an explanation of why a randomised controlled trial was chosen as the most suitable method for meeting these. The changes to the rehabilitation programme that were introduced in order for a randomised controlled trial to be possible are then outlined. Once this important groundwork has been established the details of the research design for the randomised controlled trial are discussed.

Chapter four reports the results of the bone marrow and stem cell transplant rehabilitation trial. The chapter includes a description of the study sample and compares the demographic characteristics of those who took part with those who did not. The reasons participants gave for not wishing to take part are also reported. Detailed demographic and clinical details as well as baseline scores for the outcome measures are provided for participants randomised to both the health profession led and self managed rehabilitation programmes. The results of analysis carried out on the primary and secondary outcome data is then presented. Exploratory analysis is presented and finally the SF 36 data from this trial is compared with some normative data from the UK population.

Chapter five reports the findings of the qualitative data analysis conducted on the semi structured interviews that were carried out with 15 trial participants and five members of staff. The findings from each group of interviews are presented separately. Firstly, the views of participant interviewees on the experience of participating in a randomised controlled trial are presented. Secondly, the acceptability of each programme to participants is discussed. Finally, the experiences of the staff interviewees are explored.

Chapter six presents a discussion on the findings of the stem cell transplant trial and the associated qualitative investigation. This is followed by an examination of the methodology employed in this study. The rationale for using a randomised controlled trial is reconsidered and the potential merits and limitations of alternative designs that could have been employed are debated. Finally, consideration is given to the implications of this research for practice.

## **Chapter 2 - Literature Review**

### **2.1 Introduction**

This chapter discusses the use of stem cell transplantation as a treatment for haematological malignancies. The positive and negative sequelae associated with haematological malignancy and stem cell transplantation are considered in order to explore the long-term consequences of this diagnosis and its treatment. Consideration is also given to the research concerning the amelioration of these long-term effects and also to the wider literature relating to cancer rehabilitation.

### **2.2 Haematological Malignancies**

The majority of haematological malignancies fall into one of three broad diagnostic groups: leukaemia, myeloma or lymphoma. Leukaemia accounts for approximately three percent of all cancers in the United Kingdom. Each year in the UK almost 7,000 people are diagnosed with leukaemia and the disease causes more than 4,250 deaths (Cancer Research UK, 2006). Leukaemia is a neoplastic proliferation of cells of haematopoietic origin. It can be treated with chemotherapy which, in some cases, is combined with stem cell transplantation. The symptoms of leukaemia are due to the proliferation of leukaemic cells and their infiltration into normal tissue (Bratt-Wyton, 2000). Infiltration of leukaemic cells into the bone marrow leads to anaemia, neutropenia and thrombocytopenia, which can lead to infection and haemorrhage (Dexter, 1977). The four most common types of leukaemia are acute myeloid leukaemia, acute lymphoblastic leukaemia, chronic myeloid leukaemia and chronic lymphoblastic leukaemia (Bratt-Wyton, 2000).

Myeloma is a disease arising from uncontrolled growth of plasma cells (Dowling, 2000). It accounts for approximately one percent of all cancer diagnoses in the United Kingdom. Each year in the UK more than 3,600 cases of multiple myeloma are diagnosed and the disease causes more than 2,600 deaths (Cancer Research UK 2006). Symptoms of the disease occur either directly from the excessive malignant plasma protein in the bone or indirectly from the secreted products of abnormal immunoglobulins. The majority of patients present with symptoms which are secondary to bone destruction resulting from osteolytic lesions. Since myeloma is incurable the goal of treatment is symptom control (Dowling, 2000).

Lymphomas are a diverse group of diseases arising from lymphoid tissue. Lymphomas comprise two distinct groups: Hodgkin's lymphoma and non-Hodgkin's lymphoma. According to data gathered from 1973-1996 by the World Health Organisation International Agency for Research on Cancer the world-wide incidence of non-Hodgkin's lymphoma is rising steadily and incidence rates are observed to be higher in western Europe, North America and Australia (Parkin et al., 1997). The incidence of Hodgkin's lymphoma is consistently lower than that of non-Hodgkin's lymphoma. In contrast to the steady rise seen in incidence rates for non-Hodgkin's lymphoma, there was a 16% decrease in the incidence of Hodgkin's lymphoma from 1973-1996 (Parkin et al., 1997). Presenting symptoms for lymphoma can include localised lymphadenopathy, malaise, fever, night sweats and unexplained weight loss (Grundy, 2000). Both Hodgkin's lymphoma and non-Hodgkin's lymphoma are treatable, although non-Hodgkin's lymphoma in particular is still associated with significant mortality rates (Grundy, 2000).

## **2.3 Development of stem cell transplantation as a treatment for haematological cancers**

The first known medical use of bone marrow was by Brown-Sequard in 1891. Marrow was given orally after meals for the treatment of leukaemia (Benjamin, 1995). Between 1891 and the middle of the 20th century a number of attempts were made to use marrow in a variety of ways, albeit unsuccessfully, to cure diseases of the blood (Whedon, 1995). Animal experiments in the 1950's demonstrated that marrow cells could be successfully transfused, following destruction of haematopoietic cells with toxic radiation, resulting in engraftment of the transfused cells and restoration of haematopoiesis (Duncombe, 2003). However, attempts to replicate this finding in humans were hindered by a lack of understanding in the field of immunology. The first successful human bone marrow transplant was between identical twin siblings. Successful transplantation and engraftment of marrow between non-identical siblings and unrelated individuals only became possible with the discovery of the human leukocyte antigen (HLA) system. Human leukocyte antigens are a major component of the immune system and allow the body to recognise foreign material and attack it. If a donor and recipient are not well HLA-matched, transplanted cells recognise the recipient's body as foreign and attack it. This reaction is now known as graft versus host disease. The key historical milestones in the development of allogenic stem cell transplantation are summarised in figure 2.1.

Not all haematopoietic transplants require that donor cells be used. For some conditions it is sufficient to remove haematopoietic cells from an individual, treat the person with chemotherapy and/or radiotherapy and then re-infuse the person's own cells. Whilst from an immunological

perspective this procedure is far simpler than using donor cells, its development as a treatment was only possible following the development of cryopreservation - a process whereby cells are preserved by cooling them to sub-zero temperatures (approximately  $-196^{\circ}\text{C}$ ) so that biological activity is effectively stopped.

**Figure 2.1: Historical milestones in the development of allogeneic stem cell transplantation.**

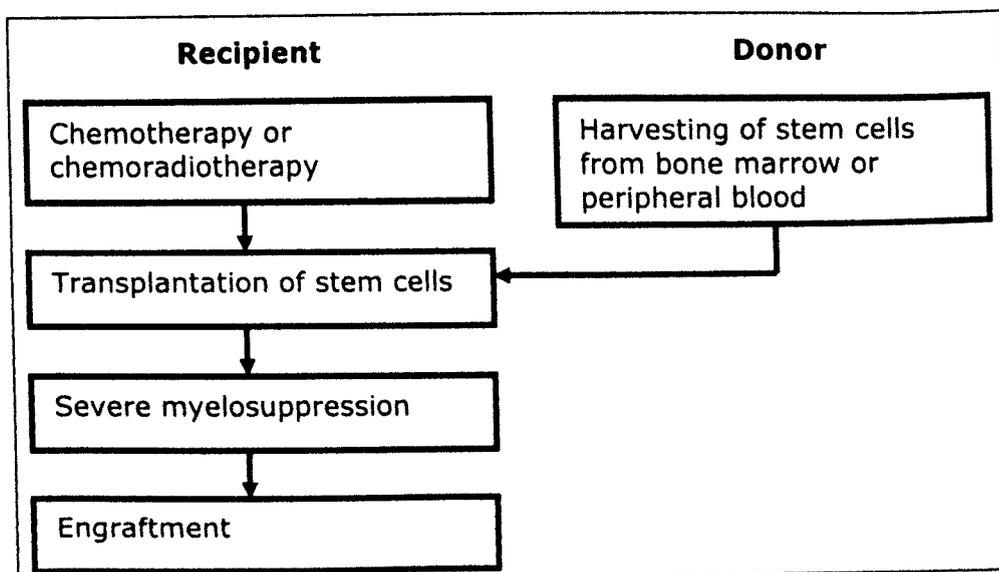
- 1950's - Animal experiments demonstrate that marrow cells can be successfully transfused.
- 1956 - First successful human bone marrow transplant was carried out between identical twins.
- 1958 - Discovery of the HLA system and first human histocompatibility antigen described.
- 1968 - First successful transplantation between non-identical siblings was carried out.
- 1973 - First successful unrelated bone marrow transplant carried out.

## **2.4 Allogeneic Transplantation**

Allogeneic transplants use stem cells that have been harvested from the peripheral blood, bone marrow or umbilical cord blood of a healthy matched donor. The donor may be a family member, most frequently a sibling, or an unrelated volunteer. The major limiting factor for the number of allogeneic transplants performed is the availability of suitable donors (Lennard and Jackson, 2000). Donors and recipients need to be HLA matched to reduce the likelihood of the transplanted cells attacking the recipients own cells causing potentially fatal graft versus host disease. Population based studies indicate that only 20%-25% of patients eligible for allogeneic transplantation will have a HLA matched sibling (Lennard et al., 1998). A number of registries of volunteer stem cell donors have been

developed in order to increase the likelihood of finding an unrelated matched donor. There are now over six million donors registered on national donor registers worldwide (Lennard and Jackson, 2000). Allogeneic transplants are used in the treatment of chronic myeloid leukaemia, acute myeloid leukaemia, myelodysplasia, acute myeloid leukaemia, acute lymphoblastic leukaemia, thalassaemia, multiple myeloma, Hodgkin's lymphoma and Non-Hodgkin's lymphoma (Lennard and Jackson, 2000). The process of treatment with an allogeneic transplant is summarised in figure 2.2. Before the transplant can take place the recipient must undergo a course of chemotherapy which may or may not be combined with radiotherapy. Stem cells which have previously been collected from the bone marrow or peripheral blood of a donor are then transfused into the recipient. Between transplantation and engraftment of the donated cells there is a period of severe myelosuppression which results in profound neutropenia. As the donated stem cells become engrafted into the recipient's marrow, blood cell production gradually increases and recovery begins.

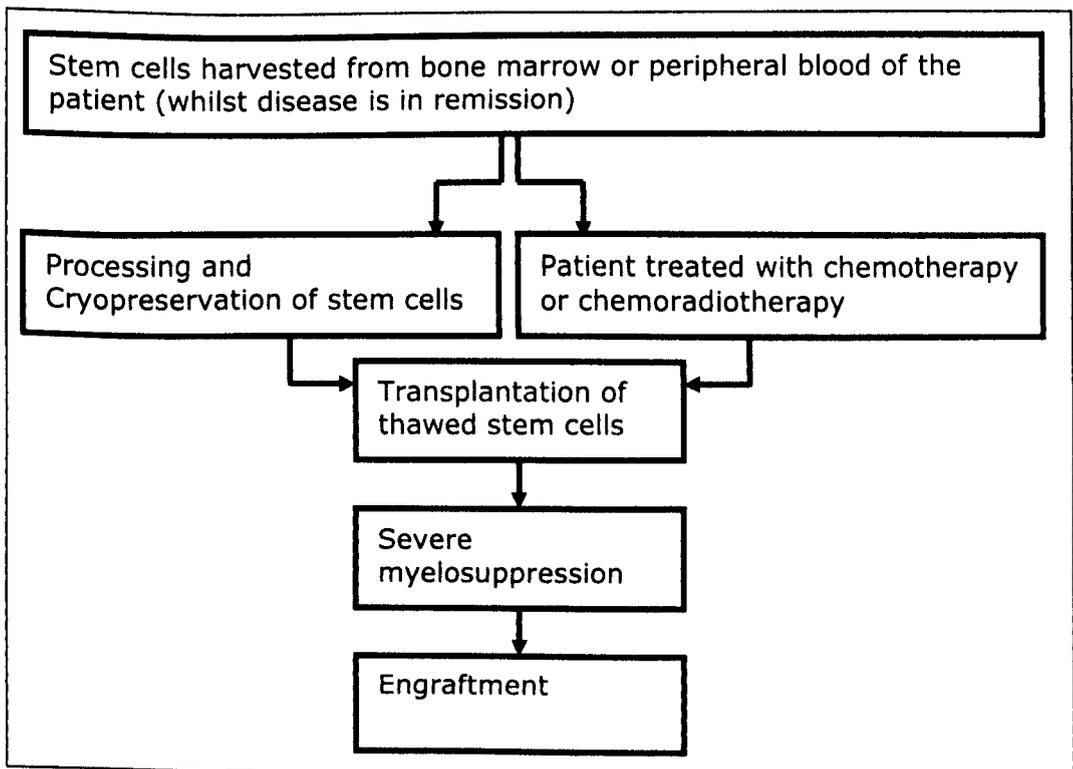
**Figure 2.2: Procedure for treatment with an allogeneic transplant** (adapted from Duncombe 2003)



## 2.5 Autologous Transplantation

Autologous transplants use stem cells which are collected from the patient's own bone marrow or peripheral blood. The cells are processed and cryopreserved while the patient undergoes a conditioning regime of chemotherapy or chemoradiotherapy. After this treatment period the stem cells are thawed and returned to the patient. As with allograft transplants following transplantation there is a period of severe myelosuppression before engraftment of the transplanted cells. The process of treatment with an autologous transplant is summarised in figure 2.3. Autologous transplantation is the most common type of stem cell transplantation (Lennard and Jackson, 2000). Autologous transplants are used in the treatment of acute lymphoblastic leukaemia, Hodgkin's lymphoma, Non-Hodgkin's lymphoma, multiple myeloma, chronic myeloid leukaemia, acute myeloid leukaemia (Lennard and Jackson, 2000).

**Figure 2.3: Procedure for treatment with an autologous transplant** (adapted from Duncombe 2003)



## **2.6 Biopsychosocial Framework**

The effects of these illnesses and treatments are complex and affect not only the physical but also the psychological and social functioning of individuals. Therefore it is important that this topic is viewed within a dynamic framework that enables consideration of the many and varied problems associated with haematological malignancy and stem cell transplantation.

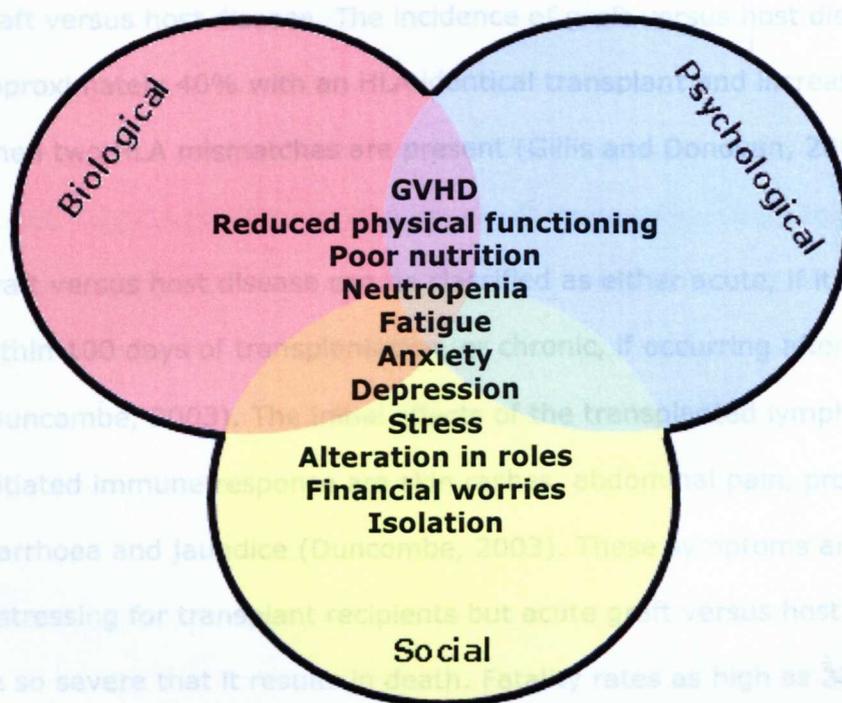
The biopsychosocial framework highlights that not only are biological aspects crucial in the assessment of health but that social, psychological and behavioural dimensions are of equal importance. The biopsychosocial framework recognises that the boundaries between health and disease, between well and sick, are far from clear and that these concepts are diffused by cultural, social and psychological considerations (Engel, 1977).

Engel (1977) in his seminal work on the framework discusses the complex issue of health specifically in situations where the doctor and the patient experience differing perspectives of health. Engel uses the examples of diabetes and schizophrenia to highlight the issues, but haematological malignancy can serve as an equally good illustration. Many patients feel healthy but medical tests reveal changes in blood cell counts that are indicative of life threatening malignant disease. Conversely, patients may come to the end of treatment and be told that the transplant procedure has been successful yet they may feel worse in themselves than before treatment started. Clearly, a model of health based on organic mechanisms alone is inappropriate for consideration of this topic. However, to dismiss the importance of the biological aspects of treatment would be equally remiss.

The biopsychosocial framework is appropriate for the consideration of diagnosis of a haematological malignancy and treatment with a stem cell transplant because both are associated with biological, psychological and social consequences. These sequelae need to be considered within a structure that does not include an inherent hierarchy since biological symptoms are not necessarily more important than psychological or social ones. The model also recognises that these aspects of health are not necessarily distinct categories and a symptom, treatment or sequelae may be associated with biological, psychological and social health.

The principles of the biopsychosocial framework and the negative side-effects associated with a diagnosis of a haematological malignancy and treatment with stem cell transplantation have been combined to develop figure 2.4. The model highlights that illness and treatment has an effect on physical, psychological and social health but that the effects do not necessarily fall into distinct categories. Fatigue, for example, has physical, psychological and social causes and consequences.

**Figure 2.4: The negative biopsychosocial sequelae associated with stem cell transplantation**



## **2.7 The negative consequences of haematological malignancy and stem cell transplantation**

The most common negative side-effects associated with haematological malignancy and stem cell transplantation are summarised in figure 2.4.

These biological, psychological and social problems will now be considered in more detail.

### **Graft Versus Host Disease (GVHD)**

Graft versus host disease is a common consequence of allogeneic stem cell transplantation (Wingard, 1998). Graft versus host disease occurs when transplanted lymphocytes recognise the recipient's own cells as 'foreign' and initiate an immune response (Mehta and Hoffbrand, 2005). Several factors influence the likelihood of a graft versus host reaction occurring. Since the HLA system is the principal system by which cells of the immune

system recognise foreign cells, the degree of HLA mismatch between donor and recipient is a crucial factor influencing the development of graft versus host disease. As the degree of HLA mismatch increases so does the risk of graft versus host disease. The incidence of graft versus host disease is approximately 40% with an HLA identical transplant and increases to 70% when two HLA mismatches are present (Gillis and Donovan, 2000).

Graft versus host disease can be classified as either acute, if it occurs within 100 days of transplantation, or chronic, if occurring after that time (Duncombe, 2003). The initial effects of the transplanted lymphocyte initiated immune response are skin rashes, abdominal pain, profuse diarrhoea and jaundice (Duncombe, 2003). These symptoms are not only distressing for transplant recipients but acute graft versus host disease can be so severe that it results in death. Fatality rates as high as 20% have been found for acute graft versus host disease (Bron, 1994).

Between 30% and 70% of allograft recipients develop chronic graft versus host disease (Atkinson et al., 1990, Ochs et al., 1994). The clinical features associated with chronic graft versus host disease are sclerotic atrophic skin, sicca syndrome, mucosal ulceration, malabsorption syndromes, recurrent chest infections, jaundice, joint movement restriction, hyposplenic infections (e.g. Pneumococcus), and myelosuppression (Duncombe, 2003). Previous research has indicated that chronic graft versus host disease is associated with decreased quality of life (Sutherland et al., 1997), decreased functional status (Syrjala et al., 1993, Duell et al., 1997, Worel et al., 2002), higher levels of depression (Syrjala et al., 2004) and incomplete resumption of social activities (Duell et al., 1997, Worel et al., 2002). Chronic graft versus host disease is the leading cause of late

treatment related death amongst recipients of allogeneic transplants (Duncombe, 2003, Duell et al., 1997, Worel et al., 2002).

There are a number of mechanisms by which the prevention and treatment of graft versus host disease are managed. By depleting T cells from the donor marrow prior to transplantation the incidence and severity of graft versus host disease can be decreased. Suppression of the recipient's immune system can also be an effective preventative measure. Ciclosporin and methotrexate are commonly used immunosuppressive agents which have been shown to be effective in reducing the incidence of graft versus host disease (Bolwell et al., 2004, Ruutu et al., 2000). The primary treatment for graft versus host disease is corticosteroids and consequently steroid myopathy results for most patients (Gillis and Donovan, 2000).

Despite the many negative consequences of graft versus host disease, its presence has been shown to reduce rates of disease relapse (Lee et al., 2002). The transplanted lymphocytes recognise not only the host but also the tumour as 'foreign' and the resulting immune response attacks the tumour as well as the host's healthy tissue. This graft versus tumour effect has been shown to have a significant positive impact on disease free recovery (Horowitz et al., 1990).

### **Reduced Physical Functioning**

Reduced physical activity is common in patients undergoing stem cell transplantation, leading to numerous physiological consequences. A reduction in physical activity can be caused by both the side effects of treatment such as nausea, pain and fatigue and the boredom and physical lack of space associated with protective isolation. Levels of activity may be

further reduced by patients being advised not to exercise due to low platelet counts. This is due to concern that exercise may result in injury that causes uncontrolled bleeding.

Inactivity has dramatic effects on both the musculoskeletal and cardiovascular systems. Musculoskeletal effects include muscle atrophy, decreased strength of tendons and ligaments, osteoporosis, cartilage degeneration and synovial atrophy (Topp et al., 2002). The speed with which these problems occur varies but one study with healthy volunteers demonstrated that one to two days of bed rest are sufficient to exacerbate bone loss (Baecker et al., 2003) and four to six weeks of bed rest can result in dramatic changes in muscle mass, accompanied by a decrease of up to 40% in muscle strength (Bloomfield, 1997). Cardiovascular effects include increased heart rate, decreased stroke volume, decreased cardiac size/volume and decreased left ventricular end-diastolic volume (Topp et al., 2002). One study has shown that maximal oxygen uptake (used to evaluate cardiovascular function) decreased by 26% in healthy male subjects after 21 days in bed. These reductions in physical functioning can take weeks or months to recover from depending on the length of time of decreased physical activity (McTiernan, 2004).

In their study of the long term impact of lymphoid malignancies treated with autologous stem cell transplantation, Vose et al. (1992) found that there was a minimal effect on pulmonary and cardiovascular functioning one year after treatment. Molassiotis and Morris (1999b), investigated quality of life in 28 patients diagnosed with chronic myeloid leukaemia and treated with an unrelated bone marrow transplant. This study found that impaired physical functioning was affecting activities of daily living in a considerable number of survivors. Difficulty doing strenuous activities (i.e.

carrying a heavy shopping bag or a suitcase) was reported by more than 50% of the sample. Half of the sample had trouble taking a long walk and approximately ten percent had trouble taking even a short walk. 50% of the sample experienced shortness of breath as a problematic symptom and 32% experienced muscle pain (Molassiotis and Morris, 1999a). The duration of this reduction in physical functioning has not been clearly established. A follow up study of patients after allogeneic bone marrow transplantation identified that physical performance continued to be affected ten years after treatment (Kiss et al., 2002).

The reduction in physical functioning caused by a reduction in physical activity can be compounded by a number of further problems associated with stem cell transplantation. In particular, inadequate nutritional intake and neutropenia are two problems that most patients recovering from stem cell transplantation experience and which have a negative impact on physical functioning.

### **Nutritional Problems**

Many of the side-effects experienced by stem cell transplant patients have the potential to cause difficulty in maintaining adequate nutrition. These side effects include nausea, vomiting, constipation, diarrhoea, taste and smell changes, mouth sores, mouth dryness, difficulty swallowing, dental problems and lack of appetite (Zittoun et al., 1999). A study by Larsen et al. (2004) investigated symptom occurrence, symptom intensity and symptom distress in 47 patients who were undergoing stem cell transplantation. Loss of appetite, mouth dryness, nausea, diarrhoea, and taste changes were reported by more than 50% of patients. Loss of appetite and mouth dryness were reported as two of the three symptoms

that patients found most intense and distressing (Larsen et al., 2004). The same study found that over 50% of the sample were still experiencing one or more of these distressing symptoms when they were discharged from hospital (Larsen et al., 2004).

A study of similar size (n=50) conducted by Molassiotis et al. (1995) reported that patients who have undergone treatment with an allograft transplant may still experience problems related to a dry and painful mouth more than six months after their treatment. 38% of the study sample reported ongoing problems related to a dry mouth and 15% reported a sore mouth and pain when swallowing. However the results also indicated that problems with diarrhoea and vomiting tended to be resolved within six months of treatment (Molassiotis et al., 1995). In another study, undertaken with patients who had been treated with an autologous transplant more than one year previously, 96% of patients thought that their appetite was good and 86% reported that their weight was either stable or that they had gained weight since transplant (Vose et al., 1992). These findings are supported by the work of Molassiotis (2003) who reanalysed data gathered in two other studies carried out with patients with haematological malignancies. The results from this reanalysis indicated that nutritional problems did not cause long-term concern for this patient population.

### **Neutropenia**

Neutropenia is a problem that is commonly associated with cancer and its treatment. This is particularly true for patients with a haematological malignancy for whom alteration in blood cell counts can be one of the first indications of disease (Bratt-Wyton, 2000, Dowling, 2000, Grundy, 2000).

Hayes et al. (2003) investigated immunological changes after autologous stem cell transplantation. The patients were immunocompromised before their transplants and the transplant procedure caused further adverse changes to leukocyte and lymphocyte counts. Leukocyte counts had returned to normal within three months of transplantation. However other immunological parameters remained depressed at three months post transplant (Hayes et al., 2003). Immunocompromisation is an unavoidable consequence of stem cell transplantation and therefore post transplant infections are common. In one study conducted with patients who had been treated with an autologous transplant found that 39% of the sample had no problem with infection post treatment. However, 24% became infected with herpes zoster four to eight months post transplant. Other less common infections included bacterial pneumonia, CMV pneumonia, Cystitis, pyelonephritis, aseptic meningitis and Hickman line infections. In this study 16% of patients experienced four or more upper respiratory tract infections per year (Vose et al., 1992). In order to protect patients and to minimise the risk of infection during the initial post transplant period, patients are nursed in protective isolation. Laminar air flow systems are used to try and prevent airborne infections and special precautions are often taken with food and drink to reduce the risk of enteric infections.

## **Fatigue**

Fatigue is one of the most common problems experienced by cancer patients (Dimeo, 2001). Patients being treated for haematological malignancy are no exception to this (Wang et al., 2002, Lee et al., 2001). In one study 50% of patients being treated for haematological malignancy reported severe fatigue (Wang et al., 2002).

Fatigue, which is relieved by rest, can be a normal response to physical and/or mental exertion. However, in a variety of circumstances this normal response mechanism can become particularly prolonged, severe and difficult to resolve. Cancer, its diagnosis and its treatment are associated with particularly disabling fatigue.

Cancer-related fatigue has been characterised as a multidimensional subjective phenomenon (Winningham et al., 1994) that develops over time, diminishes energy, mental capacity and the psychological condition of cancer patients (Cella et al., 1998). Fatigue has been described by patients as tiredness, weakness, lack of energy, exhaustion, lethargy, depression, inability to concentrate, malaise, boredom, sleepiness, lack of motivation and decreased mental status (Winningham et al., 1994).

Fatigue is known to affect patients undergoing treatment with both autologous and allograft transplants (Knobel et al., 2000). Research has also shown that these patients may continue to experience fatigue for many years after their treatment. Fatigue has been shown to be highly prevalent in lymphoma patients four to ten years after treatment (Loge et al., 1999). Similarly fatigue was one of the three most commonly reported problems in a study of 125 adult survivors, six to eighteen years after treatment (Andrykowski et al., 1990).

Distinguishing between the causes, indicators and effects of cancer-related fatigue is challenging (Winningham et al., 1994). The mechanisms which cause fatigue are complex and poorly understood (Gutstein, 2001). A patient's underlying disease, its treatments and the psychological stresses associated with cancer all contribute to the development of cancer-related fatigue (Winningham et al., 1994).

Cancer fatigue has been shown to affect many aspects of people's lives including general activity, work, enjoyment of life, mood, mobility and walking, as well as their relationships with others (Pederson and Parran, 1999). Transplant survivors who continue to suffer from fatigue report poor vitality and poor role functioning (Sadler et al., 2002). Fatigue is also associated with depressive symptoms (Wang et al., 2002).

Some biological causes of fatigue can be identified and treated. For example anaemic individuals can be given a blood transfusion. However, for the majority of cancer patients a single treatable explanation for their fatigue does not exist. Recent research has explored the impact of a number of different therapies on cancer-related fatigue including exercise, relaxation, complementary therapies and massage (Adamsen et al., 2004, Oldervoll et al., 2003, Kim and Kim, 2005, Ahles et al., 1999). These are discussed in more detail in section 2.9.

### **Psychological Impact of Stem Cell Transplantation**

It has been suggested that anxiety regarding painful procedures and strict isolation, along with depression, are universal reactions during autologous stem cell transplantation (Wolcott et al., 1987). A degree of anxiety and depression can be a normal psychological reaction to adverse situations. It could be argued that a patient has not comprehended the nature of their treatment if they were to have no anxieties about it, and given the distressing symptoms experienced during hospitalisation such as pain, nausea, fatigue, hair loss and appetite loss (Carlson and MacRae, 2002) feelings of anxiety and depression are hardly surprising. However, for some individuals anxiety and depression are not simply natural responses to a

stressful situation but on-going and persistent problems that can have a considerable impact on daily functioning and well-being.

As part of an investigation into quality of life, Zittoun et al. (1999) measured anxiety and depression during intensive chemotherapy and/or bone marrow transplantation using the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983). They did not identify any significant changes in anxiety and depression over time. However, between 23% and 35% of participants did have scores that were indicative of clinical anxiety or depression. It could be argued that this finding is to be expected in a population of patients undergoing such intensive and distressing treatment. But for some patients these symptoms do not necessarily resolve on completion of treatment. Molassiotis and Morris (1999b) also measured anxiety and depression using the HADS. Their sample consisted of 28 participants who had undergone unrelated bone marrow transplantation an average of 41.2 months previously. Of the sample, 7% were identified with symptoms of clinical anxiety and a further 25% were classified as borderline cases of anxiety, with sub-clinical symptoms. No cases of clinical depression were identified but four people (14%) were within the borderline range (Molassiotis and Morris, 1999a). This was a small exploratory study and general conclusions cannot be drawn, however it does indicate that for some patients anxiety and/or depression may be ongoing problem following stem cell transplantation.

One of the earliest studies investigating the psychosocial effects of bone marrow transplantation was conducted by Wolcott et al. (1986). The study assessed 26 adult patients who had survived for one year or more following transplantation. About one quarter of the participants said that they were experiencing significant emotional distress, chronic physical symptoms, low

self-esteem and below optimal life satisfaction. Brown and Kelly (1976) used a qualitative approach to explore psychological reactions to stress over eight stages of the stem cell transplant process. They identified that after discharge from hospital people experience a range of psychological reactions and that in particular people may struggle with attempting to balance feelings of entitlement at being the survivor of such a challenging process with feelings of persistent indebtedness, having needed so much help from their donor and others. Another issue raised by the study was concern about whether the individual who had been treated with a stem cell transplant had been permanently altered by the illness and its treatment. Fear of recurrent disease/death, and coping with memories from the transplant were causes of psychological distress identified in a qualitative study investigating the effects of unrelated donor bone marrow transplants (Molassiotis and Morris, 1998a). Lesko et al. (1992) have suggested that whilst many acute leukaemia survivors experience overall psychological well-being and social adjustment, they carry a psychological burden of distress that does not reach a psychiatric threshold.

### **Social Impact of Stem Cell Transplantation**

Prolonged periods of time spent in hospital, anxiety over the future and the inevitable change in social roles that accompanies treatment with a stem cell transplant can all have an impact on the social functioning of survivors. A qualitative study investigating the effects of unrelated donor bone marrow transplants asked 28 participants about difficult areas to deal with after returning home. Responses included difficulty in coping with family life, problems with social life, increased dependency on others, difficulty in returning to work and dealing with financial restrictions (Molassiotis and Morris, 1998a). These findings are supported by a small scale quantitative

study (n=29) conducted by Whedon et al. (1995). They found that as many as 93% of autologous bone marrow transplant survivors reported experiencing moderate to severe distress over the effect of illness on their family more than one year after treatment (Whedon et al., 1995). Similarly, marital difficulties post autologous bone marrow transplantation were noted as a problem in a study by Vose et al. (1992).

However stem cell transplantation does not necessarily have only negative effects on social relationships. A study investigating the impact of autologous and allograft transplants on the family relationships of survivors several years after treatment found that family relationships tended to be more integrated and lower in conflict compared with non transplant-affected families (Molassiotis et al., 1995). Similarly, a follow up study of patients at least ten years after allogeneic bone marrow transplantation noted a high degree of satisfaction with interpersonal relationships (Kiss et al., 2002).

A larger study (n=131) was conducted by Langer et al., the primary focus of which was to explore prospectively patient and caregiver marital satisfaction following stem cell transplantation. Interestingly couples were matched in their perceptions of their relationship prior to transplantation but grew mismatched over time. However, change in marital satisfaction was not associated with change in physical or psychosocial characteristics. The study also indentified that female caregivers were more depressed and anxious, and less satisfied with their marriages compared to male caregivers (Langer et al., 2003). This study raises some interesting issues and highlights that the physical, cognitive and emotional challenges of stem cell transplantation are rarely, if ever, handled in isolation. Patients,

family members, care givers and significant others all need to adapt to the challenges presented to them.

Several studies have investigated the impact that treatment with stem cell transplantation has on sexual relationships. One recent study has investigated reproduction and sexuality after total body irradiation and stem cell transplantation. The sample included 34 men and 36 women. Out of these 70 patients 41 reported experiencing a negative change in sexual relations. None of the patients were fertile following treatment and 24 of the women experienced menopausal symptoms (Claessens et al., 2006). One systematic review of studies investigating quality of life following autologous stem cell transplantation suggests that over half of autologous transplant patients report a decrease in sexual pleasure and/or activity long after their treatment is completed (Carlson and MacRae, 2002). Clearly changes in sexual functioning following stem cell transplantation are an important issue that has been shown to have a negative effect on quality of life (Claessens et al., 2006).

A further aspect of social functioning is employment. Several studies have investigated employment status five years after autologous and allograft transplantation. Employment status consistently appears high at this time point with one study finding that 89% of patients had returned to work (Duell et al., 1997) and another suggesting that 84% had returned to work (Syrjala et al., 2004). However a small scale study by Molassiotis and Morris (Molassiotis and Morris, 1999b) conducted with survivors of unrelated bone marrow transplantation an average of 41.2 months post treatment, found that 46% of the participants had needed to either considerably modify or completely change their goals concerning their job/education and that 11% of the sample reported experiencing either a

moderate or great increase in problems with co-workers since their illness. These results suggest that survivors may experience problems with employment that a simple measure of employment status, i.e. employed or unemployed, is unable to detect.

## **Quality of Life**

Traditionally, health has been measured by assessing reductions in functioning. The focus on quality of life represents an important attempt to view health as a positive construct. Unfortunately the term 'quality of life' is frequently ill-defined. Therefore before considering studies that have investigated the quality of life of stem cell transplant patients it is worth exploring the concept in order to provide a definition for use in the present study.

No common definition or definitive theoretical framework for the concept of quality of life has emerged from the research community (Bowling, 2005). The terms 'quality of life', 'health-related quality of life', 'health status' and 'functional assessment' are often used interchangeably to describe the same concepts and even the same instruments (Beckie and Hayduk, 1997). This inconsistency undermines the value of quality of life research and causes confusion when making comparisons between studies.

Bowling (2005) comments that quality of life is an amorphous concept. However, if any meaningful research is to be undertaken in relation to quality of life it is crucial that some structure is applied to the term. Quality of life has been described as a multidimensional concept (Mandzuk and McMillan, 2005). Edman et al. (2001) argue that an operational consensus is emerging among health researchers that the domains of quality of life

assessment are physical function, psychological function, social-role function and disease/treatment symptoms.

A reduction in physical functioning may cause deterioration in quality of life. Yet good physical functioning is not intrinsically necessary in order for an individual to experience a good quality of life. The impact that physical functioning has on quality of life will depend on the value or importance placed on physical functioning by each individual at a given point in time. Studies on health related quality of life often present significant differences between global life satisfaction and physical functioning (Fegg et al., 2005). In one study more than half of the sample reported impaired physical functioning and a high incidence of negative symptoms two to four years after stem cell transplantation. Despite this 80% of the participants rated their general health as quite good or excellent (Edman et al., 2001). Whilst this was a small exploratory study (n=25) it serves as an excellent example of the difference between specific issues of physical functioning and patients' perceptions of their general well being. Physical functioning has been used here as an example - the same arguments apply to any other domains that are attributed to quality of life. Each will only be as important as the individual in question perceives it to be. Furthermore the considerations used by people in assessing their own quality of life may be different at varying time points (Graham and Longman, 1987).

Any conceptualisation of quality of life must acknowledge the potential for the disease and its treatment to have a positive influence on some aspects of quality of life. Several studies have shown that some patients perceive that their quality of life has been increased by the experience of life threatening disease and its treatment (Cella and Tross, 1986, Ferrell et al., 1992a, Molassiotis and Morris, 1998b) . Specifically, these studies have

identified that some patients experience a greater appreciation of life (Cella and Tross, 1986, Ferrell et al., 1992a, Molassiotis and Morris, 1998b) and/or an improved or more optimistic outlook on life (Ferrell et al., 1992a), following diagnosis and treatment with a life threatening illness.

Reflecting the work of Graham and Longman (1987), in this study quality of life is defined as 'the degree of satisfaction with current life circumstances, as perceived by the patient'. A number of studies have used global quality of life measures in the assessment of stem cell transplant survivors. Results consistently suggest that survivors of stem cell transplantation rate their own quality of life as good to excellent. Broers et al. (2000) found that quality of life was rated by participants as good to excellent using a two item scale three years after bone marrow transplantation. Similarly a comparatively large study conducted with 106 patients who had received an allograft transplant more than five years previously found that 78% of the sample reported good to very good quality of life (Worel et al., 2002). In a study by Molassiotis et al. (1995) the majority of participants rated their quality of life as good to excellent following both allograft and autologous stem cell transplantation. Bush et al. (1995) conducted a large descriptive survey of adults surviving between six and eighteen years after bone marrow transplantation. When asked about their current quality of life 74% of participants reported that their current quality life was the same or better than before transplantation and 80% rated their current quality of life as good to excellent.

This evidence from quantitative studies is supported by a qualitative study conducted by Haberman et al. (1993) that analysed the responses to a postal questionnaire of 125 survivors, six to eighteen years after bone marrow transplantation. The study concluded that "... most long-term

survivors, despite the persistence of lingering side effects, perceive themselves as cured and well, leading full and meaningful lives” (Haberman et al., 1993)

## **Summary**

Haematological malignancy and stem cell transplantation are associated with numerous biological, psychological and social side-effects. These can be profound immediately following transplantation and reduce with time. When considering the consequences of stem cell transplantation it is easy to lose sight of the benefits that have come from the ability to treat haematological cancers with stem cell transplantation. Therefore this section is concluded with some quotes taken from a qualitative study that explored quality of life in stem cell transplantation survivors (Ferrell et al., 1992b).

*“well, I’m still alive and the transplant taught me a whole new look on life and priorities.”*

*“I try to enjoy each day with a good deal of enthusiasm knowing I have been given a second chance at living”.*

*“the consequence of BMT is that I’m alive and that’s really important”.*

## **2.8 Current post discharge care**

Duncombe (1997) states that regular haematological follow-up is mandatory following stem cell transplantation. Furthermore, psychological support from not only family and friends but also the transplant team is vital for readjustment to normal life (Duncombe, 1997). A previous study conducted at the unit where this research was carried out indicated that

patients feel very well supported by the transplant team during the hospitalised period of their treatment (Stone 1999). However, a study of patients' perceptions of daily life after discharge indicated that they felt that service provision after discharge from in-patient care was inadequate to meet their needs (Stone 1999).

Regular contact with hospital staff is maintained through appointments at clinic. The constraints of the clinic schedule and environment mean that a visit to clinic does not necessarily provide the emotional support and information desired by patients. Suggestions for improvement to the service were provided by patients. They felt that guidance on exercise, sharing experiences with other patients and gaining information on what to expect after transplant would have aided their recovery after stem cell transplantation (Stone, 1999).

## **2.9 Rehabilitation after Stem Cell Transplantation**

Research has clearly demonstrated that diagnosis with a haematological malignancy and treatment with a stem cell transplant has a significant impact on physical, psychological and social functioning i.e. on almost every aspect of an individual's life. Therefore attention has begun to focus on how health professionals can help to reduce the extent of the impact of these diseases and their treatment of patients' lives. Gunn (1984), one of the first people to define the concept of cancer rehabilitation, wrote that cancer rehabilitation is "the restoration of a patient with individual defects as a result of treatment or disease to as normal and functional a state as possible" (Gunn, 1984). There have been numerous studies that have evaluated methods for promoting a return to usual functional activity following cancer and its treatment. There is also a significant body of research that has been built up specifically in the field of haematological

malignancies and stem cell transplantation. There are a number of potential components to rehabilitation following stem cell transplantation. These include exercise, social support, informational support and relaxation or other stress reduction techniques.

## **Exercise**

A number of studies have investigated the effectiveness of exercise at ameliorating the negative effects of haematological malignancy and stem cell transplantation. It has been suggested that exercise may be effective in reducing not only the physical effects of diagnosis and treatment but that it may also have an affect on psychological and social functioning.

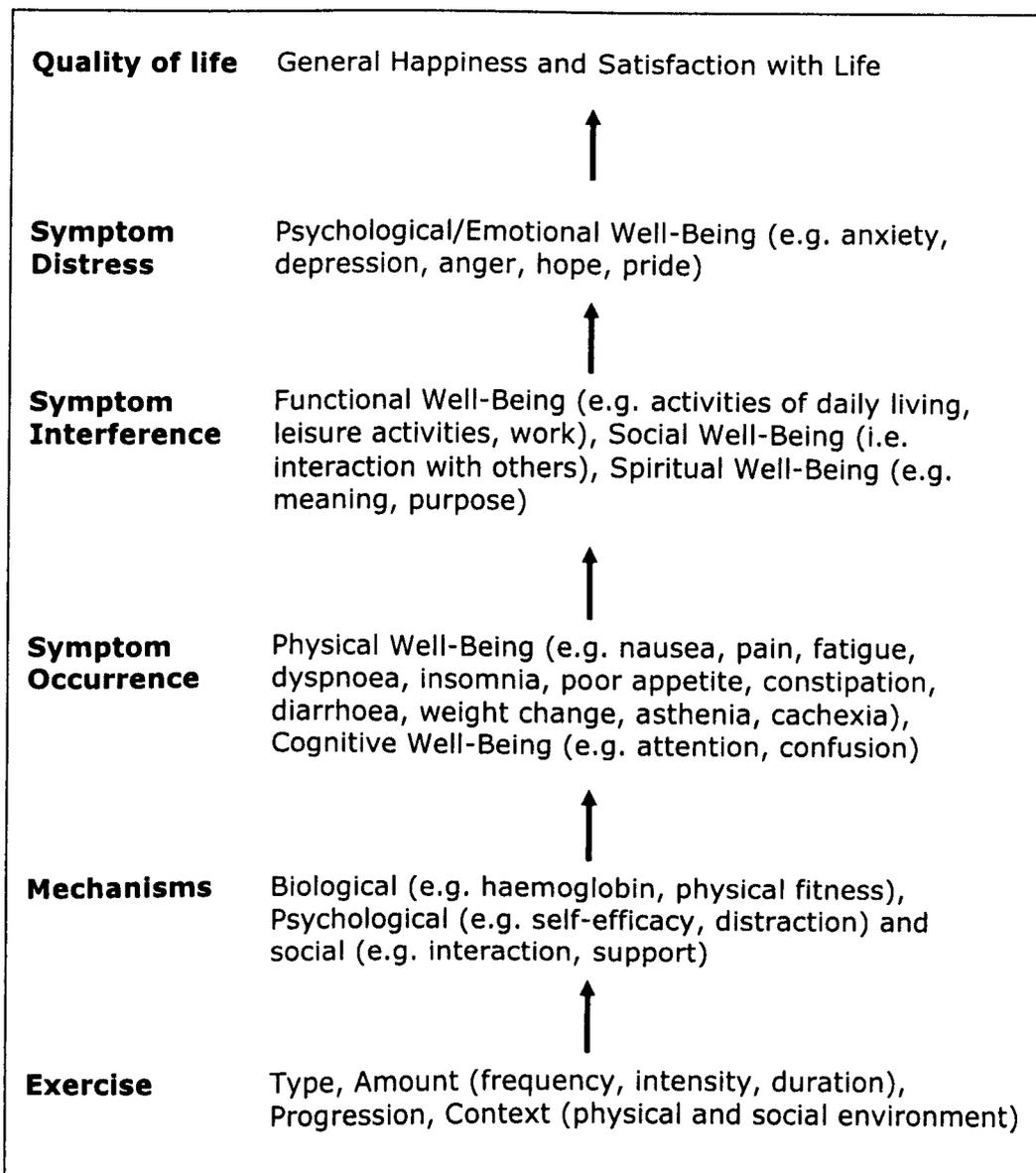
### Theoretical explanations for the efficacy of exercise

Several theories have been proposed to explain the beneficial effects of exercise on psychosocial functioning. These can broadly be divided into two groups – physiological theories and psychological theories. Psychological theories include the distraction hypothesis, the self-efficacy hypothesis and the social interaction hypothesis. The distraction hypothesis suggests that during exercise people are distracted from unfavourable stimuli leading to an improvement in mood (Morgan, 1985). The self-efficacy hypothesis is based on the assertion that gaining confidence in mastering a new set of skills or behavioural changes leads to higher levels of self esteem (North et al., 1990). The social interaction hypothesis suggests that the social interaction that is often associated with exercise results in a beneficial change in mood (Peluso and Guerra de Andrade, 2005). The two most commonly suggested physiological explanations for the association between exercise and mood are the endorphin hypothesis and the monoamine hypothesis. The endorphin hypothesis proposes that the

release of endorphins during exercise has an inhibitory effect on the central nervous system and is responsible for the sensation of calm and improved mood experienced after exercise (Dunn and Dishman, 1991). The monoamine hypothesis proposes that the increase in synaptic transmission of monoamines during exercise causes an anti-depressive effect (Peluso and Guerra de Andrade, 2005).

Courneya (2001) has summarised the various mechanisms associated with exercise and developed the model shown in figure 2.5, which explains how exercise may influence quality of life during cancer treatment. The model proposes that exercise has an effect on the biopsychosocial mechanisms that are thought to underlie coping and adjustment to cancer. In turn, changes in these mechanisms may alleviate or prevent the occurrence of the symptoms associated with cancer and its treatment. Amelioration of these symptoms may then reduce their level of interference with the daily activities of living and working. The ability to participate in physical and social activities may promote psychological and emotional well-being, thereby improving overall quality of life (Courneya, 2001).

**Figure 2.5: Model showing potential mechanisms for the effect of exercise on quality of life (Courneya (2001))**



Safety of Exercise

Dimeo et al. (1997b) used a randomised study design to assess the effects of exercise during autologous stem cell transplantation. This small scale study indicated that aerobic exercise is safe immediately after high dose chemotherapy. Furthermore the study suggested that exercise can partially prevent the loss of physical performance associated with chemotherapy and stem cell transplantation (Dimeo et al., 1997b). Further evidence that

exercise does not harm patients who have undergone stem cell transplantation is provided by Hayes et al. (2003). A small scale randomised controlled trial was used to assess the impact of exercise on immune cell recovery following autologous stem cell transplantation. Participation in the exercise programme did not hinder or delay immune cell recovery (Hayes et al. 2003).

### Benefits of exercise

Courneya et al. (2000) used a prospective design to explore the possible benefits of exercise for autologous stem cell transplant patients. The study demonstrated that there were statistically significant correlations between exercise and physical well-being, psychological well-being, depression, anxiety and days hospitalised. However, due to the design of the study it was unable to indicate whether exercise was a cause (or an effect) of the better physical and psychological well-being. Oldervoll et al. (2003) conducted a pilot study to explore the effect of exercise for Hodgkin's lymphoma survivors who had been identified as suffering from chronic fatigue. Results indicated that a home based aerobic exercise programme had a positive effect on fatigue, physical functioning and maximal aerobic capacity. However, this finding must be viewed with caution as this was not a randomised controlled study and it is possible that other factors accounted for the changes in fatigue, physical functioning and aerobic capacity.

These studies indicate that exercise is associated with an improvement in physical and psychological well-being but are unable to demonstrate causation. Dimeo et al. (1997c) used a controlled trial to investigate the effects of exercise for stem cell transplant patients. The exercise

intervention consisted of daily training on a treadmill on weekdays for six weeks. After seven weeks four people in the control group reported fatigue and low physical performance compared to none in the intervention group. However, this study involved only a small number of participants (n=16) and allocation to intervention or control was according to distance lived from hospital rather than random. Mello et al. (2003) conducted a study with a population of patients undergoing allogeneic bone marrow transfusion. In this study muscle strength was assessed at three time points - before bone marrow transplantation, after marrow engraftment and six weeks after engraftment. During the six weeks between engraftment and the third data collection point patients completed either a daily exercise programme consisting of an active range of motion exercises, stretching exercises and treadmill walking or usual care. The results indicated that the exercise programme was effective in promoting an increase in muscle strength after allogeneic bone marrow transplantation (Mello et al., 2003). These results suggest that exercise may have a beneficial effect on reducing fatigue and increasing muscle strength in stem cell transplant patients.

The research that has been carried out with patients who have a haematological malignancy tends to be restricted to studies of small sample sizes. In part this may be due to the relatively low incidence of these cancers in the general population. To find trials with larger sample sizes, consideration must be given to research into cancers with higher incidence rates. Mock et al. (2001) conducted a large (n=119) multi-institutional randomised controlled trial to determine the effects of a home based exercise programme on levels of fatigue during treatment for breast cancer. Intention-to-treat analysis revealed no significant differences between the intervention and control groups. The authors suggest that this

was due in part to a dilution of the treatment effect as 39% of the usual care group exercised and 28% of the exercise group did not.

Courneya et al. (2003) conducted a randomised controlled trial to determine if group psychotherapy combined with exercise improved quality of life in cancer survivors compared to group psychotherapy without exercise. This was a comparatively large study (n=108) and included participants who had been treated for a variety of malignant diseases. The study found significant improvements in functional well being and fatigue, and borderline significant results for physical well being, satisfaction with life and flexibility in the exercise group in comparison to the non-exercise group (Courneya et al., 2003).

Segal et al. (2001) randomly allocated 123 women with breast cancer to one of three programmes - a home based walking programme, a hospital and home based programme, and usual care. Participants allocated to the solely home based programme showed a significant improvement in physical functioning compared to the usual care group. Interestingly, the participants allocated to the hospital and home based programme showed only a borderline significant improvement in physical functioning compared to the usual care group (Segal et al., 2001). In 2003 Segal et al. conducted another exercise study, this time with 155 men being treated for prostate cancer. The men were randomly allocated to either supervised strength training exercises three times a week for 12 weeks, or to a waiting list. Fatigue and health-related quality of life improved in the exercise group and deteriorated in the control group (Segal et al., 2003).

A small scale randomised controlled trial (n=18) carried out by Burnham and Wilcox (2002) allocated patients recovering from treatment for either

breast, colon or lung cancer to one of three treatment groups - a moderate intensity exercise group, a low intensity exercise group and a control group. After the intervention period was complete there were no differences found between the two exercise groups on any of the physiological variables. For the final analysis, data from both exercise groups was combined and compared to data from the control group. The results indicated statistically significant increases in aerobic capacity, lower-body flexibility, energy levels and quality of life, measured with the Quality of Life Index for Cancer in the exercise group compared with the control group. There were no significant differences between the two groups for measures of anxiety or depression (Burnham and Wilcox, 2002).

Following consideration of the research relating to exercise following stem cell transplantation it is possible to conclude that exercise appears to be safe for this group of patients and that a number of studies indicate that completing exercise after a stem cell transplant is associated with improved physical and psychosocial functioning. There have been relatively few randomised controlled trials carried out. The evidence available from the studies that have been conducted is supportive of the use of exercise as a rehabilitation intervention but insufficient to be certain of its efficacy.

### **Social Support**

Social support has been defined as the provision of information, practical assistance and emotional empathy and comfort (Campbell et al., 2004). It can be helpful to consider three separate aspects of support - informational, emotional and instrumental support (Campbell et al., 2004). Informational support, meaning the provision of information, can increase knowledge, understanding and coping skills. Effective informational support

may be useful in enhancing a patient's sense of control over adverse situations (Helgeson and Cohen, 1996). Emotional support is based on empathetic communications between patients and their support networks. It is intended to enhance self-confidence and self-esteem, reduce negative feelings and improve relationships. Instrumental support is the provision of practical assistance with activities of daily living, finances, transport and other illness related activities (Campbell et al., 2004). Social support interventions may aim to provide one or more of these types of support.

### Theoretical explanations for the efficacy of social support

Several mechanisms by which social support may influence physical, psychological and social health have been suggested. Social comparison theory suggests that patients benefit from being able to compare their own experience with that of others in a similar position. This contact with people who have been through the same experience may provide an opportunity for positive role-modelling, encourage health-promoting behaviours and enhance self esteem (Campbell et al., 2004). A further mechanism which has been proposed to explain the benefit received by patients from social support is the helper therapy principle. This principle proposes that patients who are given the opportunity to help others benefit from improved self esteem (Campbell et al., 2004). Coping has been defined by Lazarus and Folkman as constantly changing cognitive and behavioural efforts to manage specific external and/or internal demands that are appraised as taxing or exceeding the resources of the person (Folkman and Lazarus, 1988). Modes of coping include both behaviours aimed at changing the stressor and psychological responses aimed at preserving emotional integrity (Backer et al., 2000). The stress and coping theory suggests that social support including informational support improves health directly by

enhancing coping skills and indirectly by mediating the stress response (Bloom, 1990).

### Informational Support

Informational support interventions with cancer patients involve providing information about disease, treatment and managing the side-effects of these. Assisting patients to gain information about their condition has been associated with enhanced patient involvement in decision making, improved adherence to treatment regimens, increased patient satisfaction, increased ability to cope with distressing symptoms and side effects and enhanced post-treatment recovery (Fernsler and Cannon, 1991, Johnson, 1996).

Roberts et al. (2002) conducted an evaluation of an educational support programme for cancer patients and their families and friends. The evaluation indicated that participation in the programme resulted in a significant improvement in coping abilities, knowledge, communication and relationships. This was a large study involving 1460 participants, however it was not a randomised controlled trial and therefore consideration must be given to the possibility that these changes were due to factors other than those under evaluation.

Several studies have investigated minimal contact interventions with cancer patients. Minimal contact interventions can include any method of providing informational support with minimal contact between the patient and health care professionals. These include information leaflets, workbooks and telephone contact. Several studies have shown that individuals who receive educational material exhibit increased compliance,

improved knowledge and increased satisfaction with treatment compared to individuals who do not receive educational information (Brandenberg et al., 1994, Eardley, 1988). However, a more recent study found that distress did not vary over the course of the study between participants allocated to a workbook and those allocated to usual care (Trask et al., 2003). The authors suggest that this finding was at least in part due to the fact that many participants allocated to the workbook did not look at the material. This study highlights that psychosocial interventions are arguably only beneficial for patients who perceive that they need the intervention that is being provided and who are able and willing to engage with the intervention in the format in which it is being provided.

Evaluation of a stress and activity management programme for cancer patients that involved education, relaxation, problem solving and exercise found that at the end of a six week programme individuals randomly assigned to the intervention group had increased cancer knowledge compared with that of individuals in the control group but there were no group differences in psychological adjustment (Neinrich and Schag, 1985). Similarly a large scale randomised controlled trial was conducted with men who had recently been treated for prostate cancer. The participants were randomly assigned to a control group, a group education intervention or a group education plus discussion group. Men who had participated in either the education group or the education plus discussion group showed increased prostate cancer knowledge in comparison to the control group (Lepore et al., 2003). However this increased knowledge did not translate into meaningful changes in other outcome measures. Whilst increasing the knowledge that patients have about their disease and its treatment can be argued to be an innately worthwhile activity, these studies highlight that

demonstrating that increased knowledge leads to a beneficial change in psychological adjustment is extremely difficult.

### Emotional support

Emotional support can be provided by a patient's existing interpersonal relationships, nursing and medical relationships and through friendship and camaraderie between fellow patients. A number of different methods have been used within health care to try and provide increased emotional support for patients.

A qualitative study carried out by Feigin et al. (2000) investigated the experiences of women who had been treated for breast cancer and who were attending support groups. The study was relatively large for a qualitative piece of work and considered 45 women attending five different support groups. The results indicate that all of the women found the support groups had value and significance for them. More specifically participants expressed the view that it was helpful to meet with other people who had been through a similar experience (Feigin et al., 2000).

This qualitative evaluation provides helpful information about the elements of the support programme found to be helpful by attendees. However, it must be remembered that the study was with people who had chosen to attend a support group and had chosen to take part in an evaluation of the group. Therefore the participants' views are unlikely to be representative of those people who chose not to attend a support group.

Ussher et al. (2006) conducted an in-depth qualitative evaluation of support groups for people with cancer. The participants indicated that they

felt that support groups provided a unique sense of community, unconditional acceptance and information about cancer and its treatment. This study included participants who had been diagnosed with a variety of malignant diseases. The sample was made up of 75 women and only 18 men. The authors do not provide further comment on this uneven distribution of men and women. However, it can be argued that some men may be put off the idea of a support group because of pre-conceptions that they hold about what it is to be masculine and what it is like to attend a support group. One of the benefits of combining support with an intervention such as exercise or other action-orientated activity is that many men may find it more acceptable and appealing to attend (Adamsen et al., 2001, Harrison et al., 1995, Gray et al., 1997).

Bordeleau et al. (2003) conducted a large randomised controlled trial with women with metastatic breast cancer. In this multi-centre study 235 women were randomly allocated to either a weekly 90-minute therapist led support group or to a control arm. Quality of life measured by the EORTC QLQ-C30 was the primary outcome measure and analysis at baseline, four, eight and twelve months revealed no significant differences between the two arms of the study. There are two possible explanations for this finding. Either that there were no changes as a result of the support group or that the EORTC QLQ-C30 was not able to detect any changes.

After consideration of the research relating to social support it is possible to suggest that information and emotional support may be of assistance to some patients recovering after stem cell transplantation. There is a sound theoretical base for informational or emotional support interventions; however the available evidence is inconclusive as to the efficacy of many of the interventions that have been trialled.

## **Complementary therapies**

The potential benefit of complementary therapies is a growing area of research in both cancer care and health care more generally. Unfortunately studies of complementary therapies with patients who have undergone stem cell transplants are infrequent. Furthermore much of the research into the effectiveness of complementary therapies has been criticised for a lack of methodological rigour. However, there may be benefits of complementary therapies for patients being treated with a stem cell transplant including reductions in fatigue (Kim and Kim, 2005), psychological distress (Ahles et al. 1999), pain, nausea and vomiting (Syrjala et al. 1992) and improvement in physiological indicators such as time taken for engraftment of transplanted cells (Smith et al. 2003).

Kim and Kim (2005) investigated the potential benefit of completing relaxation exercises for patients undergoing allogeneic stem cell transplantation using a randomised controlled trial. In the study 35 patients were randomly allocated to either a relaxation group or to routine care. The intervention period lasted six weeks and the participants allocated to the intervention showed a greater reduction in fatigue scores after completing the six weeks than those individuals assigned to the control group (Kim and Kim, 2005).

Ahles et al. 1999 conducted a study to examine the impact of massage therapy on psychological and physical measures in patients undergoing autologous transplantation. Patients were randomly assigned to receive either massage therapy or standard treatment. The effects of massage therapy on anxiety, depression, and mood were assessed before, during, and after treatment. Patients in the massage therapy group demonstrated

significantly larger reductions in distress, fatigue, nausea, and anxiety than the standard treatment at some but not all of the three time points.

Nausea and vomiting are common side-effects of stem cell transplantation and a number of studies have investigated the use of complementary therapies in alleviating these symptoms. There is evidence to suggest that relaxation techniques and hypnosis are not effective in reducing nausea in patients being treated with a stem cell transplant (Syrjala et al., 1992). However, a study by Ezzone et al. (1998) reported that patients undergoing stem cell transplantation who were assigned antiemetics plus music distraction reported significantly less nausea and vomiting than those assigned antiemetic drugs alone.

The effectiveness of relaxation techniques in the management of pain is a comparatively well researched concept and systematic reviews of the use of relaxation for the relief of both chronic (Carroll and Seers, 1998) and acute (Seers and Carroll, 1998) pain have been carried out. These reviews conclude that there is some weak evidence to support the use of relaxation in acute pain (Seers and Carroll, 1998) but that there is insufficient evidence to confirm that relaxation can reduce chronic pain (Carroll and Seers 1998).

Smith et al. (2003) investigated the effects of therapeutic touch and massage therapy on engraftment time, occurrence of complications and benefit of the therapy as perceived by the patient. The study recruited 88 adults receiving stem cell transplants, who were randomly assigned to receive therapeutic touch, massage therapy or a 'friendly visit'. A significantly better score for central nervous system or neurological complications was noted for subjects who received massage therapy

compared with the 'friendly visit' group; however, no differences were found among the three groups with respect to other complications. The massage therapy component was most popular with patients with the perception of the benefits of massage therapy being significantly higher than in the 'friendly visit' group.

The present study includes the use of relaxation techniques and massage in a rehabilitation programme. Current evidence suggests that relaxation techniques in the form of either massage or relaxation exercises may be associated with a reduction in fatigue (Kim and Kim, 2005), anxiety, depression and stress (Ahles et al. 1999) but that there is insufficient evidence to suggest that such interventions have an impact on pain (Carroll and Seers, 1998), nausea and vomiting (Syrjala et al. 1992) or on engraftment of transplanted cells (Smith et al. 2003). Complementary therapies, especially massage, as an adjunct to usual care have a high level of acceptability and popularity with patients (Vickers and Cassileth, 2001, Smith et al., 2003) however evidence as to their efficacy remains scant.

## **2.10 Summary**

Stem cell transplantation is increasingly used in the treatment of haematological malignancies. However, it has been shown that haematological malignancy and stem cell transplantation have a considerable impact on the physical, psychological and social well-being of patients. In particular, these illnesses and their treatment can cause reduced physical functioning, fatigue, graft versus host disease, psychological distress and changes in social circumstances and relationships. Reducing the negative impact of haematological malignancy

and stem cell transplantation is clearly desirable and therefore research is expanding into rehabilitation for this group of patients. Several studies have investigated the potential benefit of exercise for stem cell transplant patients and report favourable results in reducing fatigue, maintaining physical function and assisting recovery. Research has also investigated the provision of informational and emotional support to patients. These interventions have been associated with high levels of patient satisfaction and there is encouraging evidence that they may improve post treatment recovery. However no studies have investigated the effectiveness of a multidimensional rehabilitation programme which provides structured exercise, relaxation, emotional support and information related to the side-effects of haematological malignancy and its treatment in reducing the biopsychosocial impact of haematological malignancy and stem cell transplantation.

## **Chapter 3 - Research Design**

### **3.1 Introduction**

In the previous chapter it was shown that patients who have been diagnosed with a haematological malignancy and undergone treatment with a stem cell transplant have a range of physical, psychological and social rehabilitation needs. There is some evidence that a combination of exercise, emotional and instructional support may be effective in meeting this need. However, further research in this area is required since a comprehensive understanding of rehabilitation for this patient group does not currently exist. In particular the optimum method for the delivery of rehabilitation is unknown.

In this chapter the methods employed in this study are described. Consideration is first given to the structure and content of the rehabilitation programme. This programme was originally proposed by a clinical team in response to an unmet need that they had perceived in patient care. Details are provided of a preliminary study that was carried out by this clinical team to assess the acceptability and feasibility of the programme. The aim and objectives for the current study are set out, followed by an explanation of why a randomised controlled trial was chosen as the most suitable research design. The changes to the rehabilitation programme required in order for a randomised controlled trial to be possible are outlined. After establishing this important groundwork the details of the research design are discussed.

### **3.2 Preliminary Work**

Nursing staff working at a large regional centre which carries out numerous stem cell transplantations each year identified that a rehabilitation

programme might be an appropriate method for providing additional support and information to individuals recovering after stem cell transplantation. In particular, staff identified that due to the constraints of the clinic environment individuals were having the chance to discuss biological health concerns but that little attention was being given to their psychosocial health. Furthermore, during clinics patients were restricted to meeting the doctor and the transplant co-ordinator or the nurse consultant. However, there was no provision to meet with physiotherapists, dieticians, social workers or to have in depth discussions with the nursing staff. In order to provide a more comprehensive service to patients a rehabilitation programme was devised. It was proposed that the programme should be ten weeks in duration and consist of weekly sessions lasting between two and three hours each. The different elements of the programme are summarised by figure 3.1.

**Figure 3.1: Components of the rehabilitation programme**

<p><b>Exercise</b> Approximately 60 minutes of cardiovascular exercise Led by a physiotherapist and consisting of warm up, circuit of specific exercises based on the ability of the individual, walking and cool down</p>
<p><b>Relaxation</b> Approximately 30 minutes of relaxation and group support Opportunity for a cup of tea, a snack and a period of informal chat Followed by a relaxation exercise</p>
<p><b>Discussion</b> Approximately 40 minutes of discussion and support Different topic each week led by a relevant health professional</p> <p>Proposed topics</p> <ul style="list-style-type: none"><li>Nutrition</li><li>Benefits of exercise</li><li>Stress management and relaxation</li><li>Understanding drugs</li><li>Financial support</li><li>Relationships and roles</li><li>Meaning of life and spirituality</li><li>Fatigue</li><li>Expectations of life after transplant</li><li>Open forum for questions</li></ul>

A small scale preliminary study was conducted prior to my involvement with the project to assess the feasibility and acceptability of the rehabilitation programme that had been developed. Alongside informally assessing the feasibility and acceptability of the rehabilitation, data was collected prior to and on completion of the programme. The demographic and clinical details of the 15 participants who completed the programme are shown in table 3.1.

**Table 3.1: Demographic and clinical details of participants**

<b>Demographic variable</b>	
<b>Age</b>	
Mean	53
(SD)	(13.2)
<b>Gender (n)</b>	
Female	5
Male	10
<b>Type of transplant (n)</b>	
Autologous BMT	1
Autologous PBSCT	4
Allogeneic BMT	2
Allogeneic PBSCT	8
<b>Diagnosis (n)</b>	
Myeloma	4
Leukaemia	5
Lymphoma	4
Other	2

Feedback from participants who took part in the preliminary study suggested that the format and content of the programme was acceptable. The outcome data from the study is summarised in table 3.2. With one exception the mean scores for participants indicated better health after completion of the programme than before it. No control group was included in this initial study.

The data gathered in this preliminary study was sufficient to suggest that further evaluation of the programme was warranted. The improvement shown between baseline and completion of the programme was particularly encouraging for the shuttle walk test scores and for several elements of the SF-36. However, there was no formal statistical analysis of this data.

A progressive improvement in functioning is to be expected after stem cell transplantation and from this pilot data it cannot be established if the improvements shown can be attributed to attendance at the rehabilitation

programme. Furthermore, the mean SF-36 score for role limitations due to emotional problems reduced over the intervention period indicating poorer functioning after the programme than before it. This may simply have been an erroneous finding that would not be borne out in a larger sample. Alternatively, this reduction could be due to a feeling of excitement at resuming social activities after discharge from hospitalisation and a more pessimistic outlook at the end of the intervention period when the reality of recovery was more keenly felt. However, without a comparison group it was not possible to be certain that the reduced score was not associated with attendance at the rehabilitation intervention, highlighting the need for rigorous evaluation of the programme.

**Table 3.2: Summary of Outcome Data from Preliminary Study (n=15)**

<b>Measure</b>	<b>Mean score at baseline (SD)</b>	<b>Mean score after completion of the intervention (SD)</b>
SF-36 <sup>a</sup> – Physical Functioning	49 (22.7)	60 (24.0)
SF-36 – Role Limitation - physical	13 (24.8)	22 (31.1)
SF-36 – Role Limitation - emotional	60 (44.0)	51 (43.4)
SF-36 – Social Functioning	38 (30.4)	52 (26.9)
SF-36 – Energy/Vitality	32 (23.2)	52 (22.1)
SF-36 – Mental Health	66 (13.0)	79 (13.3)
SF-36 – Pain	67 (26.0)	79 (22.4)
SF-36 General Health	41 (16.8)	50 (16.3)
Shuttle Walk Test <sup>b</sup>	296m (153.5)	491m (186.9)
HADS <sup>c</sup> - Anxiety	6 (3.3)	5 (2.5)
HADS - Depression	5 (2.4)	5 (2.8)

<sup>a</sup> Possible scores range from 0-100. Higher score indicates better functioning.

<sup>b</sup> Possible scores range from 0-1020 metres. Higher score indicates better physical functioning.

<sup>c</sup> Possible scores range from 1-14 (<7 indicates non-cases 8-10 indicates doubtful cases 11+ indicates definite cases)

SD = Standard Deviation

### **3.3 The Main Study**

Since the preliminary study indicated that the rehabilitation programme was acceptable to patients and that it potentially had a beneficial effect on recovery it was considered appropriate to progress with a more rigorous evaluation of the rehabilitation programme. The primary aim of further research was to evaluate the effectiveness of the health profession led rehabilitation programme in promoting recovery six months after stem cell transplantation. In order to clearly conceptualise this broad aim a number of specific objectives were developed:

- To test the hypothesis that:  
'Participants who attend the rehabilitation programme will show a greater improvement in physical and psychosocial recovery at twelve weeks and six months than the participants who do not attend the rehabilitation programme.'
- To assess the effectiveness of the rehabilitation programme on patients' physical recovery
- To assess the effectiveness of the rehabilitation programme on patients' psychosocial recovery
- To explore patients' experiences of the rehabilitation programme that they received.
- To explore the experiences of staff members involved in the provision of rehabilitation following stem cell transplantation.

### **3.4 Rationale for the study design**

Considerable debate exists as to the most appropriate way to assess the effectiveness of health service interventions. This debate intensifies when the focus of discussion is the evaluation of complex interventions such as

the one in this study. Traditionally randomised controlled trials have been seen as the 'gold standard' of evidence based medicine (Barton, 2000). The Cochrane Glossary defines a randomised controlled trial as "an experiment in which two or more interventions, possibly including a control intervention or no intervention, are compared by being randomly allocated to participants". The importance of the randomised controlled trial in developing new drugs and technologies is well established and this approach has produced much of our current medical knowledge. However, the appropriateness of using randomised controlled trials to evaluate complex interventions is more contentious.

The MRC document 'A Framework for the Development and Evaluation of Randomised Control Trials for Complex Interventions' attempts to clarify the term complex intervention and suggests that "the greater the difficulty in defining precisely what are the active ingredients of an intervention and how they relate to each other, the greater the likelihood that you are dealing with a complex intervention" (Medical Research Council, 2000). It is precisely this difficulty in understanding the interaction of complicated factors in a complex intervention that results in debate over the use of randomised controlled trials in their evaluation.

Hawe et al. (2004) suggest that too often a complex intervention is reduced to its constituent parts in order for it to fulfil the strict requirements of a randomised controlled trial. In effect this results in a complex intervention being reduced to a series of simple interventions and in doing so fails to acknowledge that a complex intervention has the potential to be more than the sum of its parts (Hawe et al., 2004). The authors suggest that expensive and inconclusive trials could be avoided if standardisation of the function of an intervention rather than of its form

was more widely utilised. This would allow for context level adaption and enable tailoring of the intervention to the local environment, which would potentially improve efficacy (Hawe et al., 2004).

Given the problems that can be associated with using a randomised controlled trial design to evaluate a complex intervention many authors argue for more use of well designed observational studies in health evaluation research (for example Black (1996)). However, there are advantages in the randomised controlled trial approach that are not readily available from observational designs. The primary advantage of using a randomised controlled trial design is that it is conceptually easier to attribute any observed effect to the treatment being tested (Barton, 2000). Observational studies can highlight associations between variables but it is very difficult to use data from an observational study to indicate causation. Randomisation is important because it reduces bias in the distribution of known and unknown confounding factors across groups (Watson et al., 2004) and therefore makes it more likely that an observed effect is due to the manipulation of the independent variable.

After consideration of both the advantages and disadvantages, a randomised controlled trial design was chosen as the method for this study. This decision reflected the fact that the primary aim of the study was to investigate the effectiveness of the rehabilitation programme. Steps were taken to recognise and reduce the impact of the potential complications associated with using a randomised controlled trial to evaluate a complex intervention. These included using qualitative interviews to provide additional depth to the quantitative data, having a broad range of outcome measures, drawing on preliminary data to guide

the methodology and seeking a way of providing standardisation without restricting the dynamic nature of the programme.

### **3.5 Changes to the rehabilitation programme required by the randomised controlled trial design**

The most significant change to the rehabilitation programme was the inclusion of a series of information leaflets. These leaflets were intended to complement the discussion part of this intervention and to provide some degree of standardisation in order to ensure that approximately the same information was given each time the session was run. The leaflets were designed to be used by the health professions who led each session to guide the discussion and they also enabled participants to revisit each topic at home between sessions. I wrote and produced the leaflets in collaboration with the health professional responsible for each component of the programme. The leaflets reflected current advice available in the literature and the clinical experiences of the various health professionals. In total eight leaflets were produced and these are shown in Appendix A (page 201).

A randomised controlled trial by definition requires a comparator. In planning this study considerable attention was given to finding an appropriate comparator for the rehabilitation programme. I was concerned to ensure that the trial met the conditions of equipoise. There is no evidence on the efficacy of multidimensional rehabilitation programmes for patients who have undergone treatment with a stem cell transplant. However, sufficient evidence does exist to suggest that some aspects of the rehabilitation programme are beneficial to patients. For example it is widely acknowledged that exercise is beneficial for health in general (NHS

Choices, 2008) and therefore it would be inappropriate to not encourage all patients including those recovering after stem cell transplantation to complete some form of exercise regularly. In order to ensure that all participants were receiving advice of known benefit I decided to provide the control group with the same information leaflets as were used in the rehabilitation programme. However, the control group were not provided with any contact time with health professionals beyond that provided by usual care.

Since one of the differences between the two programmes was the contact with health professionals, the intervention was referred to as the health profession led programme and the control was referred to as the self-managed rehabilitation programme.

### **The Health Profession Led Rehabilitation Programme**

The health profession led programme consisted of three elements, exercise, relaxation and information. The programme was design to last ten weeks and consisted of weekly sessions lasting between two and three hours.

#### The exercise component

The exercise element consisted of approximately one hour of group cardiovascular exercise directed and supervised by a team of physiotherapists. Three different exercise programmes were designed to suit individuals with a variety of exercise capacities. The participants were assigned to an appropriate level of exercise programme in accordance with their shuttle walk test results. The shuttle walk test is an incremental walking test conducted on a 10 m course where walking pace is dictated by bleeps on an audio CD . The three programmes are shown in Appendix B

(page 250). Physiotherapy staff adjusted the programmes and moved participants on to a harder programme as appropriate. Each exercise session consisted of a warm up period, the circuit of specific exercises, walking and a cool down period.

#### The relaxation component

This exercise component was followed by a period of relaxation. The first part of this time was spent informally as participants and staff had drinks and biscuits together. This provided an informal environment for conversation to flow between fellow participants and between staff and participants. This was followed by a more formal relaxation component. When volunteers from the hospitals massage service were available participants were given a hand, foot or shoulder massage. When this service could not be provided the group were led by the physiotherapist in a relaxation exercise.

#### The information component

Each week a discussion was led by a relevant health professional on one of ten topics.

#### Benefits of exercise

In this information session the physiotherapist provided information on the benefits of exercise, guidance on how much and what type of exercise might be appropriate and how to exercise safely. This session was complemented by the booklet 'Exercising after your bone marrow transplant' which summarised the information presented by the physiotherapist and also included a programme of home exercises which participants were encouraged to complete two to three times a week between rehabilitation sessions.

## Nutrition

During this information session the dietician would provide information on common problems that frequently present after haemopoietic transplants including the need for a neutropenic diet, taste changes, poor appetite, dry mouth, weight loss, nausea, diarrhoea and healthy eating. The session was supported by the booklet 'Eating after your bone marrow transplant'.

## Stress management and relaxation

This session was led by a nurse and provided advice on managing stress and relaxation techniques. It was accompanied by the booklet 'Coping with stress after your bone marrow transplant' which provided explanations of common relaxation techniques and gave the contact details of a variety of organisations where participants could go for more information.

## Fatigue

This session was led by an occupational therapist and gave information about techniques for minimising and coping with fatigue. It was accompanied by the leaflet 'Managing fatigue after your bone marrow transplant'.

## Financial support

A social worker led the session on financial support and provided information on the benefits that are available to support people during illness and in returning to work. This session was complemented by the leaflet 'Financial support after your bone marrow transplant'.

## Expectations of life after transplant

This session was led by a nurse and a patient who is now several years post transplant. The session provided the opportunity for patients to

discuss life after a transplant with someone who has been through it. The session was complemented by the leaflet 'My life after a bone marrow transplant, by someone who has been through it'.

#### Relationships and roles

This session was also led by a nurse and an ex-patient. The session was fairly flexible and provided a time for patients to discuss the effect that their treatment has had on their relationships with family members and friends. Participants were invited to bring significant others along to this session if they wished. The session was supported by the leaflet 'Relationships after your bone marrow transplant' in which previous patients and their family members shared how the treatment process had affected them. The leaflet also contained the contact details for a wide variety of services which offer support to people affected by cancer.

#### Understanding drugs

The pharmacist led this session in which information on the medicines most commonly used after bone marrow transplants were discussed. Information that was presented included the usual dose of medications, the therapeutic benefits of different medications, how long participants might expect to continue on each medication, special instructions for taking medications and any possible side effect that patients should look out for. This session was supported by the leaflet 'Medication after your bone marrow transplant'.

#### Meaning of life and spirituality

This session provided an opportunity for participants to talk with the hospital chaplain. Since the session was primarily directed by the participants it was not feasible to produce an accompanying booklet that

summarised the content of the session. However participants were given information on how to contact the chaplain or one of the other faith workers associated with the hospital if they wanted to seek further advice or support as part of the relationships leaflet.

#### Open forum for questions and answer session

This session provided an opportunity for participants to ask questions. The session was attended by some of the individuals involved in giving information on the other topics and when available a doctor from the haematology team also attended. Given the informal nature of this session it was not feasible to produce an accompanying booklet.

#### **The self managed rehabilitation programme**

The self managed rehabilitation programme consisted of an information pack that contained the eight leaflets that were used as part of the health profession led programme. Participants were encouraged to read these booklets at home and to regularly complete the exercise programme contained within the leaflet 'Exercising after your bone marrow transplant'. Participants were informed that they were welcome to ask for clarification or seek further information about any of the content of the leaflets when they attended clinic appointments.

### **3.6 Study Design**

A randomised controlled trial was used to compare a health profession led rehabilitation programme with a self managed rehabilitation programme.

### **3.7 Setting**

This research was carried out at a large teaching hospital in the East Midlands which provides health services to a local and regional population. The clinical haematology unit at the hospital is a specialist centre for bone marrow transplantation and carries out upwards of 140 stem cell transplants each year on patients from across the Midlands. All subject recruitment took place in the Clinical Haematology department where data collection also took place.

### **3.8 Participants**

The inclusion and exclusion criteria for participation in this trial were that the patient was required to

1. Have undergone any type of stem cell transplant between six to eight weeks prior to recruitment,
2. Be deemed physically able as identified by their medical consultant,
3. Be 18 years of age or older.

The inclusion criteria were broad in order to ensure that the study would be representative of the wider stem cell transplant population. However, the trial was not open to all patients recovering after stem cell transplantation regardless of their time since transplant since it was perceived that if the inclusion criteria were too broad the study would be unable to detect important differences in intervention effects.

Those patients for whom participation would increase the risk of an adverse event occurring were excluded. Therefore before patients were admitted to the study their medical consultant was asked to confirm that they were well enough to take part. Throughout the intervention period patients blood

counts were checked to ensure that they were safe to participate in exercise.

This study only recruited people who were over the age of 18 at the time of their transplant. This decision was made because it was anticipated that the rehabilitation needs of children and young teenagers who undergo stem cell transplantation differ to those of adults.

### **3.9 Sample size**

The Short Form 36 Health Survey (SF-36) physical function score was chosen as the primary outcome measure and was used to calculate the sample size required for the study. After looking at the data obtained from the preliminary study, consideration of previous studies (Adamsen et al., 2001, Shephard and Franklin, 2001, Walters and Brazier, 2003) and reading the information provided by the tool's authors (Ware et al., 1993) the decision was taken that it was appropriate to look for a ten point difference between the two groups in the mean physical function score of the SF-36. A ten point difference in scores represents a moderately large clinically and socially relevant difference (Ware et al., 1993).

Whilst a study power of 90% is ideal, in this study a concession to the small study population had to be made and on the grounds of feasibility the power calculations were made assuming a power of 80%. This study followed statistical convention (Pocock, 1983) and set the significance level at 0.05. Data from the pilot study was used to provide an estimation of the standard deviation. The standard deviation used in the calculation was 18.9.

It was calculated that 57 patients would be required in each arm of the study (114 in total) to have an 80% chance of detecting as significant (at the two sided 5% level) a ten point difference between the two groups in the mean physical function score of the SF-36. We aimed to recruit a total of 132 patients to allow for a 15% attrition rate. This attrition rate was estimated using data from the preliminary study. The power calculation is shown in Appendix G.

### **3.10 Recruitment, consent, baseline data collection and randomisation**

The process of recruitment, gaining consent, baseline data collection and randomisation can be best summarised by figure 3.2.

**Figure 3.2: Recruitment through to randomisation**

<b>Procedure</b>	<b>Personnel involved</b>	<b>Location</b>	<b>Timing</b>
<b>Initial approach</b>	Staff involved in the patient's routine care	The ward	Prior to discharge from inpatient care
<b>Consent</b>	A senior nurse or I asked patients to consent	Routine clinic appointments	A minimum of several days after patients were first approached
<b>Baseline data collection</b>	A senior nurse or I collected baseline data	Routine clinic appointments	Between six and eight weeks after the patients SCT
<b>Randomisation</b>	A senior nurse or I liaised with a secretary at Nottingham University who held a list of the randomised allocation	Patients were informed before leaving clinic as to the randomisation result	Immediately after baseline data collection

### **Initial approach**

Patients were approached by a member of the clinical team and given information about the study when they were in hospital recovering after their stem cell transplant. In order to ensure that all patients received the salient information at this point a letter and information sheet (shown in Appendix C – page 257) were given to patients alongside verbal information. It was decided that no patient should be approached prior to

their stem cell transplant, since this is a period of time when patients may experience increased anxiety and depression (Gaston-Johansson and Foxall, 1996). It was decided that the optimum time to approach people was likely to be as they were preparing for discharge from hospital. Patients were approached by members of staff, normally a nurse or physiotherapist, involved in the patient's routine care. During this initial approach patients were given the option of not being contacted again if they felt confident that they did not want to take part in the study. Occasionally patients were discharged from hospital prior to being approached about the study, these patients were seen and given information about the study at their first post discharge clinic appointment. In exceptional circumstances the first approach was made by phone and the information sheet was posted to participants.

## **Consent**

At routine clinic appointments the researcher or a member of staff met with patients, providing an opportunity to discuss the study and to answer questions. If patients were willing to take part written consent was obtained (consent forms are shown in appendix D - page 266). No one was asked to consent on the same day as they were initially approached about the study. This was to ensure that everyone had time to think about participation and discuss it with significant others if they wished.

## **Base-line data collection**

After patients had given their consent and prior to randomisation, baseline data were collected. The data collected is summarised in table 3.3 and copies of both the data collection sheets and questionnaires used are shown in appendix E (page 275).

**Figure 3.3: Summary of baseline measures**

<b>Demographic Information</b>	<b>Clinical Information</b>	<b>Psychometric and Symptom Specific Questionnaires</b>
Age Gender Social circumstances	Diagnosis Type of transplant Blood counts Presence and degree of GVHD	The SF-36 The Graham and Longman Q of L Scale The GHQ – 12

Demographic information

The demographic information that was gathered on all participants is summarised in table 3.3. It was important to record the age of all participants since side effects such as fatigue and pain as well as a reduction in functional ability have been shown to correlate with age (Hensel et al., 2002). The relationship between gender and recovery after haemopoietic transplantation is not clearly understood. A study by Hensel et al., investigating quality of life after transplantation, found that male and female survivors did not differ for any QLQ-C30 items. However a study by Syrjala et al. (1993) found that women were more depressed after transplantation. Other authors have suggested that the acceptability of some forms of rehabilitation and post treatment support is gender related (Adamsen et al., 2001). It recorded whether or not patients lived with their next of kin in order to provide a crude measure of their social circumstances.

## Clinical Information

A number of clinical details were gathered directly from the medical notes of all participants. The clinical information of primary importance was transplant type. This is due to the variation that has been shown in the frequency and severity of the side-effects associated with the different transplant procedures (Duncombe, 1997). The origin of the transplanted cells i.e. whether cells have been collected from the patient themselves (autologous) or a donor (allogeneic) has an impact on recovery since the transplantation of donor cells is an immunologically more complicated procedure. These patients must take immunosuppressants and are at high risk of developing graft versus host disease.

For patients who had been treated with an allogenic transplant it was also important to record whether the donor was either a sibling or a matched, unrelated donor since research has shown that transplant related mortality is 20-30% for individuals who receive sibling HLA matched allografts and up to 45% for recipients of allografts from matched, unrelated donors (Duncombe, 1997).

It was also important to know whether the patient received stem cells which had been collected from the bone marrow or from the peripheral blood system. The use of stem cells that have been harvested from the peripheral blood is a relatively recent medical development and it is gradually replacing bone marrow transplantation as the procedure of choice. This is because engraftment is more rapid and patients can normally be discharged from hospital earlier. A study by Vellenga et al. (2001) indicates that treatment with stem cells rather than bone marrow cells correlates significantly and positively with several important outcomes including quality of life (Vellenga et al., 2001).

The purpose of performing a stem cell transplant and the side-effects induced by treatment differ for different cancers (Outhwaite, 2004). Therefore the type of haematological malignancy with which each participant had been diagnosed was recorded. The approximate date of the patient's diagnosis was noted in order to give an indication of the length of time between diagnosis and treatment in which the participant had been able to psychologically adjust to the concept of needing a stem cell transplant.

As previously discussed the process of preparation for a stem cell transplant causes the destruction of blood cells that are crucial for oxygen carriage, clotting and immune defence. During the recovery phase levels of these cells gradually increase. Individuals with inadequate levels of these cells are at risk of bleeding and severe breathlessness particularly during exercise. Therefore participants' haemoglobin, platelet, white cell and neutrophil counts were checked prior to their commencement of the trial and regularly throughout the intervention period in order to ensure that they were safe to complete the exercise component of the intervention.

#### Psychometric and Symptom Specific Questionnaires

A number of general health status questionnaires exist. The SF-36 (Ware, Snow et al. 1993) was chosen in preference to alternatives because the SF-36 is particularly appropriate for use with patients who are recovering from major illness. It was also important that the tool chosen was suitable for self administration and not too burdensome to complete. This was particularly important as bone marrow and stem cell transplant patients

are susceptible to fatigue. The SF-36 contains 36 questions which can be used to calculate eight sub-scales

1. physical functioning
2. role limitation due to physical health
3. bodily pain
4. social functioning
5. general mental health
6. role limitations due to emotional problems
7. vitality, energy or fatigue
8. general health perceptions

The SF-36 has been shown to have good psychometric properties and high levels of reliability and validity (Ware et al., 1993). Ware et al. (1993) report the results of a factor analysis of the SF-36 and suggest that there is strong evidence for the conceptualisation of health on which the scale is built. This factor analysis indicated that some components of the scale effectively measure physical health, some mental health and some measure both (Ware et al., 1993). Brazier et al. (1992) investigated the acceptability, validity and reliability of the SF-36 and reported that the SF-36 had good construct validity and that it was able to detect low levels of ill health. This study identified evidence that the SF-36 was more sensitive to gradations in health than either the Euroqol or the Nottingham Health Profile (Brazier, Harper et al., 1992). Considerable evidence was found for the reliability of the SF-36 (Cronbach's alpha  $>0.85$ , reliability co-efficient  $>0.75$ ) for all dimensions except social functioning (Brazier et al., 1992). A number of other studies have also demonstrated that the SF-36 has acceptable internal consistency measured using Cronbach's alpha (Jenkinson et al., 1997, Garratt et al., 1993).

The SF-36 is one of the most widely used measures of health status (Bowling, 2001). It has been used in a number of previous studies with cancer patients (Ingram, 2002, Berger and Walker, 2001, Helgeson et al., 2000) and in several studies conducted with stem cell transplant patients (Gruber et al., 2003, So et al., 2003). Furthermore SF-36 population norms have been established for the UK population (Jenkinson et al., 1993) allowing comparisons to be made between the sample in this study and the wider UK population.

In recognition of the fact that health as defined by the health professionals may not accurately reflect the factors that are important to patients, a quality of life scale was included as a further outcome measure. Quality of life was measured using the Graham and Longman's two item Quality of Life Scale (QL Scale), which asks patients to rate their current quality of life on a scale from 1 (poor) to 10 (excellent), and their degree of satisfaction with their current quality of life from 1 (not satisfied at all) to 10 (very satisfied). Participants completed the questionnaire themselves, which took less than five minutes. The scale does not define quality of life and therefore it allows patients to rate their own quality of life according to the factors that are important for them. This scale has been shown to be a valid and reliable tool (Graham and Longman, 1987) and when tested with cancer patients it has been shown to have an inter-item correlation of less than 0.05 (Porock et al., 2005) suggesting that the two items measure different aspects of quality of life.

Since anxiety and depression are potential side effects of treatment with a bone marrow and stem cell transplant it was also important that a specific measure of psychological health was included as an outcome measure. Therefore the General Health Questionnaire, GHQ-12 (Goldberg, 1978) was

also used. The GHQ-12 is a state measure of psychiatric disturbance, assessing current state in relation to usual state. The GHQ-12 is a short item version of the long (60 item version), both versions having been shown to be reliable and valid. It has been suggested that the GHQ-12 is the scale that has been most extensively tested for reliability, validity and sensitivity (Bowling, 2001). The GHQ-12 has been shown to correlate well with psychiatric diagnoses of morbidity and depression. Internal consistency has been reported to range from 0.77 to 0.93 (Cronbach's alpha) and test-retest correlations range from  $r=0.51$  to 0.90 (Goldberg and Williams, 1988). The GHQ-12 was chosen in preference to the GHQ-60 in recognition of the fact that instrument burden was a potential problem given the number of questionnaires participants were asked to complete.

#### Other baseline measures

A standardised measure of exercise capacity was also included as an outcome measure. Exercise capacity was measured using the shuttle walk test. This measure was included to provide an objective measure of improvement in physical functioning. The reliability and validity of the shuttle walk test have been shown in studies with different patient populations including patients with cancer (MacSween et al., 2001, Ngaage et al., 2004, Win et al., 1996). It took participants approximately 20 minutes to complete the test.

During the collection of baseline data participants were also asked if they had a preference which programme they were allocated to. This was done to assist with data analysis. It was probable that some patients taking part in the trial would have a strong preference for one or other of the programmes. Their pleasure at being allocated their preferred programme or their disappointment at not getting their preferred programme might

have influenced the extent to which they engaged with their allocated programme which in turn might have influenced its effectiveness. Therefore it was important to establish if participants had a preference for one or other of the programmes. It was reiterated to patients that their stated preference did not influence the randomisation process.

### **Randomisation**

Patients that met the inclusion criteria and who gave written consent were randomly assigned to one of two groups (group SM "self managed rehabilitation programme", and group HPL "health profession led rehabilitation programme"). Facilitated by the website [www.randomization.com](http://www.randomization.com) an independent person used computer randomisation to generate randomisation lists. After the baseline measures had been completed a telephone call was made by the researcher to a member of administrative staff who held the randomisation lists. This individual was not otherwise involved in the study. The researcher was told which group the patient has been allocated to and the researcher then informed the participant. The participant's study number and randomisation result were logged in the trial records to enable verification after the completion of the trial that the randomisation process had not been manipulated.

In order to ensure that there was not too great an imbalance in the number of participants completing each arm of the trial at any one time, block randomisation was used. However a system of randomised block sizes was used to ensure that as the trial progressed it was not possible to work out the block sizes. If block size is known the final allocation in each block would be apparent and this would have made it easier for staff to

manipulate allocation if they so desired. The block sizes that were randomly assigned were six, eight and ten. The health care team and I were blind to block sizes until after the completion of the data collection.

### Stratification

Randomisation is designed to ensure that an imbalance in prognostic factors does not occur across arms of a trial. However, in practice, particularly in small trials such imbalances can occur. Stratification is used to control the imbalance between groups (Matthews, 2000).

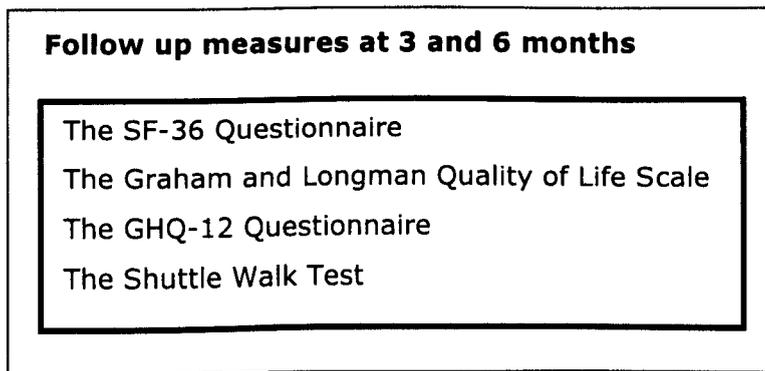
Receiving donated cells is immunologically more complicated than being re-infused with your own cells. Therefore allogenic transplants are associated with greater risk than autologous transplants (Outhwaite, 2004).

Transplant type is therefore a crucial prognostic factor in recovery after stem cell transplantation. Therefore there was stratification into two groups according to transplant type (autograft and allograft) prior to randomisation.

### **3.11 Follow Up Measures**

Data was gathered from participants on two further occasions, at the end of the intervention period and six months after randomisation. The rehabilitation programmes were ten weeks in duration. Therefore the first of these time points was chosen in order to assess the immediate impact of the health profession led and self managed programmes on the physical and psychosocial recovery of participants. The final data collection point was set at six months post randomisation in order to provide an indication as to the sustained effect of the programmes. At both time points the participants were asked to complete the measures shown in figure 3.4

**Figure 3.4: Follow up measures**



### **3.12 Qualitative Interviews**

Randomised controlled trials can provide information on how effective an intervention is, but are unable to provide insights into the overall experience of the patient who receives the intervention (Seers and Crichton, 2001). The addition of a qualitative component can compensate for this limitation and provide information about the intervention from the perspective of patients (Seers, 1994).

Semi structured interviews allow the researcher to set the agenda in terms of the topics covered but the interviewees responses' determine the kind of information produced and the relative importance of each topic (Green & Thorogood, 2005). A strength of using a guided approach is that it enables a systematic approach to data collection (Patton, 1990) which may increase the breadth, although not the depth, of the data generated.

Interview schedules (shown in Appendix F – page 285) were developed in order to assist the interviewer in conducting the interviews. These topic guides were developed through a process considering the different elements of the rehabilitation programmes and of exploring these in relation to the existing literature on the topic. The guides were reviewed by clinical and research colleagues, who provided suggestions for any further

topics for inclusion. The guides were then re-examined after the first couple of interviews had been conducted. The guides were used purely as a guide and did not stipulate exact phrasing of or a predetermined sequence to the questions.

The semi-structured interviews were used to explore the patients' experiences of recovering after a stem cell transplant, their experience of either the health profession led programme or the self managed programme and their experience of participation in a randomised controlled trial. It was anticipated that the interviews would provide additional depth to the quantitative data collected and allow participants the opportunity to express their thoughts and opinions about their recovery after stem cell transplantation and how the programmes provided, did or did not aid that recovery.

Semi structured interviews were also conducted with members of staff involved in either the health profession led programme or the provision of medical care to patients recovering after stem cell transplantation. It was expected that these interviews would provide an insight into the staff members experiences of being involved in a randomised controlled trial.

The semi structured interviews were conducted at the end of the study period, six months after randomisation and focused on the patients' perceptions of their quality of life and their recovery from stem cell transplantation. These interviews were conducted in a location convenient for the participant. This tended to be in a quiet side room during a clinic visit or at a visit by the researcher to the participant's home.

Participants were selected to ensure that the sample included individuals not only from each arm of the study but also from both transplant types, both genders and a range of ages. Furthermore it was important to ensure that within the group of interviewees there were participants with differing reactions to the two programmes. For example it was necessary that interviews were conducted with individuals whose attendance at the health profession led programme had been high and with individuals whose attendance had been sporadic or even non-existent. Staff members were selected for interview according to their involvement in the trial or their acknowledged expertise in the field of stem cell transplantation.

### **3.13 Trial Outcomes**

#### **Primary Outcome**

Change in the mean SF-36 physical functioning summary score at six months was chosen as the primary outcome measure. The time point of six months was chosen for the primary outcome measure since establishing if the rehabilitation programmes had any ongoing effectiveness was considered to be more important than assessing the effects of the programmes immediately after their completion. Since the programme has a considerable focus on the physical components of health it was appropriate to choose a measure of physical functioning as the primary outcome measure.

#### **Secondary Outcomes**

A wide range of secondary outcome measures were chosen in recognition of the complex nature of the health profession led programme. Given the

biopsychosocial nature of the intervention under evaluation it was important to choose measures that reflected each element of the study.

The secondary outcome measures were; Change in role limitation due to physical health; bodily pain; social functioning; general mental health, role limitations due to emotional problems; vitality, energy or fatigue and general health perceptions as measured by the SF-36 between baseline and six months; Change in physical functioning; role limitation due to physical health; bodily pain; social functioning; general mental health, role limitations due to emotional problems; vitality, energy or fatigue and general health perceptions as measured by the SF-36 between baseline and three months; Change in quality of life, as measured by the Graham and Longman two item quality of life scale, between baseline and six months; Change in quality of life, as measured by the Graham and Longman two item quality of life scale, between baseline and three months; Change in psychological health, as measured by the General Health Questionnaire, between baseline and six months; Change in psychological health, as measured by the General Health Questionnaire, between baseline and three months; Change in exercise capacity, as measured by the shuttle walk test, between baseline and six months; Change in exercise capacity, as measured by the shuttle walk test, between baseline and three months.

### **3.14 Data management and analysis**

#### **Quantitative data management**

The statistical software package SPSS (v14) for windows was used to manage and analyse the quantitative data. Prior to data analysis an analysis plan was devised. This approach was used to avoid data dredging,

a process whereby multiple analyses are conducted increasing the risk of making a type I error. Descriptive statistics were used to summarise the questionnaire and shuttle walk test data. The outcome data was analysed using linear regression models. Data was checked to ensure it met the assumptions required for linear regression analysis. In particular the distribution of residuals was checked for all data. The analysis plan included the proviso that if results that were indicative of a difference between the two arms of the trial occurred for data where there was any evidence to suggest the assumptions of linear regression had been violated, then non-parametric tests would be used to see how robust the results were.

Exploratory analysis using linear regression models was conducted to explore if a patient's programme preference had a modifying effect on the relationship between physical functioning and programme allocation. Further exploratory analyses were considered but the study was considered to be insufficiently powered to allow this. Since one of the advantages of using the SF-36 health survey was that population norms exist for the UK population, the SF-36 data from six months post recruitment was compared to the UK population norms. This enabled a comparison to be made between the health of individuals recovering after stem cell transplantation and that of the general public. The SF-36 data was adjusted for both age and gender.

### **Qualitative data management**

The interviews were transcribed into word documents and then analysed. The decision was taken not to use any additional computer packages (other than Microsoft word) in the analysis of data but to adapt the 'scissor and

'paste' approach described by Krueger and Casey (2000). The volume of data was comparatively small and a non-computerised method was both feasible and appropriate.

A thematic content approach to data analysis was used. This is a commonly used approach in health research and is appropriate for interview data (Green and Thorogood, 2004). Following transcription which was carried out by a combination of the researcher and an employed transcription service, the interview transcripts were checked for accuracy, read for context and then coded. Respondents' accounts were categorised and compared enabling identification of the themes that were common in the data set. Individual themes were then considered in more detail, with attention being paid to contradictory accounts or unusual cases. The findings were then interpreted within the context of the existing literature.

Green and Thorogood (2004) suggest a number of features of rigorous qualitative analysis. These include transparency, providing a clear account of the procedures used, the analysis of deviant cases and disconfirming data, analysis of the whole data set, using more than one analyst, providing simple frequency counts of key themes, comparing findings to other studies and accounting for the role of the researcher in the research. Unfortunately the study did not have the resources to use more than one analyst to analysis the data. Therefore, several full transcripts were reviewed by an experienced researcher and checks were made on the interpretation of data. All the rest of the principles outlined above were applied to the analysis of the qualitative data generated in this study.

### **3.15 Ethical considerations**

There were a number of ethical concerns that required consideration during the planning of this study. A concern of all studies is to ensure that consent is both informed and voluntary. It is clearly unethical to mislead people or dupe them into participation. However, ensuring that consent is informed consent, requires more than just a commitment to not deliberately mislead people. For example, the initial draft of the information letter to be used in the study informed participants that the allocation of rehabilitation programmes would be on a random basis. This was clearly a truthful statement but research has shown that participants often have very little understanding of what random allocation actually means (Stead et al., 2005). Therefore the final draft of the information letter (shown in Appendix C – page 257) stated that “participants are randomly assigned to one or other of the groups by a computer that does not have any information about the individual – i.e. by chance”. Throughout this study we attempted to fully explain concepts in order to ensure that as far as possible patients had not only been given accurate information but that they had understood it. In order to ensure that participation was voluntary we informed all potential participants that their routine care would be unaffected by their decision either to or not to participate and that they were free to withdraw at any point without giving a reason.

In order for a randomised controlled trial design to be ethically viable it is crucial that genuine uncertainty exists as to which arm of the trial will provide the most benefit to patients. It is of fundamental importance that this equipoise exists in order to justify having a control group. It is clearly unethical to deprive participants of an intervention that is of proven benefit. Therefore the existing evidence was explored at length to ensure that this research was justified and to be certain that those participants

randomised to the control group would not have any aspect of care withheld from them that was of known benefit. Since there is sufficient evidence that exercise has proven health benefits this research did not attempt to reassess this concept. This research aimed to establish whether the structure of a health profession led rehabilitation session was more effective at promoting recovery than a programme which provided patients with information and support through a self managed programme. The information pack was used in order to provide the control group with the same information that is available to the participants attending the health profession led rehabilitation programme. The participants in the control group were not discouraged from making any lifestyle changes that are thought to promote recovery and good health.

In many studies the control group consists of usual care. In these studies participants are aware before they take part that they may or may not receive any additional intervention. For the reasons outlined above I did not want to use usual care as the control in this study. However it was very important that patients were not misinformed about the nature of the self managed programme and led to expect more than was actually being provided. Therefore it was stated in the pre-trial information and reiterated verbally that the self managed programme consisted of information that was available to patients generally but that for the purposes of this study it had been gathered together into one pack.

### **Ethics and Research Governance**

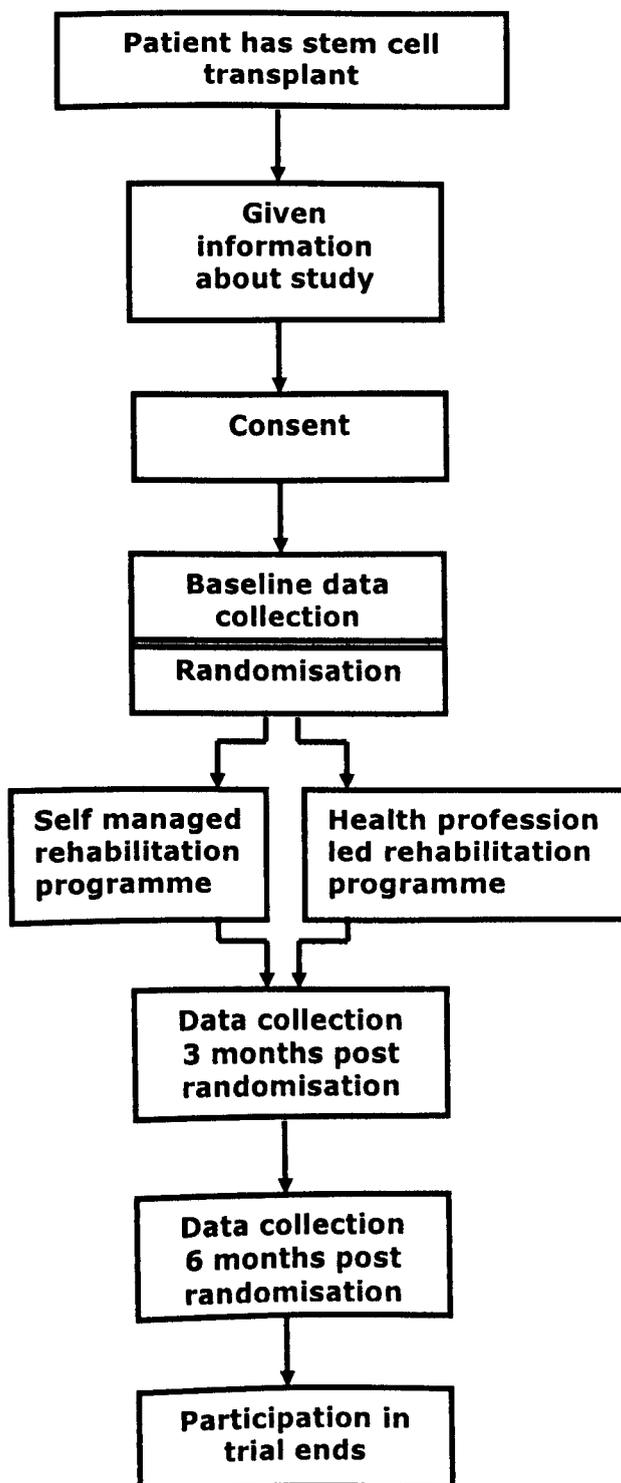
The study was reviewed by the local research ethics committee who gave approval for the study. Permission to conduct the study at the particular research site was requested and given by the appropriate research and

development committee. The progress of the trial was also monitored by the research and development department.

### **3.16 Summary**

A randomised controlled trial was used to evaluate a health profession led rehabilitation programme. The control group completed a self managed programme. The study design is summarised in figure 3.5.

**Figure 3.5: Summary of Study Design**



## **Chapter 4 - Trial Results**

### **4.1 Introduction**

This chapter reports the results of the bone marrow and stem cell transplant rehabilitation trial. The chapter includes a description of the study sample and compares the demographic characteristics of those who took part with those who did not. The reasons participants gave for not wishing to take part are also reported. Detailed demographic and clinical details as well as baseline scores for the outcome measures are provided for participants randomised to the health profession led and self managed programmes. The results of analysis carried out on the primary and secondary outcome data is then presented. Exploratory analysis is presented and finally the SF-36 data from this trial is compared with some normative data from the UK population.

### **4.2 Recruitment**

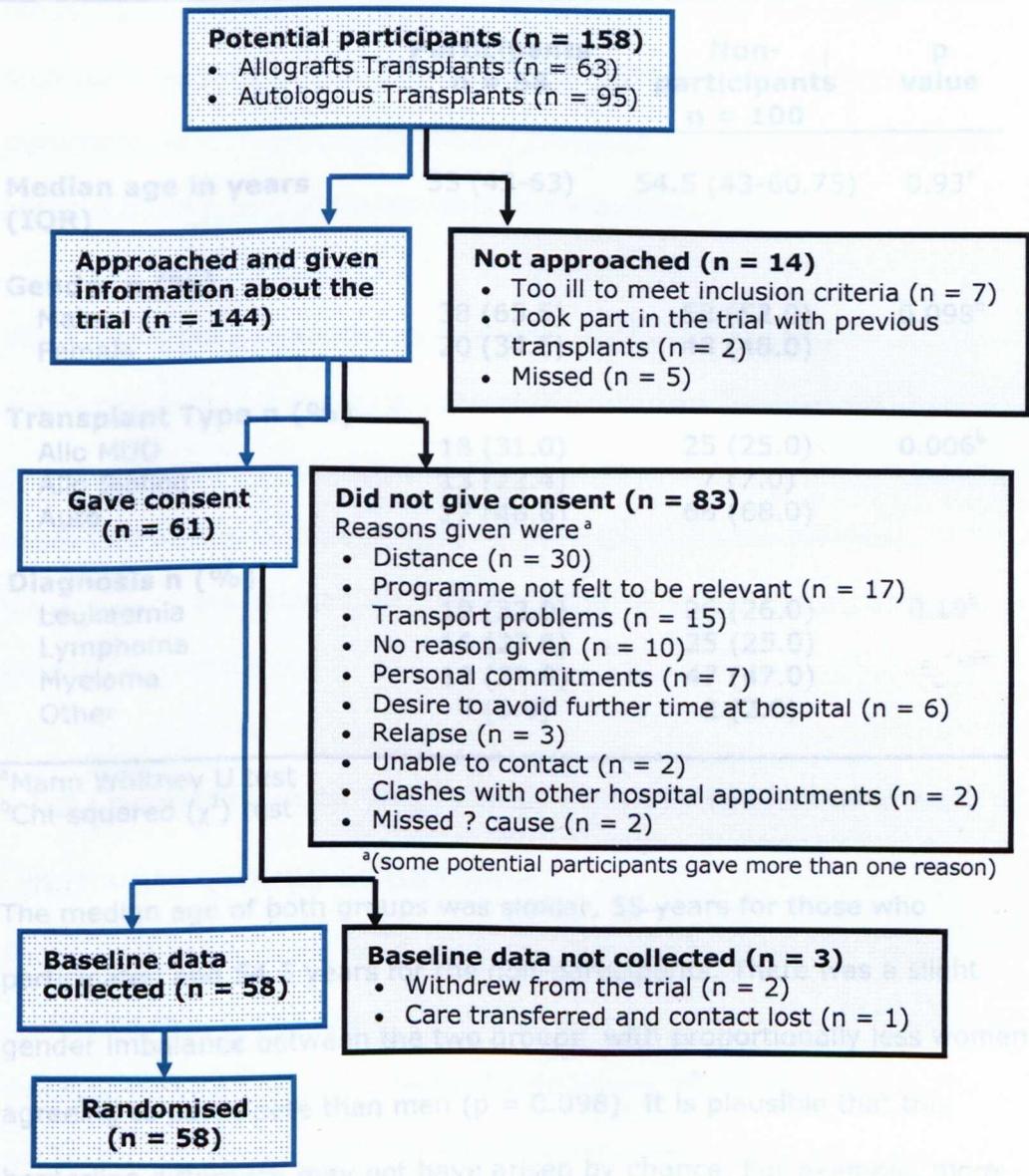
Recruitment took place over a 14 month period commencing in August 2005. Recruitment was from the allograft and autologous transplant clinics. During the recruitment period 158 people underwent treatment with either an allograft (63) or autologous (95) transplant. All 158 people were considered for entry into the trial. Of these 158 people, 144 (91%) were approached with regard to taking part. Of the fourteen potential participants not approached seven were too ill to meet the inclusion criteria and two had already taken part in the trial with previous transplants and they were therefore ineligible, five participants were missed because their care was transferred to their referring hospital immediately post transplant. Of the 144 potential participants who were approached about the trial 61 (42%) gave their consent to take part. The most frequently cited reasons for declining to take part were distance from home to hospital, and that the

programme did not seem relevant to their needs. Baseline data was collected from 58 of the 61 people who had consented to take part. Two people withdrew from the trial before their data was collected and one person had their care transferred to another hospital and contact was lost. Everyone who had baseline data collected was randomised to either the health profession led programme or the self managed programme.

It was calculated that a total of 132 participants needed to be recruited in order for the study to be adequately powered (shown in chapter three section 3.9). Despite this the decision was taken to stop recruiting after 14 months when only 58 participants had been recruited. A combination of factors including the poor rate of recruitment, changes to the clinical environment and a lack of stability of the health profession led rehabilitation programme all contributed to the decision to stop recruiting participants. These factors are explored in greater detail in the discussion of the methodology (chapter six section 6.2).

The flow of potential participants from transplant to randomisation is summarised by figure 4.1.

**Figure 4.1: The progression of participants from transplantation through to randomisation**



### 4.3 Comparison of study participants and non-participants

In order to assess how representative the sample was of the study population the demographic characteristics of those who agreed to take part were compared with those who did not take part. The data includes both potential participants who were approached but declined to take part and those who were not approached. This is shown in table 4.1.

**Table 4.1: Demographic characteristics of study participants and non-participants**

	<b>Participants n = 58</b>	<b>Non- participants n = 100</b>	<b>p value</b>
<b>Median age in years (IQR)</b>	55 (43-63)	54.5 (43-60.75)	0.93 <sup>a</sup>
<b>Gender n (%)</b>			
Male	38 (65.5)	52 (52.0)	0.098 <sup>b</sup>
Female	20 (34.5)	48 (48.0)	
<b>Transplant Type n (%)</b>			
Allo MUD	18 (31.0)	25 (25.0)	0.006 <sup>b</sup>
Allo Sibling	13 (22.4)	7 (7.0)	
Auto	27 (46.6)	68 (68.0)	
<b>Diagnosis n (%)</b>			
Leukaemia	19 (32.0)	26 (26.0)	0.19 <sup>b</sup>
Lymphoma	16 (27.6)	25 (25.0)	
Myeloma	19 (32.8)	47 (47.0)	
Other	4 (6.9)	2 (2.0)	

<sup>a</sup>Mann Whitney U test

<sup>b</sup>Chi-squared ( $\chi^2$ ) test

The median age of both groups was similar, 55 years for those who participated and 54.5 years for the non-participants. There was a slight gender imbalance between the two groups, with proportionally less women agreeing to participate than men ( $p = 0.098$ ). It is plausible that this borderline difference may not have arisen by chance. For example, more women than men (six women, one man) when asked about the study cited other commitments as the reason for their non-participation and this was frequently related to their responsibilities as a mother or grandmother.

A difference was identified between the participants and non-participants in relation to transplant type ( $p = 0.006$ ), with participants who had undergone an autologous transplant being less likely to take part in the trial. There are a number of possible explanations for this finding. It may

be that the better post transplant recovery associated with having an autologous transplant meant that individuals did not feel the need for rehabilitation. However it must also be considered that the health profession led programme was run on the same day as the allograft transplant clinic, therefore potentially providing an incentive for allograft patients to take part and a disincentive for autologous patients.

There was a good representation of each diagnostic group in the study population with no substantial differences identified between the participants and non-participants. The slight imbalance in the two groups in relation to myeloma patients is to be expected given the previous discussion on transplant type since the usual treatment for myeloma is autologous transplant.

#### **4.4 Comparison of the health profession led and self managed groups at baseline**

Participants in the study were randomly allocated to either the health profession led programme or the self managed programme. Of the 58 participants who took part, 29 participants were allocated to the health profession led programme and 29 participants were allocated to the self managed programme. The purpose of randomly allocating participants was to ensure that patients in different groups were similar in characteristics such as age, gender and any other factors that may influence trial outcomes, however randomisation cannot guarantee that imbalances will not occur especially when sample sizes are small (Wang and Bakhai, 2006). Therefore the health profession led and self managed groups were compared to check for imbalances that might have an affect on the

outcome variables. Table 4.2 provides information about the demographic and clinical characteristics of the two groups at baseline.

The health profession led group have a marginally higher median age (57 years) than the self managed group (52 years), however the interquartile ranges for the two groups were very similar (44-63.5 compared to 42.5-63). There was a modest gender imbalance between the two groups with more women being allocated to the health profession led programme (n = 13) than the self managed programme (n = 7). Wang and Bakhai (2006) recommend that adjustment of the baseline covariate is appropriate if it is known to be correlated to the outcome. They suggest a covariate that gives a correlation coefficient  $>0.5$  or  $<-0.5$  requires adjustment. Therefore the correlation coefficient between each baseline characteristic and the main outcome measure were calculated. These are shown in table 4.3. The correlation coefficient for gender was found to be -0.14 and therefore the imbalance in gender between the two groups in this sample was not considered to be important.

It was predicted that transplant type might have a major influence on the outcomes of this trial and therefore the randomisation process included stratification according to transplant type. The two groups were therefore well balanced with regard to transplant type. The health profession led programme included 15 people who had undergone an allograft transplant and 14 people who had undergone an autologous transplant. The self managed programme included 16 people who had undergone an allograft transplant and 13 people who had undergone an autologous transplant.

There was a good representation of each diagnostic group in each arm of the study with no particular imbalances between the two groups. Only six

people in the study had transplants using cells harvested from bone marrow and five of these were allocated to the health profession led programme. However the source of a participant's cells had a correlation coefficient of  $-0.004$  with the main outcome measure and therefore this imbalance was not considered to be problematic. The median time between diagnosis and transplant was similar in both groups, seven months in those allocated to the health profession led programme and six months in those allocated to the self managed programme. A crude measure of social support, i.e. does the participant's next of kin live with them indicated that individuals in both groups had a similar level of social support. In the health profession led group 22 people lived with their next of kin compared to 25 people in the self managed group.

**Table 4.2: Demographic and clinical characteristics of the health profession led and self managed groups at baseline**

	<b>HPL Group (n = 29)</b>	<b>SM Group (n = 29)</b>
<b>Median age in years (IQR)</b>	57 (44-63.5)	52 (42.5-63)
<b>Gender n (%)</b>		
Male	16 (55.2)	22 (75.9)
Female	13 (44.8)	7 (24.1)
<b>Transplant type n (%)</b>		
Allo MUD	8 (27.6)	10 (34.5)
Allo Sibling	7 (24.1)	6 (20.7)
Auto	14 (48.3)	13 (44.8)
<b>Diagnosis n (%)</b>		
Leukaemia	9 (31.0)	10 (34.5)
Lymphoma	10 (34.5)	6 (20.7)
Myeloma	9 (31.0)	10 (34.5)
Other	1 (3.4)	3 (10.3)
<b>Source of cells n (%)</b>		
Peripheral Blood	24 (82.8)	28 (96.6)
Bone Marrow	5 (17.2)	1 (3.4)
<b>Median time between diagnosis and transplant in months (IQR)</b>	7 (4-22)	6 (4-14)
<b>Does participant live with NOK n (%)</b>		
Yes	22 (75.9)	25 (86.2)
No	7 (24.1)	4 (13.8)

IQR = Interquartile Range

NOK = Next of Kin

**Table 4.3: The correlation between characteristics measured at baseline and the primary outcome measure (SF-36 Physical Functioning score at six months).**

	<b>Correlation co-efficient</b>
<b>Age</b>	-0.13
<b>Gender</b>	-0.14
<b>Transplant type</b>	0.08
<b>Diagnosis</b>	0.03
<b>Source of cells</b>	-0.004
<b>Time between diagnosis and transplant</b>	-0.008
<b>Does participant live with NOK</b>	-0.01

NOK = Next of Kin

Table 4.4 provides a comparison of the summary scores from the psychometric questionnaires at baseline. The baseline scores in both the health profession led and self managed groups are similar across the range of outcome measures.

**Table 4.4: SF-36,<sup>a</sup> general health questionnaire,<sup>b</sup> quality of life<sup>c</sup> and the shuttle walk test<sup>d</sup> scores for the health profession led and self managed groups at baseline**

	HPL Group (n = 29)	SM Group (n = 29)
<b>SF-36 Mean, (SD) &amp; Median Summary Scores</b>		
Physical Functioning	41.7 (23.6) 45.0	44.0 (25.3) 40.0
Role-Physical	20.9 (19.6) 18.8	23.2 (17.2) 25.0
Bodily Pain	63.1 (29.1) 64.0	60.6 (28.6) 62.0
General Health	49.0 (19.8) 45.0	44.5 (18.5) 42.0
Vitality	30.8 (20.9) 31.3	31.3 (19.1) 31.3
Social Functioning	37.0 (30.1) 25.0	35.8 (27.9) 25.0
Role-Emotional	54.0 (36.8) 66.7	44.5 (28.5) 50.0
Mental Health	66.6 (17.9) 70.0	62.2 (22.3) 65.0
<b>GHQ Mean Score (SD)</b>	17.4 (6.5)	16.3 (8.0)
<b>QoL Mean, (SD) &amp; Median Summary Scores</b>		
QoL Rating	5.6 (1.7) 5.0	5.5 (2.2) 5.5
QoL Satisfaction	4.7 (2.6) 4.5	4.7 (2.6) 4.5
<b>SWT Mean, (SD) &amp; Median Summary Scores (Metres)</b>	235.9 (150.4) 260.0	233.1 (133.9) 220.0

<sup>a</sup> Possible scores range from 0-100. Higher score indicates better functioning.

<sup>b</sup> Possible scores range from 0-36. Higher score indicates worse mental health.

<sup>c</sup> Possible scores range from 0-10. Higher score indicates better quality of life.

<sup>d</sup> Possible scores range from 0-1020 metres . Higher score indicates better physical functioning.

GHQ = General Health Questionnaire, QoL = Quality of Life, SWT = Shuttle Walk Test  
SD = Standard Deviation

## 4.5 Participation in the health profession led programme

Table 4.5 shows the attendance levels for participants allocated to the health profession led programme. There was considerable variability in the attendance level of participants with some participants attending for the entire programme whilst others never attended. No measure of

participation is reported for those allocated to the self managed programme.

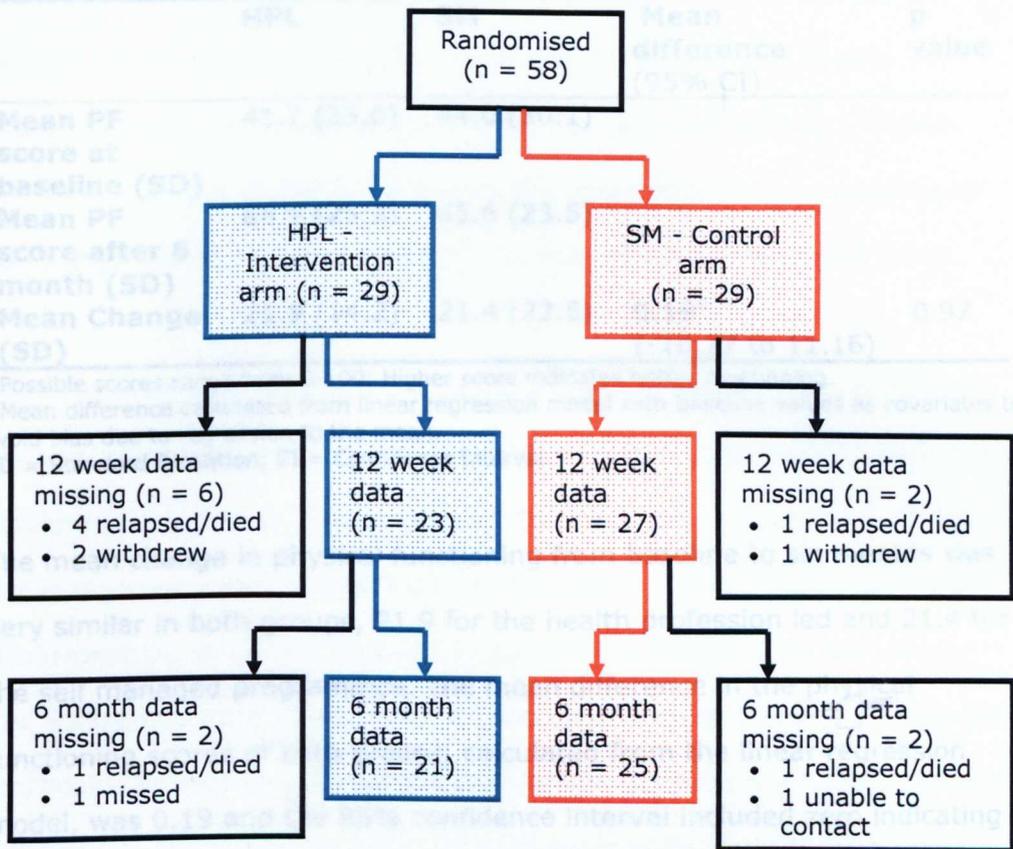
**Table 4.5: Distribution of number of health profession led rehabilitation sessions attended out of a total of ten by participants allocated to the HPL programme (n = 29).**

<b>% of rehab sessions attended</b>	<b>Number of participants</b>
0-3	10
4-6	6
7-10	13

## **4.6 Attrition**

Data was collected from 50 participants at the 12 week data collection point. 23 of these participants were in the health profession led group and 27 were in the self managed group. Of the eight participants from whom 12 week data was not collected three participants had chosen to withdraw from the trial and five participants were either undergoing active treatment again because their disease had relapsed or they had died. By the six month data collection point a further two participants had either relapsed or died, one participant was missed and it was not possible to contact one further participant. Data was collected on the remaining 46 participants. This information is summarised by figure 4.2.

**Figure 4.2: The progression of participants from randomisation through to trial conclusion**



#### 4.7 Primary outcome of the trial

The primary outcome measure was the physical functioning score of the SF-36 at six months which was analyzed using linear regression with baseline physical functioning and intervention group as covariates. This analysis and the mean physical functioning scores at baseline and after six months are shown in table 4.6.

**Table 4.6: Change in the primary outcome measure, SF-36 physical functioning score,<sup>a</sup> between the study groups at 6 months**

	<b>HPL</b>	<b>SM</b>	<b>Mean difference (95% CI)</b>	<b>p value</b>
<b>Mean PF score at baseline (SD)</b>	41.7 (23.6)	44.0 (30.1)		
<b>Mean PF score after 6 month (SD)</b>	64.9 (25.3)	65.6 (23.5)		
<b>Mean Change (SD)</b>	21.9 (14.2)	21.4 (22.5)	0.19 <sup>b</sup> (-10.77 to 11.16)	0.97

<sup>a</sup> Possible scores range from 0-100. Higher score indicates better functioning.

<sup>b</sup> Mean difference calculated from linear regression model with baseline values as covariates to avoid bias due to regression to the mean.

SD = Standard Deviation, CI = Confidence Interval

The mean change in physical functioning from baseline to six months was very similar in both groups, 21.9 for the health profession led and 21.4 for the self managed programmes. The mean difference in the physical functioning scores of both groups, calculated from the linear regression model, was 0.19 and the 95% confidence interval included zero indicating that no evidence of a difference between the two modes of rehabilitation could be observed. However, the confidence interval around the estimated difference in physical functioning could not exclude differences of up to 10 points in either direction.

## **4.8 Secondary outcomes of the trial**

The secondary outcomes of the trial were change in the SF-36 scores, the general health questionnaire, quality of life ratings and the shuttle walk test scores between baseline and six months and also between baseline and three months. Table 4.7 presents the mean change from baseline to six months for all outcome measures broken down by treatment group.

The mean changes in the SF-36, general health questionnaire, quality of life and the shuttle walk test scores from baseline to six months were very similar in both groups. The smallest mean difference calculated from the linear regression model was 0.02 (for the quality of life rating data) and the largest mean difference was -15.06 (for the shuttle walk test data).

The 95% confidence intervals for all outcomes included zero indicating that the health profession led rehabilitation programme did not have an impact on recovery that could be detected in this size sample six months after randomisation.

**Table 4.7: Change between baseline and six months for the HPL and SM scores of the SF-36,<sup>a</sup> GHQ,<sup>b</sup> quality of life scale<sup>c</sup> and the shuttle walk test<sup>d</sup>**

	<b>HPL group</b>	<b>SM group</b>	<b>Mean Difference<sup>e</sup> (95% CI)</b>	<b>p value</b>
<b>Physical Function</b>				
Mean Change (SD)	21.85 (14.22)	21.38 (22.54)	0.19 (-10.77 to 11.16)	0.97
<b>Role-Physical</b>				
Mean Change (SD)	33.44 (28.41)	34.25 (27.43)	-1.17 (-18.05 to 15.70)	0.89
<b>Bodily Pain</b>				
Mean Change (SD)	8.86 (24.93)	11.96 (26.65)	-1.37 (-14.19 to 11.46)	0.83
<b>General Health</b>				
Mean Change (SD)	7.24 (23.08)	10.40 (15.71)	-1.21 (-12.76 to 10.34)	0.83
<b>Vitality</b>				
Mean Change (SD)	21.73 (17.07)	22.50 (23.87)	-0.15 (-11.62 to 11.32)	0.98
<b>Social Function</b>				
Mean Change (SD)	32.14 (38.64)	35.00 (31.25)	-2.64 (-19.21 to 13.93)	0.75
<b>Role-Emotional</b>				
Mean Change (SD)	17.91 (27.61)	27.00 (33.70)	2.28 (-13.17 to 17.73)	0.77
<b>Mental Health</b>				
Mean Change (SD)	5.95 (16.48)	6.40 (21.14)	1.57 (-8.36 to 11.50)	0.75
<b>GHQ</b>				
Mean Change (SD)	-5.95 (7.63)	-4.96 (9.39)	-0.36 (-4.60 to 3.88)	0.87
<b>QoL Rating</b>				
Mean Change (SD)	1.60 (1.99)	1.69 (2.53)	0.02 (-1.16 to 1.20)	0.97
<b>QoL Satisfaction</b>				
Mean Change (SD)	2.14 (2.50)	2.44 (3.64)	-0.06 (-1.53 to 1.42)	0.94
<b>SWT</b>				
Mean Change (SD)	126.11 (107.71)	140.91 (99.85)	-15.06 (-82.45 to 52.33)	0.65

<sup>a</sup> Possible scores range from 0-100. Higher score indicates better functioning.

<sup>b</sup> Possible scores range from 0-36. Higher score indicates worse mental health.

<sup>c</sup> Possible scores range from 0-10. Higher score indicates better quality of life.

<sup>d</sup> Possible scores range from 0-1020 metres.

<sup>e</sup> Mean difference calculated from linear regression model with baseline values as covariates to avoid bias due to regression to the mean.

GHQ = General Health Questionnaire, QoL = Quality of Life, SWT = Shuttle Walk Test

SD = Standard Deviation, CI = Confidence Interval

The trial design included testing for differences between the health profession led programme and the self managed programmes immediately after the end of the intervention period (three months after randomisation). Table 4.8 presents the mean change from baseline to three months for all outcome measures broken down by treatment group.

As with the six month data, the mean changes at three months for the SF-36, general health questionnaire, quality of life and the shuttle walk test scores were very similar in both groups. The smallest mean difference calculated from the linear regression model was 0.09 points, for the quality of life rating data, and the largest mean difference was 34.7 metres, for the shuttle walk test data. The 95% confidence intervals for all outcomes included zero indicating that no evidence of any difference in recovery between the health profession led and self managed rehabilitation groups could be observed.

**Table 4.8: Change between baseline and three months for the health profession led and self managed group scores of the SF-36,<sup>a</sup> GHQ,<sup>b</sup> quality of life scale<sup>c</sup> and the shuttle walk test<sup>d</sup>**

	<b>HPL Group</b>	<b>SM group</b>	<b>Mean Difference<sup>e</sup> (95% CI)</b>	<b>p value</b>
<b>Physical Function</b>				
Mean Change (SD)	15.96 (16.38)	11.91 (21.62)	3.94 (-7.13 to 15.00)	0.48
<b>Role-Physical</b>				
Mean Change (SD)	16.85 (20.94)	21.76 (27.59)	-4.89 (-19.17 to 9.40)	0.50
<b>Bodily Pain</b>				
Mean Change (SD)	7.48 (29.49)	10.74 (19.05)	-1.27 (-13.81 to 11.26)	0.84
<b>General Health</b>				
Mean Change (SD)	4.13 (16.57)	9.30 (17.92)	-3.93 (-13.75 to 5.89)	0.43
<b>Vitality</b>				
Mean Change (SD)	16.39 (13.71)	14.74 (21.11)	2.17 (-8.16 to 12.49)	0.68
<b>Social Function</b>				
Mean Change (SD)	20.11 (30.32)	25.46 (31.29)	-3.96 (-18.93 to 11.00)	0.60
<b>Role-Emotional</b>				
Mean Change (SD)	5.43 (29.15)	25.30 (38.01)	-12.76 (-30.82 to 5.30)	0.16
<b>Mental Health</b>				
Mean Change (SD)	5.54 (13.44)	6.67 (20.94)	0.99 (-7.99 to 9.97)	0.83
<b>GHQ</b>				
Mean Change (SD)	-4.27 (7.49)	-4.84 (8.29)	1.15 (-3.04 to 5.35)	0.58
<b>QoL Rating</b>				
Mean Change (SD)	0.89 (1.60)	0.98 (1.92)	-0.09 (-1.01 to 0.84)	0.85
<b>QoL Satisfaction</b>				
Mean Change (SD)	1.32 (1.49)	1.78 (2.73)	-0.38 (-1.50 to 0.73)	0.49
<b>SWT</b>				
Mean Change (SD)	145.00 (170.51)	106.54 (110.85)	34.67 (-43.01 to 112.34)	0.37

<sup>a</sup> Possible scores range from 0-100. Higher score indicates better functioning.

<sup>b</sup> Possible scores range from 0-36. Higher score indicates worse mental health.

<sup>c</sup> Possible scores range from 0-10. Higher score indicates better quality of life.

<sup>d</sup> Possible scores range from 0-1020 metres.

<sup>e</sup> Mean difference calculated from linear regression model with baseline values as covariates to avoid bias due to regression to the mean.

GHQ = General Health Questionnaire, QoL = Quality of Life, SWT = Shuttle Walk Test

SD = Standard Deviation, CI = Confidence Interval

## 4.9 Confirmatory Analysis

In the data analysis plan it was stated that the data would be checked to ensure it met the assumptions required for linear regression analysis.

Furthermore, if results that were indicative of a difference between the two arms of trial occurred for data where there was any evidence to suggest the assumptions of linear regression had been violated, then non-parametric tests would be used to see how robust the results were.

The distribution of residuals was checked for all data. No confirmatory analysis was carried out as no results indicated a difference between the health profession led and the self managed arms of the study and there was therefore no risk of a type I error.

## 4.10 Exploratory Analysis

Prior to randomisation, participants were asked if they had a preference as to which programme they received. Table 4.9 illustrates the preferences expressed by participants.

**Table 4.9: Programme preference expressed by participants**

	<b>No Preference</b>	<b>Preference for HPL</b>	<b>Preference for SM</b>
<b>All participants</b>	17 (29.3%)	28 (48.2%)	13 (22.4%)
<b>Participants allocated HPL</b>	9 (15.5%)	11 (19.0%)	9 (15.5%)
<b>Participants allocated SM</b>	8 (13.8%)	17 (29.3%)	4 (6.9%)

It is clear from these numbers that in each group there were a considerable number of people who stated a preference for the programme which they were not allocated to. Given the potentially important contribution of personal motivation to the impact of the programmes in the

trial it was considered important to explore this concept of programme preference and its impact on outcome. Specifically, it was of interest to explore if a participant being allocated the programme for which they had a preference had an impact on outcome. Therefore the interaction effect for preference and allocation on the mean physical functioning scores of participants at six months was explored. This analysis is shown in table 4.10.

**Table 4.10: The interaction effect for preference and allocation on the mean physical functioning scores of participants at six months**

Preference	Allocation	Mean Physical Functioning score, (SE)	Mean difference <sup>a</sup> (CI)	p value
None	SM	28.2 (8.5)		
None	HPL		-2.4 (-23.9 to 18.8)	
HPL	SM		6.7 (-10.8 to 24.1)	
HPL	HPL		5.5 (-13.5 to 24.4)	
SM	SM		-2.3 (-29.2 to 24.7)	
SM	HPL		8.4 (-13.9 to 30.7)	
				0.73

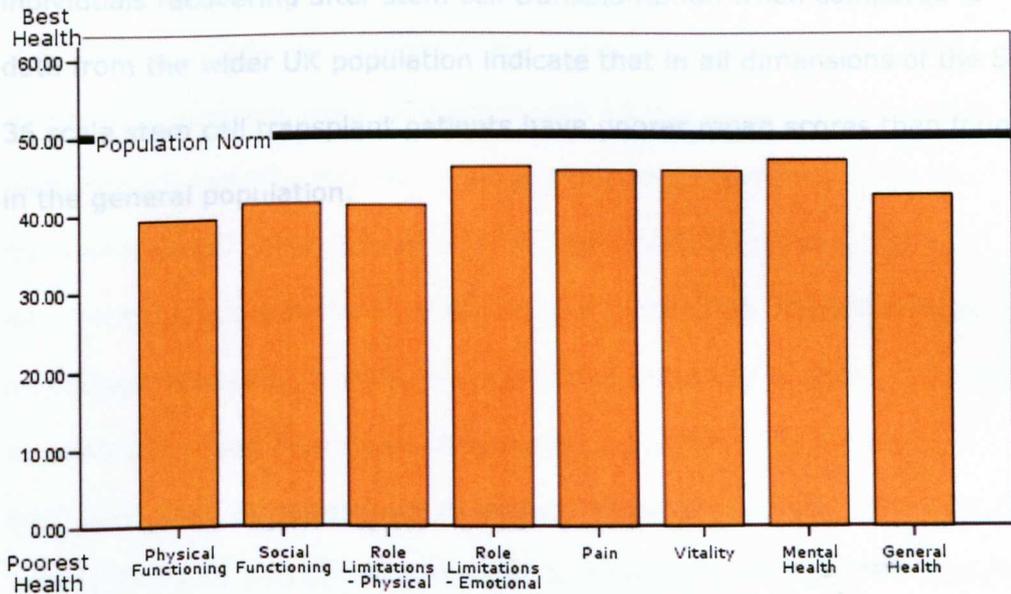
<sup>a</sup> Mean difference in PF score according to allocation & group compared to participants with no preference who were allocated the SM programme, calculated from linear regression model with baseline values as covariates to avoid bias due to regression to the mean.

This exploratory analysis provided no evidence to support the theory that preference was an effect modifier of the relationship between an individual's allocated treatment and their physical functioning score at six months.

#### **4.11 Comparison to population norms**

The SF-36 data collected at six months post randomisation from both arms of the trial was combined and compared to UK age group and gender specific population norms for the SF-36 health survey (Jenkinson et al. 1993). The results of this analysis are presented in figure 4.3.

**Figure 4.3: Norm-based scoring of the SF-36 for stem cell transplant recipients<sup>a</sup>**



All Scales: Mean = 50, SD = 10

<sup>a</sup>Using SF-36 data collected at 6 months post transplant adjusted for age and gender.

The comparison of the SF-36 scores collected from stem cell transplant patients six months after their transplants with data from the wider UK population indicates that in all dimensions of the SF-36 scale stem cell transplant patients have poorer mean scores than found in the general population. Predictably, given the nature of the stem cell transplant procedure, the greatest variation between the two sets of data was seen in the physical functioning dimension of the SF-36. Encouragingly, there was least variation in the scores for the mental health dimension of the scale. This comparison used the SF-36 data collected from stem cell transplant patients six months after their transplants indicating that recovery after transplantation can be protracted and therefore endorsing the concept of rehabilitation for this patient group.

#### **4.12 Summary**

There was no evidence of any difference in recovery between the health profession led and self managed rehabilitation groups. The SF-36 scores of individuals recovering after stem cell transplantation when compared to data from the wider UK population indicate that in all dimensions of the SF-36 scale stem cell transplant patients have poorer mean scores than found in the general population.

# **Chapter 5 - Results from the qualitative interviews**

## **5.1 Introduction**

This chapter reports the findings of the qualitative data analysis. Semi structured interviews were carried out with 15 trial participants and five members of staff. The interviews ranged from approximately 15 to 60 minutes in length. The participant interviews were designed to explore each participant's experience of taking part in the trial. Therefore these interviews focused on two key issues; the acceptability of each programme to participants and the burden of participation in the trial. The staff interviews were an opportunity to explore issues around both providing the intervention and also of being involved in a randomised controlled trial. The findings from each group of interviews are presented separately. Firstly, the views of participant interviewees on the experience of participating in a randomised controlled trial are presented. Secondly, the acceptability of each programme to participants is discussed. Finally, the experiences of the staff interviewees are explored. Before these findings are presented a summary is given of the characteristics of those who took part in the interviews.

## **5.2 Interviewee characteristics**

Table 5.1 shows the characteristics of those who agreed to be interviewed. Of the 15 participant interviewees seven were male and eight were female. A range of age groups were represented. The youngest participant interviewee was 20 years old and the oldest was 73 years old. Eight participant interviewees were aged over 50 years and seven were 50 years old or younger. Five of the participant interviewees had been treated with an allograft transplant and ten had been treated with an autologous

transplant. Eight participant interviewees had been allocated the self managed programme and seven had been allocated the health profession led programme. Of the seven who had been allocated the health profession led programme their attendance at the programme had varied considerably. The least attendance was none and the most was all ten sessions. Three participant interviewees had attended between four and seven sessions and three had attended three or fewer sessions. All patients and every member of staff who was approached with regard to being interviewed, agreed to be interviewed. Five members of staff were interviewed. Of these one was a physiotherapist, two were nurses and two were doctors. The nurses and physiotherapist were directly involved in providing rehabilitation following stem cell transplantation. The two doctors were not directly involved in running the provision of rehabilitation although they were highly experienced in the field of haematology and were very influential in the clinical environment where the trial took place. It was therefore useful to explore their perceptions of the rehabilitation needs of patients recovering after stem cell transplantation and of the programmes on trial in this study.

**Table 5.1: The characteristics of the interviewees**

	<b>HPL</b> (n = 7)	<b>SM</b> (n = 8)	<b>Total</b>
<b>Participant Interviewees (n = 15)</b>			
<b>Gender</b>			
Male	2	5	7
Female	5	3	8
<b>Age</b>			
<=50	3	4	7
>50	4	4	8
<b>Transplant type</b>			
Allograft	3	2	5
Autologous	4	6	10
<b>Attendance at programme</b>			
0-3 sessions	3	n/a	n/a
4-7 sessions	3	n/a	n/a
8-10 sessions	1	n/a	n/a
<b>Staff Interviewees (n = 5)</b>			
<b>Occupation</b>			
Physiotherapist			1
Nurse			2
Doctor			2
<b>Direct involvement in the intervention</b>			
Yes			3
No			2

### **5.3 Participant interviewees' experiences of taking part in a randomised controlled trial**

Participants expressed two key motivations for agreeing to take part in the trial; that their own health might benefit and that future patients might benefit. Participant interviewees expressed that they did not find the trial overly burdensome. Some participants had clearly understood that the trial was randomised and the reasons behind using this approach. Others were less clear in their understanding of the randomisation process. One participant suggested that the investigators must have had some control over the allocation because they lived a long way from the hospital and received the self managed programme. Another suggested that they wished that they had agreed to take part on the condition that they were allocated the home programme. There also appeared to be confusion over

why everyone could not receive the hospital programme, two participants indicated that they believed the study had two arms because limited resources within the NHS meant that not everyone could have the health profession led programme. These comments raise questions about how much participants understood the information that had been given to them in relation to the randomisation process. This is a widely acknowledged problem in randomised trials (Stead et al. 2005). In this study considerable effort was spent on producing understandable patient information leaflets. However, Featherstone and Donovan (1998) suggest that since the provision of clear and accurate patient information alone does not ensure consistent interpretation of difficult concepts such as randomisation, patients may need to discuss the purposes of randomisation in order to understand them fully enough to give truly informed consent (Featherstone and Donovan, 1998). In this study there was a passive approach to such conversations with potential participants. Staff did not actively promote discussion on topics such as randomisation but they were available to answer questions if patients initiated the discussion.

Participant interviewees indicated that completing the questionnaires whilst waiting for clinic appointments was no inconvenience and that on the whole the questionnaires were easy to understand and complete. One person commented that the questionnaires were not sufficiently plain spoken and that they had found it difficult to understand what was meant by the questions. Throughout the trial participants occasionally postponed or refused to complete the shuttle walk test. Sometimes this was due to ill health, sometimes it was perceived by the researcher that the burden of taking the test was too considerable due to the physical effort required. The participant interviewees tended to be enthusiastic about the test because when viewed in retrospect the test provided a very clear measure

of physical improvement. However, patients did report finding the test daunting as is highlighted by the following extract.

P117 (SM) commenting on the SWT

*At first I thought, 'oh my god,' but it proves to you what you can and cannot do. You know what I mean, like that last time when I was running up and down here. But, like I say, it proves to me that I can do these things, you know.*

Most participant interviewees when asked if you could step back in time would you change any of the decisions you made in relation to the trial stated that there was nothing they would change. This indicated that the trial itself had a high level of acceptability with participants and that the burden of participation was not too great.

## **5.4 Participant interviewees' experiences of the health profession led programme**

Since the health profession led programme contained three distinct elements the participant interviewees' comments on the programme are considered in three sections. Firstly, the participants' experiences of the exercise component are discussed. Secondly, their comments on the relaxation element of the programme are considered, and finally, their views and attitudes with regard to the information component are examined.

### **The exercise component of the health profession led programme**

The majority (four out of six) of those interviewed who had taken part in the HPL programme were positive about the exercise component of the

programme. Participants commented that at times taking part had been enjoyable and that whilst the programme had been tough it had been rewarding. Participants stated that the exercises were simple, manageable, and did not require a lot of specialist equipment which made them easily transferable to home. Participants expressed some surprise at the nature of the exercises as illustrated by the following quote.

*P326 (HPL) Well I mean the first week I obviously didn't know what to expect, I knew it was certain exercises, and some of them were so hard, you know I never thought you could actually do something so difficult just by getting up off a chair and lifting a book up and some of them were really hard, so no I didn't really expect, I thought for it to be hard you had to be sort of running or, you know what I mean, it was like something that seemed more physical but actually it was really very hard, but you didn't need a lot of equipment in order to do it, that was what was really amazing for me. So it was sort of things that you can do. I'm always telling my friends you know if you do this or do that, so it's been pretty useful.*

Participant interviewees frequently expressed a dual reaction to having completed the exercises, both exhaustion and satisfaction. Satisfaction was frequently related to a sense of achievement, in particular participants appreciated being able to see an improvement in their performance from week to week.

*P315 (HPL) I was umm, I think the word is delighted, at the way I improved from one to the other. I was amazed how some of the, well I think it was about 10 exercises, erm, how some of them I was able to double week by week which was an amazing step up. Press ups for one,*

*cycling things like that. Some of them just edged up a little bit but I don't think any of them went back at all.*

Participant interviewees also expressed some degree of tiredness or exhaustion after exercising. For most people this was a temporary feeling that was relieved by resting. However this was not a universal experience and two participants found the exercises too exhausting. One participant was particularly concerned about the exercise and suggested that rather than being beneficial for their health, they felt that, it may in fact have been detrimental.

*P123 (HPL) I was a little bit concerned that I personally felt that it had perhaps done me more harm than good. And I perhaps thought it was a bit early because I wasn't coping with it very well. ... I was comfortable with the exercise part of the thing but having done it once I was sort of knackered for 3 days and that feeling never sort of went away, it sort of hung about when I was expecting to feel better.*

Both of the individuals who did not find the programme helpful commented that they believed it had been offered too early in their recovery. This may have been a consequence of the trial protocol which had an entry criterion of six to eight weeks post transplant.

*P114 (HPL) I wish I'd done it a few months later when I was a month or so down the line I was feeling a lot better and had slightly more energy. When I did it I just couldn't handle it. Couldn't cope with it. My muscles were shaking and I just had to sit down. I didn't get a lot out of actually going to the gym, but still built it up slowly doing bits at home.*

One participant could not comment on the exercise programme because they did not attend any of the sessions. When interviewed this participant suggested that a combination of ill health and the thought of having to make another trip to hospital were key factors that affected their decision not to attend the health profession led programme. With specific reference to the exercise component of the programme the individual indicated that the programme was not very appealing and that they were particularly put off because they knew it involved using exercise bikes.

*P317 (HPL) The one other factor, because you mentioned a bicycle, right and because of my last infection which was three big balls between my legs including a cyst that burst open. There's no way I could have done it. I mean its still sore now. ... So there's no way back then I could have even done that, so what was left of the program I don't know. Just to walk round cones.*

Researchers and the clinical team were unaware during the trial that this individual was reluctant to attend the programme because of the exercise bikes. If this had been known it would have been easy to reassure the individual that the bikes were a small element of the programme and that they were under no compulsion to use them. In many circumstances it may be appropriate to find out why someone does not want to attend a programme and if possible to resolve the issue in order to encourage attendance. However, caution is required since there is a fine line between this and nagging or coercing people into attending. Particular caution is required in a trial situation where it is an ethical requirement that individuals are able to withdraw from the trial without giving a reason.

In this study the exercise component of the health profession led programme was acceptable to most patients. This finding is consistent with the available literature on this topic which indicates that exercise is safe for stem cell transplant patients to complete (Dimeo et al., 1997a, Hayes et al., 2003) and that patients find exercise programmes acceptable (Dimeo 2000, Courneya et al., 2000 and Oldervol et al., 2003).

In this study two participants did not find the exercise programme beneficial and both of these suggested that the programme was acceptable but that they attempted to take part in the programme too early in their recovery. The impression of the exercise component that was conveyed to one participant was very off putting and since they did not attend it is not possible to know if the reality of the exercise programme would have been equally unappealing.

### **The relaxation component of the health profession led programme**

The diagnosis and treatment of a life threatening illness combined with spending a prolonged time in hospital, often in isolation, is undoubtedly a distressing experience. It has been argued that bone marrow transplantation is one of the most stressful treatments in modern cancer care (Heinonen et al., 2005). In this study several members of staff commented on the stress associated with stem cell transplantation and suggested that patients lose the ability to relax during treatment. However this assertion was not matched by the experiences described by all participants.

P117 (SM) *I think I am quite a strong willed person anyway so I tend to just take everyday as it comes and just sort of like if it happens it happens,*

*you know what I mean. I've gone past that stage of worrying about things if you know what I mean. I know this is probably through the illness as well but I've just gone past that stage, (name of partner) is the witterer not me.*

P315 (HPL) *I don't have a great problem relaxing. I don't get very tense very often.*

Guided imagery was included in the trial to promote relaxation and target stress. Some participants clearly felt uncomfortable with this guided imagery and one suggested that taking part was like being "subjected to sort of séances". However, a proportion of the participants did report experiencing trouble relaxing. These participants who identified themselves as finding it difficult to relax were also more likely to find the guided imagery a useful exercise and a number of participants requested assistance with repeating the exercises for themselves at home.

An individual's reaction to the relaxation sessions may have been affected by their perceptions of appropriate behaviour for a group environment. One participant who had not found the exercises helpful said "*I think a couple of the grannies were nodding off. I thought for God's sake try and keep awake*" (P123) indicating that to them falling asleep would have been both undesirable and unacceptable. However one of the other participants commented that "*I love doing that kind of thing, I could kind of fall asleep*" (P326) indicating that to them falling asleep was both desirable and acceptable.

Fife et al. (2000) investigated stress during bone marrow transplantation and reported that patients experienced the greatest stress after admission

to hospital prior to their transplant and that least stress was experienced three months and one year after transplantation. This may explain why staff felt stress to be a problem in this patient population whilst many of the participants did not report currently feeling particularly stressed. Furthermore, it suggests that the timing of the relaxation component may not have been optimal. A more appropriate approach may be to provide structured advice to inpatients on relaxation techniques.

At the start of the trial the health profession led programme contained weekly massage as a form of relaxation and informal feedback from participants suggested that this had a high level of popularity. Unfortunately the massage was provided by volunteers and the service was stopped during the early stages of the trial and guided imagery was introduced as a replacement. Whilst massage has been shown to be no more effective than guided imagery using relaxation tapes in helping a sample of patients from general practice to relax (Hanley et al., 2003) the benefits of massage may not be in its efficacy but in its appeal to patients. In the paper by Hanley et al. (2003) the authors comment that whilst massage was no more effective than relaxation tapes it was more popular with participants. Likewise in this trial it was observed that massage did appear to be more popular than guided imagery and functioned as a reward after the physical discomfort of exercising and appeared to provide a motivation for individuals to attend the programme.

### **The information component of the health profession led programme**

Participants were given the opportunity to comment on each of the information sessions provided as part of the HPL programme. It was clear in the interviews that participants tended to only have vague recollections

of the different sessions. This is not surprising given the time that had elapsed since the sessions and the volume of information presented to patients throughout the transplant and recovery process. It was clear that unless something had really stood out about a session participants did not have any comments to make. Many participants were not able to identify if they had been present at any given session.

Participants' reflections on the sessions were generally positive but did not convey the same level of enthusiasm that was displayed when talking about some other aspects of the programme. The criticisms most frequently given were that the information was either repetitive, common sense or given too late in the transplant process.

P315 (HPL) *But a lot of it was repetition and there was a bit of déjà vu. I'd heard and seen a lot of it before.*

A further problem identified was that some of the information presented was only relevant to those who had undergone allograft transplants. This problem seemed to have been particularly, but not exclusively, associated with the medications session. Whilst all participants had undergone stem cell transplants there are significant differences between the transplantation of donated stem cells and an individual's own cells. Consequently, the information needed by patients particularly on topics such as medications varies considerably for the two groups. Therefore it may not be appropriate to attempt to meet the detailed informational needs of all patients in the one programme. Since it is not feasible to run two separate programmes it may be appropriate to remove the elements that have information relevant to only some patients. However, it is likely to be necessary to find an alternative way of providing this information in a

more targeted manner. Unfortunately, this has cost implications since it is generally cheaper to provide something general than to target individual needs.

The argument for not including information on topics such as medications in the rehabilitation programme is supported by the fact that many participants reported that the information given in the programme was a repetition of information that they had already received. This repetition of information is predictable given the nature of the programme. A participant may not attend the medications session for up to ten weeks after being discharged from hospital. It is not satisfactory for them to have been self medicating at home for ten weeks if they require further information about the medications they are receiving. Therefore it is highly likely and desirable that patients receive this information in preparation for discharge from in-patient care. Repeating the information as part of the programme appears to have been unnecessary and unwanted by participants.

The session facilitated by a vicar appeared to have stood out particularly strongly in a number of participants memories. Participants' feelings about the session varied considerably. Some were very enthusiastic about the session and some were not so enthusiastic, suggesting that they found it either boring or even intrusive.

*P326 (HPL) The guy who came from the church he was quite interesting, talking about death and how people feel about dying and how you know, just how people think, yeh that was interesting and just, I can remember others but I think he was the most interesting one to be honest.*

P320 (HPL) *We had the vicar and, and I felt he was a bit, he was very nice, erm but for me he was a bit intrusive and that was no fault of his that was just you know the way that I felt about it, erm.*

P114 (HPL) *I found the vicar quite boring... I'm not, not religious but I found it, talking about death and things like that [a bit depressing] ... The others, the older ones seemed to enjoy it but I really did struggle to stay awake on that one.*

The varied reactions to this session emphasise the difficulties that are inherent in trying to provide an intervention of this sort to a mixed group of people. Not only is each person different but their reaction to having had a life threatening illness will be different. It is unrealistic to expect all stem cell transplant patients to want to discuss the impact of their transplant with a vicar, who they are unlikely to have met before, and a group of fellow patients. However, the acknowledgement that having a life threatening illness does have an impact on your life and the opportunity to discuss this in a safe environment was clearly appreciated by a number of participants. An appropriate solution to this problem may be to remove the expectation that everyone will stay on for the information session that follows after the exercise component of the programme. If patients are given information about what the information session is going to be about each week they can make an informed decision about whether they want to attend or not.

## **5.5 Participant interviewees' experiences of the self managed programme**

During the interviews participants from the self managed programme were given the opportunity to reflect on each leaflet provided in the information pack. As with the health profession led programme participant interviewees often had only vague recollections of the content of the programme. The strongest opinions and recollections related to the exercise component of the programme. Adjectives used about the exercises included, "good", "enjoyable", "too basic", "monotonous", "unappealing", "boring", "difficult", and "common sense".

Several participants suggested that they never completed the exercises and others indicated that they gave the exercises a go but quickly lost interest. Reasons for this included that they lacked motivation to complete the exercises and that they found other activities more appealing, such as gardening or walking the dog. One person suggested that the exercises were too difficult for them to complete. Every participant who identified themselves as not having completed the exercise programme stated that they believed that their motivation would have been higher and their participation greater if they had been allocated to the health profession led programme. Participants attributed this to two factors: the support provided by a group environment and a feeling of greater confidence exercising where there were professionals available to ensure you did not injure yourself.

In contrast to this three participants suggested that they found the programme appropriate and helpful and that they had consistently completed the programme several times a week for a period of many

weeks. Two of these individuals had been very physically active before being ill and were highly motivated to regain their fitness and were also used to exercising alone.

*P311 (SM) I found them very good. At first, well I've come from a background where I've been very physical all my life and I've done a lot of exercise regimes through the time. I first looked at them and thought this looks too easy, but, the situation I was in at the time when I came out of hospital, nothing was easy so they erm, they were very good overall. The balance was excellent I think.*

One further person also reported consistently completing the exercises. In contrast, this person was older and had not been very physically active before being ill. However, she also reported being highly motivated to regain pre-transplant health. Interestingly, this person reported that her son had helped her to understand the exercises and had checked she was completing them correctly.

*P324 (SM) Initially my son when he used to come and see me he used to get me on there you know, 'You do some, you're not doing that right mum do it properly'. So erm, once I got in to the swing I didn't have to refer to the paper because I knew what was coming after. ... I did them for months and months and I still do them now, not all the time but I walk a lot so that's my exercise.*

With regard to the rest of the leaflets given in the information pack participants were generally positive but not overly enthusiastic. Every participant indicated that they had read the leaflets but most felt that they could no longer remember any details about them.

P324 (SM) *Well I read through them all but then I didn't refer to them after that. I only kept the exercise one.*

P318 (SM) *I read um, but to be honest with you you know I can't remember anything about um, you know.*

Participants that could remember individual leaflets tended to comment enthusiastically on the nutrition leaflet and on the leaflet about relationships. Two participants particularly remembered and commented on the leaflet written by a previous patient. One commented that

P324 (SM) *I found that quite informing really, he was quite young, half my age, poor man. And I thought gosh shall I contact him and I never got round to it.*

The reaction of the other was less enthusiastic highlighting once again that this patient group contains a wide range of individuals and that meeting everyone's needs with one intervention is not always possible.

P124 (SM) *that bloke who wrote a bit, erm, he were crap because its not from my perspective, you know what I mean, its not, it's aimed, I find it more aimed at erm, like 40 plus. It's not from like a young person's perspective, its erm, more aimed at 40 plus you know what I mean.*

## **5.6 Conclusions from the participants' experiences of the health profession led and self managed rehabilitation programmes.**

The participant interviews provide invaluable information on patients' experiences of undertaking both the health profession led and self managed rehabilitation programmes. From these interviews it is possible to draw a number of conclusions and to make suggestions for improvements to the delivery of rehabilitation services for patients who have received stem cell transplants.

### **Factors that facilitate or impede exercise**

Exercise was a key component of both rehabilitation programmes. Unlike in cardiac rehabilitation where the benefits of exercise are well documented (Williams et al., 2006) the benefits of exercise for this patient population are less well established. The current evidence supports the hypothesis that exercise can be of physical and psychosocial benefit for survivors of cancer, however, a number of questions remain. In particular, the optimal exercise programme remains unclear (Silver, 2007).

This study has identified a number of factors that either facilitate or impede stem cell transplant patients from exercising. These factors highlight some of the issues that require consideration when planning interventions for this patient population. They are summarised in table 5.2.

Motivation is clearly important in either facilitating or impeding exercise. Those individuals that were highly motivated exercised regardless of which programme they were allocated and likewise there were individuals in both programmes who were not motivated to exercise and who therefore did not

exercise. Several participants who were allocated the self managed programme indicated that they believed their motivation to exercise would have been increased by attending the health profession led programme. It was not within the scope of this study to ascertain whether this assertion would in fact have been born out in reality.

In this study there was some evidence to suggest that individuals who had been very active prior to being ill were more motivated to exercise after completing treatment. However, one individual who had been very physically active prior to treatment found the deterioration in their physical abilities depressing which acted as a deterrent to exercising. Courneya et al. (1999) investigated motivation to exercise in a sample of colorectal cancer patients. The study identified that individuals with greater intention to exercise and with higher levels of pre-diagnosis exercise were more likely to engage in post-diagnosis exercise (Courneya et al., 1999).

A number of individuals from the self managed programme indicated that lack of confidence in how to complete the exercises was a factor that hindered their participation in exercise. Linked to this was a concern that if they did not complete the exercises correctly then they could have a detrimental rather than beneficial effect on their health. One participant from the health profession led programme also expressed concern that the exercises had not been beneficial to their health and that they had therefore stopped attending the programme. Similarly, experiencing or the fear of experiencing pain or discomfort when exercising was a factor that emerged from the interviews with a number of participants. These findings are supported by the work of Emslie et al. (2007). Their evaluation of an exercise programme for breast cancer patients identified that after diagnosis and treatment women in their study felt vulnerable and were

wary of injuring themselves whilst exercising. The women reported that they felt safe and secure in an exercise class and that they valued expert instruction and support (Emslie et al., 2007).

Being able to see an improvement in performance over time was a factor that individuals from both arms of the study cited as a helpful encouragement to continue exercising. However, fatigue was mentioned by a number of participant interviewees as a factor that limited their ability to exercise. Feeling exhausted after exercising was common, however, the length of time that the feeling lasted varied and was a factor that affected participants' willingness to exert themselves.

Finding exercise boring or uninteresting were cited as reasons why people stopped exercising and finding the exercises interesting and enjoyable was a factor that individuals in the health profession led programme particularly identified as helping them to exercise. A sense of sportsmanship and competition was a factor that one member of staff identified as helping some individuals to exercise. However, one participant commented on what a disincentive to exercise it was to feel that one was the least physically able in the group.

**Table 5.2: Factors identified that facilitate or impede exercise**

<b>Factors that facilitate exercise</b>	<b>Factors that impede exercise</b>
Good personal motivation	Poor personal motivation
Confidence in how the exercises should be completed	Lack of confidence in how the exercises should be completed
Visible improvement over time	No visible improvement over time
Confidence that exercise beneficial to health	Concern that exercise detrimental to health
Improving energy levels	Fatigue
Comfortable and confident in own bodies reaction to exercise	Physical discomfort during or after exercising
Interest	Boredom
Enjoyment	Lack of enjoyment
Sportsmanship / competition	Feeling inferior to others
Adequate time set aside for exercise	Lack of time

It was identified that it is not always easy to predict the factors that affect any one individual's desire and ability to exercise. Furthermore, several factors that facilitate exercise appeared to need to be present to be effective in prompting an individual to exercise, whereas one factor that impedes exercise appeared to be enough to stop an individual exercising. Investigating the factors that promote or impede exercise was not the primary aim of this study, however, analysis of the interviewees' comments on exercise has provided a helpful insight into this topic. More detailed research specifically investigating this issue is required.

### **Appropriate provision of relaxation techniques**

The relaxation component was the most contentious aspect of the health profession led programme. Whilst some people reported finding the techniques helpful, others reported disliking them. For at least one person this reaction appeared to be sufficiently strong as to contribute to their decision to stop attending the programme. Research has indicated that the stress experienced by patients undergoing a stem cell transplant peaks prior to the transplant and is least after discharge from in-patient care (Fife et al., 2000). Therefore assistance with relaxation techniques may be more

appropriate during hospitalisation. If alternative sources of evidence support the need for assistance post discharge an alternative approach to delivering this aspect of the programme might be appropriate. Since there is evidence to suggest that using a tape to complete guided imagery at home is as effective as using guided imagery in a formal setting (Hanley et al., 2003), the appropriate solution may be to provide an introduction to relaxation techniques and to provide the encouragement and resources for those who desire it to continue using the relaxation techniques at home.

### **Apposite information required**

During the interviews participants confirmed that apposite information was a desirable component of a rehabilitation programme. However their evaluations of the programmes suggest that there were a number of problems in the delivery of information:

- Too much information was given to participants, for example on issues that were not relevant to them due to the nature of the transplant that they had received.
- Information was not always provided at the time that it was required. In particular, participants commented that information was received after it would have been most useful.
- Information was repetitive.
- Information was common sense.

Topics that participants had found helpful included nutrition, life after transplant, relationships and facing a life threatening illness. Topics that participants did not appear to have found helpful included medications and financial support.

## **Group dynamics**

One of the key aspects of this study was to investigate the impact of being in a group programme. Participant interviewees who had been allocated to the health profession led programme were mostly (4 out of 7) enthusiastic about having been allocated the group programme. Specifically, interviewees frequently expressed finding that other people where experiencing the same things as them very helpful.

*P315 (HPL) It was also useful to have people, other patients, who were recovering from various things like bone marrow transplants and such to hear their problems and also to think that the problems I had everybody else had as well. You know shortness of breath, and the short stamina and so on. ... As I said before the sharing experiences and things with the people who are there. I thought I was the only one who felt tired and breathless and so on but of course they all do. And they ache and the rest of it. So yes it's nice to share it.*

One participant who had expressed this idea also suggested that the fact that he felt himself to be less ill than some of the other participants gave him a positive feeling. As illustrated by the following quote.

*P315 (HPL) In fact because they seemed to be a little more poorly than me it made me feel a little bit better which is an awful thing to say but its true.*

This was not a concept that other participants also expressed but this may be because as the participant indicates the idea of being cheered by another's misfortune is not particularly socially acceptable. The logical

extension of this view i.e. how terrible it feels to be the least well in the group was discussed by one participant.

The three participant interviewees who were less enthusiastic about being part of a group expressed a variety of reasons for not enjoying being part of the group. Participant 123, highlighted a gender difference that had occurred when he had been part of the group, referring to the group as a "sewing circle" and commenting that the "grannies were busy talking about children and things". Participant 114 commented that she had found the group intimidating since the other participants had been much older and were recovering faster than her having been treated with a different type of transplant. One participant who was allocated the health profession led programme but who never attended stated that

*P317 (HPL) They [would] probably [have] thought I was an absolute nutcase if I had gone along and told them, what I've told you so far, plus a lot of other stuff.*

Participant 317's belief that people would think she was a 'nutcase' suggests that she did not believe that her own reaction to treatment was similar to other peoples. Similarly, participant 317 and 114 did not find it easy to gain support from the group since they perceived themselves to be very different to the rest of the group. These experiences highlight the importance of people feeling a connection with the other people they are in a group with. It is easy to assume that since the individuals in the group had all been treated for a haematological malignancy with a bone marrow or stem cell transplant that they would feel some degree of shared experience. The reactions of these individuals highlight that in order to feel

part of a group, individuals themselves must believe that they have something in common with the other members of that group.

These findings are consistent with social comparison theory, first developed by Festinger (1954) which suggests that individuals can benefit from drawing social comparisons with others who are similar to themselves. Individuals may also draw upwards comparisons with those perceived to be in some way better off and downwards comparisons with those perceived to be in some way worse off (Festinger, 1954).

The self managed programme did not involve meeting with other participants and therefore for opportunities to gain support from others were more limited. Despite this two participants allocated to the self managed programme suggested that they had benefited from being able to compare their experience with other people through the information provided in the booklets.

*P324 (SM) It was because I knew that I wasn't the only one I thought I was imagining it but I thought I can't, nobody can feel so fatigued, especially when I was, all my life I've been up and going a very active person and I just thought it must be normal because reading those books I'm not the only person that's experiencing such horrible feelings, yes.*

One participant in particular commented that this was very helpful with regard to the information on relationships, commenting that;

*P311 (SM) I found, especially the ones about how you're feeling emotionally were, both me and my wife found the information quite useful. Because were not ones to go hunting for information over, of that*

*particular subject anyway on the net and things like that. So that information was great to us because we'd not received anything else on them, on the information, so it was good really.*

Whilst for two people the information in the leaflets provided some sense of shared experience the majority of participants (n=6), including the two people who had commented positively on the leaflets expressed that being able to share experiences directly with others was something they really felt was missing from the self managed programme.

*P324 (SM) I felt I'd missed out a wee bit, I would have loved to have spoken to other people that had been through the same as me and find out how they were getting on. That bit I missed and would have loved to have been. As I say just curiosity I suppose. Be able to chat to somebody and see how they're feeling. I felt a little bit alone.*

However, this was not a universal feeling and two participants commented specifically that they did not desire or need the support of others who had also had a bone marrow or stem cell transplant.

*P310 (SM) I haven't had any inclination to do is to join any groups or anything. You know to share your experiences.*

One participant interviewee, who was generally positive about wanting to share experiences, did raise an important consideration. They commented specifically with regard to the written leaflets that

*P323 (SM) I think its nice to read other people's experiences but I think they could be quite frightening because you know, whilst I was in hospital*

*you know they kept saying it will kick in next week, and you know it never did, I mean I was not sick even and it was all sort of tomorrow and you think oh, and then it never actually happened. So I think sometimes it can be a bit frightening because you think that's the norm and perhaps I was the exception to the rule I don't know.*

## **5.7 Summary**

The exercise component of the health profession led programme was generally well received. The evaluation of the self managed exercise programme was less positive and the programme appears to have only assisted those who were already highly motivated to exercise. A home exercise programme may be more appropriate as an add-on to the health profession led programme, encouraging participants to exercise between sessions, or as an alternative for those who cannot attend a hospital based programme.

When considering participants' reactions to the relaxation and information elements of the programmes it is clear that reactions were mixed. What one person liked another disliked. This was most clearly demonstrated with regard to the information session led by a hospital chaplain. Reactions to the session varied considerably with one individual suggesting that it had been the best of the ten sessions whilst others indicated that they had not found the session helpful. Patients are individuals and therefore they have individual desires, needs and expectations.

The conclusions drawn from the experiences of participants suggest that from the patient's perspective the ideal programme would provide an exercise component which was led by experienced health professionals. In addition to this there would be an additional home element for between

sessions and for those who do not wish to or cannot attend the hospital sessions. Relaxation techniques are not a crucial component of such a programme and should therefore be optional. Potentially, the programme could contain one session where relaxation techniques are explained and the necessary advice and/or equipment is provided in order to enable individuals to continue at home if desired. An information element is appropriate since some patients do desire the opportunity to gain further information and support. However, detailed and accurate information as to the session content should be available prior to the session enabling patients to make an informed decision about whether to attend or not.

## **5.8 Staff interviewees' experiences of being involved in a randomised controlled trial**

### **Perceived value of the intervention**

The ethos of the large and busy haematology unit where this research took place is very technical with an understandable focus on curing people from a variety of very aggressive cancers. Research has highlighted that alongside the physical issues there are many psychosocial issues associated with haematological cancers and their treatment. The unit's focus on physical health may in part be due to the fact that the illnesses and treatments seen on the unit lend themselves to hard measures of health and illness. For example, it is common for the first indication of a person's haematological malignancy to come not from symptoms experienced by the patient but from a blood test indicating unusual cell counts. Similarly, after a transplant great attention is given to the recovery of a patient's blood cell counts.

*S2 I think that we are a technical team, so we focus very much on what their blood count is, and when they come to clinic... what's your blood count, have you got, and it's all physical symptoms.*

Some staff interviewees expressed concern that this focus on the physical may be at the expense of considering the entire individual. This in turn may result in individuals being cured of their haematological cancer but experiencing considerable on-going psychosocial side-effects. Interestingly, when one senior member of the team was asked during an interview about the rehabilitation needs of this patient group, they mentioned only physical aspects of recovery in their reply.

It was within this environment that the health profession led programme was devised and trialled. It is therefore unsurprising that reactions to the programme were varied. No individuals were hostile to the concept of rehabilitation but other reactions ranged from great enthusiasm through to ambivalence and disinterest. Similarly, there was a lack of consensus about which patients were likely to benefit from rehabilitation. Some individuals, those who were very enthusiastic about the health profession led programme, believed that attending a rehabilitation programme should be a routine part of care after transplantation since all patients would potentially benefit from this type of intervention.

*S3 I wanted it to be part now of the service that, you know, for the next ten years anybody walking through the doors with a diagnosis of leukaemia or myeloma or lymphoma, after transplant, after treatment they all have a rehab programme.*

Other members of staff suggested that not all patients needed or were likely to benefit from a rehabilitation programme. One individual suggested that transplant type was likely to be a strong indicator of whether or not rehabilitation was likely to be of benefit to an individual.

*S4 My own view was that it [the health profession led programme] probably wasn't going to have a great deal of value for the autografts. It may have a lot more value for the allografts.*

Another member of staff rejected the idea that transplant type was a key factor in an individual's needs for rehabilitation, suggesting instead that it is possible to identify those individuals from a range of treatment and disease types who would benefit from such an intervention. Interestingly, this staff interviewee also suggested that a rehabilitation programme need not be confined to individuals that have had a bone marrow or stem cell transplant, but the scope of the intervention could be broadened to include other haematological malignancy patients treated with chemotherapy without a transplant. In contrast to some members of staff this individual was not advocating a routine attendance at the programme but a targeted, needs based approach.

Since there were a range of opinions over the probable value of a biopsychosocial intervention it is unsurprising that individuals also held strong and varied opinions on evaluating the intervention with a randomised controlled trial. Those individuals that did not place a high value on psychosocial care were slightly ambivalent about the rehabilitation needs of patients and therefore they were not particularly enthusiastic about the trial. One staff interviewee summarised the argument for needing a trial by stating;

*S4 It [the trial] was the right thing to try to do, yes, I think that's right because clearly it [the health profession led programme] involves expense, and the question is how much value it had.*

In this individual's opinion it was clear that the health profession led programme required testing to see if it had any or sufficient benefit to patients to justify the expense of running it. In contrast to this it was apparent that some staff members had already formed an opinion about the efficacy of the health profession led programme. These individuals were involved in the trial not because they wanted to find out if the programme worked but because they wanted to prove that it worked.

*S3 What I signed up to this trial to do was to get it [the health profession led programme] part of the service.*

One member of staff acknowledged that they felt resentful that the health profession led programme required testing and that they would rather it was simply implemented as usual care. Staff members that were particularly committed to the programme also reported finding it very difficult when participants that they perceived would particularly benefit from the health profession led programme were allocated to the self managed programme.

*S1 There were certain patients that we saw that, you know, you were desperate for them to get the hospital led programme, and, you know, quite often they didn't get the one that they wanted.*

These occasions when individuals who really wanted the health profession led programme or those that staff perceived to really need the health profession led programme were allocated the self managed programme resulted in staff members feeling further disillusioned with the trial.

### **Staff interviewees' experiences of recruiting patients to the trial**

Recruitment to the trial was problematic and this was one of the key frustrations that staff reported in the qualitative interviews. A minor annoyance was the difficulty that was encountered in seeing patients to discuss recruitment to the trial at the appropriate point in their transplant process. This was highlighted to be a particular problem when recruiting the autologous transplant patients who had a shorter stay in hospital and less frequent visits to clinic resulting in a shorter window of opportunity to approach these individuals.

The poor rate of recruitment was a considerable cause of frustration for staff. During the interviews staff expressed this frustration towards patients, fellow professionals and towards the trial itself. Staff were discouraged by the fact that not as many patients as expected agreed to take part in the trial. Whilst staff were aware of the reasons why patients might not want to take part they found it very frustrating when individuals declined to take part.

*S2 Frustrating because they had no insight into how they were, or how they might be, and how they might benefit. And you could try and tell them, but actually to them it was all a bit, oh well it's another trip to*

*hospital and this, that and the other, when actually all they're going to do is sit in their chair at home anyway, you know.*

Staff interviewees also expressed disappointment that the wider clinic environment was not more supportive of the trial. Several staff interviewees commented that patients were not being encouraged to take part by the entire clinical team. This frustration was intensified by the perception that potential participants responded differently according to who spoke to them about the trial.

*S1 I know one registrar spoke to a patient last week ... and the following week, the patient, you know, had turned up, whereas ... nurses had been trying to get them to go for about three weeks, this registrar had said it, and he was there the next week (Speaking about a patient attending the rehabilitation programme that has been implemented now that the trial has finished).*

It was suggested in the staff interviews that recruitment would have been easier if doctors had been more willing to suggest taking part in the trial to potential participants. The two doctors who were interviewed were both asked if they had discussed the trial with potential participants. One doctor indicated that they had never discussed the trial with a patient. Conversely, another reported a number of conversations about the trial with patients. Interestingly, this doctor stated that they discouraged some potential participants from taking part because the doctor perceived that the patients were too well and would not benefit from a rehabilitation intervention.

Staff interviewees also attributed some of the poor rates of recruitment to the trial itself. It was felt that the inclusion criteria were too strict and that sometimes people who wanted to take part were denied the opportunity. The majority of the inclusion criteria were included to ensure the safety of participants, however one criterion was that participants should be between six and eight weeks post transplant. This criterion was included as a means of ensuring a degree of standardisation in the participants at the start of the trial since it was perceived that the response to the programmes of those who were recently post transplant would be very different to those who were months or even years post transplant. However, in the course of the trial it became apparent that this criterion of six to eight weeks was unhelpful and that it was a factor in limiting the number of people who agreed to take part.

At the start of the trial individuals whose inpatient phase of care had lasted more than eight weeks were automatically excluded. However, it was perceived that these individuals may be the ones who most needed rehabilitation and therefore the criterion were altered to allow individuals whose inpatient care had prevented them being recruited on time to take part in the trial. A further proportion of individuals were also restricted from taking part in the trial by the six to eight week criterion. These were people who initially recovered well from their transplants and who turned down the trial when offered it but that later developed complications that made them feel more inclined to take part. However by that point they had passed the six to eight week window and were ineligible for the trial.

This issue was explored in the staff interviews. There was a consensus that any reference to time post transplant was unhelpful. It was the opinion of a number of members of staff that individuals may benefit from this type of

intervention even years after their transplant. One suggestion was that a needs based criterion may have been more appropriate. Alternatively, some staff wanted the programme to be available to everyone without any particular entry criterion. It should be noted that if the intervention was redesigned in either of these ways it would remain highly likely that individuals are likely to respond differently to the intervention according to how long after their transplant they participate. This would be a potential problem in any quantitative evaluation of the programme however a more appropriate solution to this problem may be to adjust for time from transplant in the analysis of the data.

### **Staff interviewees' experiences of providing the health profession led rehabilitation programme**

It was clear from the interviews that keeping the health profession led programme running was hard work, more so than staff expected. Some of the difficulties lay in providing a consistent service. It was necessary to liaise with a considerable number of different health professionals in order to provide the information component of the health profession led programme and this was time consuming. There were difficulties with working with the volunteer service. This was a particular problem when massage was still a component of the health profession led programme. Even after the massage component was removed the relaxation element was still identified as difficult to deliver and one staff member in particular commented that they felt self conscious leading the relaxation exercises. The issue of the repetitive nature of the programme which was highlighted in the participant interviews was also raised in the staff interviews.

*S2 It seems quite repetitive sometimes when we're doing it, mind, and with the ten sessions, that's one of the things I would say, well it did seem quite repetitive at times, but sometimes people needed to hear information more than once. And whilst, it was repetitive to me, but then I was doing a day every week, so for them it was a new session.*

### **'The trial killed the intervention'**

The small numbers of participants attending the programme at any one time was a particular problem identified by the staff. The numbers attending the programme were low for two reasons: firstly, the trial failed to recruit participants at the rate that had been anticipated, and secondly, the attendance rates at the programme were considerably lower than expected. Staff highlighted that the effect of a small group size were twofold. Staff found the small group size demoralising. It was clearly important to ensure that sufficient staff were present should all participants turn up but frequently staff were taken away from other activities unnecessarily because only a few or even no participants arrived. Not only did the small group size have a demoralising impact on the staff but it appeared to affect the very nature of the health profession led programme. It was felt that there was a critical size at which the group started to function well and when fewer participants were present the group was laboured and dysfunctional. In conversation one member of staff told me that they felt "the trial had killed the intervention" suggesting that the conditions required for a randomised controlled trial had fundamentally changed the atmosphere and potentially the efficacy of the rehabilitation programme.

*S2 I thought that the trial struggled, and I think the outcomes may be effected, because from the discussions that we had, in terms of the number of people, if there were only two or three people there, then the discussion groups are altered, you know, the, the, um, interactions, you know. So, as a result, I don't think they get the best benefit. If there's a bigger group, then you, certainly with the pilot group, we had, there was eight or ten people there, so you got some camaraderie, you got some, you know, and actually those people still see each other in clinic now, and still link up and ask how each other are and sit together and, you know, so. Whereas, I think with the trial, we didn't get that because there weren't the numbers.*

This staff interviewee referred to the differences between the health profession led programme during the pilot study and the full trial. Since poor attendance rates were not an issue during the pilot study it is necessary to consider if the poor attendance rates that occurred during the trial were, as suggested by this member of staff, a result of the trial itself and the impact that it had on the intervention. Potentially, the trial had an impact on the numbers attending in a variety of ways. The fact that the programme was part of an experiment and involved randomisation may have made some potential participants reluctant to take part reducing the number of available participants. The tight entry criteria chosen for the trial may further have restricted the pool of available participants. Furthermore, by design 50% of those who had agreed to take part were allocated to the self managed programme.

## **Summary**

The experience of being a member of staff involved in the rehabilitation after stem cell transplantation trial can probably best be summarised by the word frustrating. The research did not have the active support of the wider clinical team. Recruitment was slow and difficult and 50% of those recruited were allocated the control element of the trial. Even within those allocated to the health profession led programme attendance at the programme was poor. Running the health profession led programme was hard work and required preparation and commitment. Many members of staff became involved in the trial because they believed in the health profession led programme. The trial did not provide the evidence they desired to justify the long-term implementation of the programme. To their credit staff remain committed to the concept of rehabilitation for patients recovering after stem cell transplantation, despite these problems.

## **Chapter 6 - Discussion**

This chapter presents a discussion on the findings of the stem cell transplant trial and the associated qualitative investigation. This is followed by an examination of the methodology employed in this study. The rationale for using a randomised controlled trial is reconsidered and the potential merits and limitations of alternative designs that could have been employed are debated. Finally, consideration is given to the implications of this research for practice.

### **6.1 Discussion of the findings**

#### **The trial outcomes**

The aim of this study was to assess the efficacy of a rehabilitation programme for patients who have had a stem cell transplant, using a randomised controlled trial. The primary outcome measure was change in the physical functioning dimension of the SF-36 scale at six months post transplant. The mean change in physical functioning from baseline to six months was similar in both arms of the trial (21.9 for the health profession led programme and 21.4 for the self managed programme). The mean difference calculated from the linear regression model was 0.193 and the confidence interval included zero. Therefore it is possible to conclude that no evidence of a difference in the physical functioning of participants as measured by the SF-36 scale was observed between the two modes of rehabilitation.

The secondary outcome measures in this trial included a range of biopsychosocial outcomes measured at both three and six months after randomisation. There was no evidence of a difference in any aspect of

recovery between the health profession led and self managed rehabilitation groups.

The sample size achieved was 58 participants, only 44% of that calculated to be required for an adequately powered study. Whilst no differences between the health profession led and the self managed programmes were apparent in the findings, it is possible that clinically significant differences between the programmes were missed by a study of this size. The confidence interval around the estimated difference in the primary outcome measure of physical functioning could not exclude differences of up to 10 points in either direction.

The SF-36 data gathered at six months post transplant was compared to UK population norms. In all dimensions of the SF-36 scale the patients from this trial had poorer mean scores than found in the general population. This supports previous research indicating that recovery after transplantation can be protracted and endorses the concept of rehabilitation for this patient group.

### **The qualitative findings**

The study contained a qualitative component that provided valuable insights into the perspectives of participants and staff on rehabilitation after stem cell transplantation. The interview data highlighted that the health profession led rehabilitation programme had only a moderate level of acceptability and that there were various ways in which patients and staff believed it could have been improved. Furthermore, the interview data indicated that the self managed programme had a poor level of acceptability with the majority of patients who were allocated to it. To

better understand the qualitative findings from this study it is important to consider them within the framework of existing research. Therefore the main themes from the qualitative findings are considered below within the context of the relevant academic literature in relation to exercise, relaxation, information and social support.

#### Findings related to exercise

In relation to the exercise component of the programme it was found that amongst the participants allocated to the health profession led programme the majority of people found exercising in a group environment helpful. This is consistent with previous research and a number of other studies have shown that exercise programmes are acceptable to patients who have been treated with a stem cell transplant (Oldervoll et al., 2003, Courneya et al., 2000, Dimeo, 2000).

Individuals with a strong preference for the self managed programme, but who were allocated the health profession led programme, found exercising in a group environment unhelpful. Those participants allocated to the self managed programme, who did not desire to attend the health profession led programme, found exercising at home acceptable. In contrast individuals that expressed a preference for the health profession led programme did not find exercising alone an acceptable alternative. These findings suggest that if patients do not engage with the format in which the exercise is being provided they are less likely to complete the exercise programme.

A study by Segal et al. (2001) compared three exercise programmes - a home based walking programme, a hospital and home based programme,

and usual care amongst women treated for breast cancer. Interestingly, participants allocated to the solely home based programme in Segal's (2001) study showed a significant improvement in physical functioning compared to the usual care group, whilst the participants allocated to the hospital and home based programme showed only a borderline significant improvement in physical functioning compared to the usual care group (Segal et al., 2001). The authors were surprised by this finding and were unable to adequately account for it since there were no differences in reported adherence to exercise prescription between the two treatment groups. However, they do note that self-directed exercise is more convenient for participants and that the research population demonstrated a high level of motivation to engage in structured exercise (Segal, Evans et al. 2001).

The questions raised by both the Segal et al. (2001) study and by the qualitative findings in this study suggest that further research into the mode of delivery for exercise interventions is warranted. Whilst a consistent picture is beginning to emerge from the literature as to the benefits of exercise for cancer patients there is no such clarity in the evidence as to the best format for such exercise.

#### Findings related to stress and relaxation

It has been reported that a minority of patients suffer with clinical levels of anxiety and depression following stem cell transplantation (Molassiotis and Morris, 1999a). Other authors suggests that persistent and life affecting but sub-clinical levels of psychological distress are more common in patients who have been treated with stem cell transplantation (Lesko et al., 1992). In the present study the mean general health questionnaire

(Goldberg, 1978) scores collected throughout the study were not indicative of high levels of psychiatric distress (see chapter four section four for the GHQ scores at baseline). Furthermore, the qualitative data supports this finding with a number of participants reporting that they were not currently experiencing high levels of stress or anxiety. If patients are not experiencing levels of stress, anxiety or depression post discharge that are affecting their ability to relax it raises questions as to the necessity of providing a relaxation component as part of a rehabilitation programme following stem cell transplantation.

Exploring patients' experiences of stress across different stages of the transplant process was not within the scope of the present study. However, several participants made reference in the qualitative interviews to diagnosis and active treatment being more stressful times than the period after their discharge from in-patient care. This is supported by other research which indicates that patients' stress levels are highest whilst they are in hospital (Fife et al., 2000) and therefore it may be more appropriate to target relaxation techniques for this period of a patient's treatment. Furthermore, a study by Kim and Kim (2005) found that completing relaxation techniques whilst hospitalised for stem cell transplantation was associated with a greater reduction in fatigue than usual care. This provides further evidence that teaching relaxation techniques during acute treatment rather than post discharge may be appropriate.

#### Findings related to information

The provision of appropriate information has been shown to increase patients' control and involvement in their care, to reduce psychological distress, to increase adherence to treatment regimes and to encourage

realistic expectations in studies conducted with patients who are being treated for cancer (Mills and Sullivan, 1999). The provision of information was therefore a logical and appropriate component of the rehabilitation programmes in the present study. However, the qualitative findings of the present study indicate that the provision of information was not as well received by patients as might have been expected.

Patients found it frustrating when information was repetitive or common sense. A further problem was that since the same information was given to patients regardless of their transplant type all of the information was not relevant to all of the people who received it. It was also noted that different patients expressed different thoughts as to the quantity and depth of information required. This finding is consistent with the findings of a study conducted by Tarzian et al. (1999) which specifically investigated the information requirements of stem cell transplant patients. The study highlighted that providing appropriate information is difficult because different patients desire different amounts of information. Flexibility in the provision of information may assist patients to receive the information that they need and want (Tarzian et al., 1999).

#### Findings related to social support

Previous research has reported the potential psychosocial benefits to cancer patients of attending a support group (Feigin, Greenberg et al., 2000). The present study identified that the relationships developed with fellow patients and staff through a group programme were perceived by some patients to provide beneficial additional support. Helgeson, Cohen et al. (2000) investigated which patients are likely to benefit from social

support interventions and concluded that additional support was only likely to benefit those individuals who lack other sources of social support.

In the present study social support was provided through attendance at a group programme that included an exercise component. The provision of support through a group exercise programme was been found to appeal to people who would not consider attending a conventional support group (Adamsen et al., 2001, Emslie et al., 2007). However, in contrast to this there was some evidence in the present study that patients who were uncomfortable with the group element of the programme discontinued attending, thereby receiving neither the exercise nor the support elements of the programme.

### **Discussion of the findings in relation to the biopsychosocial framework**

This research was situated within a biopsychosocial framework emphasising that psychological and social, as well as biomedical, factors have an impact on health. Previous research has established that the effects of haematological malignancy and its treatment with a stem cell transplant are complex and affect not only the physical but also the psychological and social functioning of individuals. The development of the health profession led programme that was trialled in this study was influenced by the commitment of the health professionals involved to the provision of care that focused on the psychological and social, as well as the biological deficits caused by haematological disease and its treatment. Therefore the health profession led programme was made up of a number of component parts in an attempt to address more than the physical needs of patients.

Due to the nature of randomised controlled trials it was not possible to unravel these components and to establish if any of the separate elements were effective. However, the qualitative component of the study did highlight that the health profession led programme did not meet the biopsychosocial needs of participants in the way that had been anticipated.

The exercise component of the intervention was designed to provide physical rehabilitation through improving muscle strength and stamina but it was also envisaged that further benefits might be seen in psychosocial health. For example it was anticipated that as patients grew in confidence in their physical ability it would enable them to socialise more and potentially help to reduce negative psychosocial factors such as anxiety or boredom. For some individuals it seems that the exercise component did provide a boost to morale as people saw an improvement in their ability week on week. However other people reported feeling discouraged and exhausted by attending the programme which arguably hindered their psychosocial recovery.

The information component of the health profession led programme was designed to provide additional information about recovery after stem cell transplantation. It was hoped that this would reduce anxiety and stress by ensuring that patients were adequately informed about the recovery process and by allowing additional contact with health professionals thereby providing an opportunity to discuss concerns not addressed at clinic. Similarly it was envisaged that the relaxation techniques included in the health profession led programme would enable participants to release any tension and anxiety associated with having been treated with a stem cell transplant. Reactions to these components were varied. It was suggested that additional information had the potential to increase anxiety

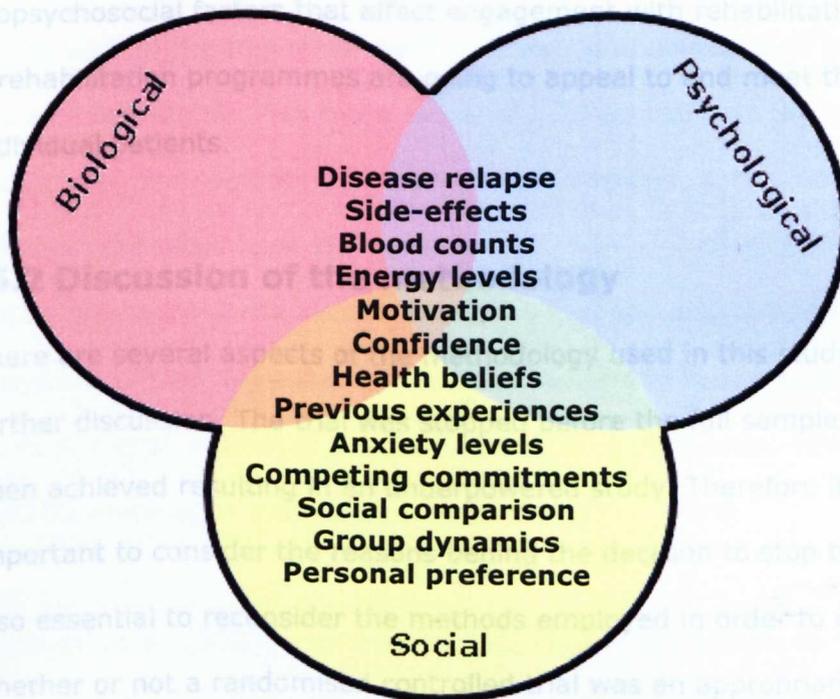
rather than reduce it and many individuals disliked the relaxation techniques.

A further key aspect of the health profession led programme was the group nature of the programme. It was anticipated that this would provide the opportunity for social support through comradeship, shared mutual experiences and friendship. The group dynamic of the programme did not function as was hoped. In part this was related to the small group size, however the qualitative findings indicate that whilst some participants enjoyed being part of a group others disliked the group environment because they did not feel any connection with the other people present.

These issues highlight the complexity of trying to meet the psychosocial needs of individuals. Whilst the biological consequences of stem cell transplantation respond to treatment in a relatively predictable fashion, the psychological and social issues associated with stem cell transplantation are unique to each individual. In recognition of this a more flexible patient centred approach to rehabilitation following stem cell transplantation is required.

Whilst the success of the health profession led programme as a biopsychosocial intervention can be questioned the findings from this study do provide a number of insights into the biopsychosocial factors that influence participation in rehabilitation. Figure 6.1 has been developed to highlight the biopsychosocial elements affecting rehabilitation following stem cell transplantation and complements figure 2.4 which is shown in chapter two section six.

Figure 6.1: The biopsychosocial factors affecting rehabilitation following stem cell transplantation.



It was observed in this study that a number of different biopsychosocial factors affecting rehabilitation following stem cell transplantation. The predominant biological factors are an individual's disease status, the extent and intensity of any side-effects that they are experiencing, their blood cell counts and their energy levels. All of these factors will impact an individual's willingness and ability to engage in rehabilitation. The findings also highlight a number of psychological factors that may have an impact on rehabilitation. An individual's level of motivation, their confidence (both in their own abilities and in the expertise of other such as physiotherapists) their health beliefs, previous experience particularly with regard to exercise and their anxiety levels will all potentially effect how they engage with rehabilitation. The study also identified a number of social factors affecting rehabilitation. These were competing commitments, such as role as a mother or an employee, desire or otherwise for social contact and meeting

people who had been through a similar experience. Finally this study identified the importance of personal preference and individual taste or desires in the process of rehabilitation. Consideration of these biopsychosocial factors that affect engagement with rehabilitation is crucial if rehabilitation programmes are going to appeal to and meet the needs of individual patients.

## **6.2 Discussion of the methodology**

There are several aspects of the methodology used in this study that merit further discussion. The trial was stopped before the full sample size had been achieved resulting in an underpowered study. Therefore it is important to consider the reasons behind the decision to stop the trial. It is also essential to reconsider the methods employed in order to explore whether or not a randomised controlled trial was an appropriate design. It is also of interest to assess what steps could have been taken to avoid some of the difficulties that were encountered.

### **Rationale for early trial termination**

After a data collection period of approximately one year it was clear that the trial was not progressing as intended. The greatest area of concern was the rate at which participants were being recruited to the study. It had been anticipated that approximately 65% of the transplant population would agree to take part. In the event, only 37% actually took part.

### Factors affecting recruitment

It was noticed that fluctuations in recruitment were related to the enthusiasm and availability of members of staff. During the pilot study and at the start of the trial when staff were very enthusiastic and committed to the trial recruitment was more successful. In contrast, as the trial progressed and competing time pressures emerged, it was hard for staff to maintain the same level of dedication and rates of recruitment fell. This is not an unusual occurrence in trials. The work load and competing time pressures of staff were two of the many barriers to recruitment identified by Fayter et al. (2006) in their review of the barriers, modifiers and benefits involved in participation in cancer clinical trials.

Donovan et al. (2002) explored the recruitment of patients to a randomised controlled trial. The study identified that the language used by practitioners and researchers had an impact on whether or not participants agreed to take part. By giving feedback to researchers and practitioners they were able to increase the recruitment from 40% to 70% over the course of the trial (Donovan et al., 2002). The study by Donovan et al. (2002) highlights the need for clinicians to be engaged in the process of recruiting patients. In the stem cell transplant rehabilitation trial it became clear that whilst some doctors were keen to talk to patients about the trial others were not. Unfortunately, it was observed that potential participants responded differently to information from different members of staff. In particular, it was observed that if a doctor spoke to a patient about the trial then the patient was more likely to agree to take part. Since not all doctors were willing to discuss the trial with their patients it was questioned whether a substantial change in rates of recruitment could be achieved.

It was also clear that the entry criteria for the trial had an impact on recruitment. In particular the criterion that participants should be six to eight weeks post transplant when recruited negatively affected the rate of recruitment. The effect of the six to eight week recruitment window was that some participants turned down the trial when they were offered it because they felt their recovery was progressing well. Subsequently, their recovery did not progress as they had hoped. By the point that they then felt a rehabilitation programme would be of benefit this six to eight week window had passed and it was not possible for them to take part.

A small number of potential participants were restricted from taking part because they were too ill to be recruited during the six to eight week window. However, this problem was identified early in the trial and the protocol was adjusted so that individuals could take part in the trial if they had missed the six to eight week window because they had not been discharged from in-patient care by week eight.

A number of factors that were potentially affecting recruitment were identified, relating not to the trial but to the health profession led programme. During the early stages of the trial a lack of independent transport to attend the health profession led programme was consistently cited by participants as a reason for non-participation. In order to reduce the impact of this problem on rates of recruitment, taxis were provided for travel to and from the hospital. Interestingly, the rate of recruitment did not increase after this measure had been introduced.

Two other practical barriers to recruitment identified were participants' desire not to spend more time at the hospital, and journey time to the hospital. It would have been interesting to relocate the programme away

from the hospital and to assess the impact that this had on attendance rates. Situating the health profession led programme in the community might have helped to remove these barriers to participation, but since the transplant population was from a wide geographical area there was no obvious location for the group to meet that would be convenient for a majority of patients.

Lower than expected rates of recruitment are common in research studies. Research investigating rehabilitation with cancer patients is no exception to this. Previous studies have also identified the practical barriers to recruitment that were found in this present study (Campbell et al., 2005, Stevinson and Fox, 2006, Fayter et al., 2006). Since recruitment problems are a recurring theme in the literature on rehabilitation for cancer patients future research specifically investigating this issue may be of benefit to the research community.

#### Implications of the slow recruitment rate

The rate of recruitment was considered to be crucial to the success or failure of the trial since it had an undeniable impact on the health profession led programme itself in that if people were only recruited a few at a time, and 50% were allocated the self managed programme, only one or two participants filtered through to the health profession led programme at a time. It is highly questionable whether a group intervention with an average weekly attendance of just three people is actually a group intervention at all. It had been anticipated that up to ten participants would take part in the health profession led programme at any one time, providing a potentially lively group with a good sense of camaraderie and companionship. However, the group size never exceeded six participants

during the trial with an average weekly attendance of three. This small group size was perceived by the staff to affect the nature of the group, which the staff argued in turn affected participants' enjoyment, motivation and commitment to the group. In effect, the small group size, it was argued, had a downwards spiral effect whereby newly recruited individuals turned up to the health profession led programme, they did not encounter a lively dynamic group, and they were less motivated to continue attending, contributing further to the small group size for future recruits. This argument was supported by the fact that attendance rates at the programme were very poor with 34.5% of those allocated the health profession led programme attending for three or fewer of the ten sessions. Without a dynamic and lively group there was genuine concern that the efficacy of the intervention was being affected.

Given these concerns simply extending the time allowed for the trial to be completed in order to recruit more patients was not an appropriate response. With some reluctance, consideration was given as to whether stopping the trial early was the most appropriate response to these problems. This was not an easy judgement to make and a number of further factors were taken into account when considering the decision.

The poor attendance rate at the health profession led programme has already been mentioned as a problem. However, an additional problem caused by the fact that less than half of the individuals allocated to the programme attended for seven or more of the sessions was the resulting dilution effect that was caused whereby individuals allocated to the health profession led programme were effectively receiving the self managed programme. This increased the likelihood that any benefit of the health profession led programme would not be detected. It is possible to account

for a dilution effect when calculating the sample size required for a study (Wang and Bakhai, 2006). This precaution was not taken with this study since the pilot data did not indicate that this was likely to be a problem. If such a calculation had been performed it would have further increased the sample size required. Achieving a larger sample size was unfeasible given the problems that were encountered with recruitment. It therefore became increasingly clear that even if the trial continued until the sample originally calculated had been recruited the study would still have been underpowered.

One further factor that compounded this problem was that it was proving difficult to ensure a consistent study environment for the duration of the trial. The framework for the development and evaluation of RCT's for complex interventions to improve health published by the Medical Research Council states that once a randomised control trial begins the intervention must not evolve (Medical Research Council, 2000). Whilst the logic behind this requirement is clear, achieving such a condition can be difficult if not impossible. In the present trial the intervention underwent some minor changes. However, the environment within which the trial was run underwent some significant changes, which undoubtedly affected the self managed programme in particular. In part these were due to the merger of two acute hospital trusts. The merger resulted in the increased provision of some services. Most significantly, the level of physiotherapy support increased and a physiotherapist became available to see patients whilst they were attending clinic. Likewise, the level of dietetic support also increased and many patients started to see the dietician at clinic appointments. Prior to the trial, out-patients could not be referred to hospital based social workers. But during the trial, the service provided by the social work department evolved and it became possible for out-patients

to see a hospital social worker. These changes reflect important steps forward in the provision of care for people who have undergone stem cell transplantation. However, these changes caused the health profession led and the self managed programmes to become less distinct, since elements that were previously only available to the health profession led group became available to both groups. The issues raised by the changes in usual care were not sufficiently serious when considered alone to cause the continuation of the trial to be questioned. However, they further increased the likelihood that the study would be underpowered and unable to reach genuine conclusions as to the efficacy of the health profession led programme.

When all of these factors were taken into account it was clear that the most appropriate course of action was to stop recruiting to the trial. All individuals who had already been recruited continued through the trial as previously planned. Relevant stakeholders, the ethics committee and the research and development department were all informed of the decision and the reasons for it.

### **Suitability of a randomised controlled trial**

Given the problems that were encountered in this study it is reasonable to ask if a randomised controlled trial was the most appropriate method for evaluating the health profession led programme. Traditionally, randomised controlled trials have been seen as the 'gold standard' of evidenced based medicine (Barton, 2000) and the importance of the randomised controlled trial in developing new drugs and technologies is undeniable.

On rare occasions, the effects of a new treatment are so dramatic that there can be little doubt as to their importance. For example, the effectiveness of penicillin to treat bacterial infections is unquestionable. However, many potentially worthwhile interventions will never hope to have such an unquestionable impact and therefore it is important to have a method of evaluating more subtle health benefits. The advantage of using a randomised controlled trial design is that it allows greater confidence in attributing any observed effect to the intervention being tested (Barton, 2000). If assignment to treatment group is not random then it is impossible to be certain that known or unknown confounding variables are not the cause of any difference observed between the two groups (Watson et al., 2004). Proponents of the randomised controlled trial, for example Pocock (2006), argue that this method is the only way to establish the efficacy of a treatment.

The primary aim in this study was to investigate the efficacy of a new intervention and therefore a randomised controlled trial was an obvious approach to take. However, the intervention was undeniably complex making the use of a randomised controlled trial more contentious. During the planning of this study and it was perceived that by creating information leaflets to support the different elements of the programme a consistent structure could be provided without inhibiting the complex nature of the health profession led programme. However, as the trial progressed it became apparent that it was not the individual sessions that needed flexibility but that the actual programme needed to be able to adapt and change according to the needs of different patients. It had been envisaged that all patients allocated to the health profession led programme would complete the entire programme. Potentially, the most effective way to utilise the health profession led programme would have been for staff using

their skills, experience and expertise to work with patients to identify which elements of the programme would be of benefit to them and in so doing provide care that was tailored to meet the needs of individuals. This approach would not have precluded the use of a randomised controlled trial.

Black (1996), in his defence of the use of observational studies highlights four limitations on the use of randomised controlled trials suggesting that there are occasions when experimentation is unnecessary, inappropriate, impossible or inadequate. He argues that randomised controlled trials are inappropriate in a number of circumstances such as when evaluating interventions designed to prevent rare events, when the outcomes of interest are far in the future and when the use of a trial is self-defeating. Black (1996) uses the term self-defeating to refer to trials in which the act of randomisation may reduce the effectiveness of the intervention being tested, suggesting that this occurs "when the effectiveness of the intervention depends on the subject's active participation, which, in turn, depends on the subject's beliefs and preferences" (Black 1996 pg 1217). Many complex interventions, including the one in this study, fall into this category and therefore Black (1996) would question the appropriateness of using a randomised controlled trial in its evaluation. Black (1996) argues that "it is at least as plausible to assume that experimentation reduces the effectiveness of such interventions as to assume, as most researchers have done, that the results of observational studies are wrong" (Black 1996 pg 1217).

The qualitative finding that individuals who expressed a preference for the group programme did not find exercising alone acceptable and stopped exercising, but that participants allocated to the self managed programme

who did not desire to attend the group programme found exercising at home acceptable, is an example of precisely the problem addressed in Black's (1996) argument. The extent to which participants engaged with the programme they were allocated inevitably affected their commitment to exercise. The extent to which this problem affects the validity of the randomised controlled trial is a contentious issue. There are a number of potential solutions to this problem and these are discussed in the following section.

### **Alternative research designs**

Since there are a number of problems associated with using randomised controlled trials it is important to consider the alternative approaches that could have been employed in the evaluation of the stem cell transplant rehabilitation programme.

One alternative to conducting a single centre randomised controlled trial is to conduct a multicentre trial. This is a trial that is conducted simultaneously at many centres following the same protocol synchronised from a single command centre (Wang and Bakhai 2006). All data gathered is analysed collectively. The advantages of this type of trial are that it allows for a larger number of participants to be recruited in a shorter period of time and it has been argued that the results are more generalisable. However, the resource implications of a multicentre trial are considerable and therefore the majority of these trials have commercial funding and are driven by pharmaceutical sponsors (Wang and Bakhai 2006).

Since the rate of recruitment was a key difficulty in this study a multicentre approach is an attractive alternative to the single centre design that was employed. Unfortunately, the resource implications of such a decision were too prohibitive. Even if funding for a large scale study had been available it is likely that a number of difficulties would have been encountered with this approach. In particular, providing comparable complex interventions at different sites is a potential problem in the use of multicentre trials to evaluate complex interventions. In this study ensuring consistent provision of the health profession led programme in one setting was challenging, and a number of unavoidable changes to the programme occurred in the course of the trial. Therefore keeping an intervention stable across a number of centres may have proved impossible.

Furthermore, whilst a multicentre trial would have increased overall recruitment, it is likely that the recruitment at each individual centre would have been on a par with that achieved in this study. Presuming, as is the norm in multicentre trials, that the intervention was provided at each site, then numbers attending each intervention would not be increased in this approach. Since it has been argued that failure to achieve a sufficient group size for the health profession led programme impacted the nature and potentially the efficacy of the programme, to pursue a conventional multicentre trial design would have been irrational. A potential solution to this problem would be to use a multicentre approach with cluster randomisation.

Cluster randomisation uses a group of individuals, a hospital, or a community as the unit of randomisation and therefore provides a useful alternative in situations where it is not feasible or desirable to randomise each individual participant in a trial (Wang & Bakhai 2006). Cluster

randomisation is a particularly useful tool in the evaluation of complex interventions and successful studies have been reported that have utilised this design (Moore et al., 2002, Graham et al., 2002). A cluster randomised trial is an attractive option for studies of interventions that require group participation, such as the stem cell rehabilitation trial. In a traditional multicentre trial where four centres are involved, if 240 participants are recruited, 120 will be allocated the intervention and these will be distributed randomly between the four centres with approximately 30 participants from each receiving the intervention. Since in cluster randomisation it is the centre rather than the individual that is randomised the participants receiving the intervention in this example would only be at two sites and therefore the group size at each would be greater.

A further advantage of cluster designs is that they reduce the likelihood of contamination between treatment arms occurring since individual participants are only likely to have contact with other participants and medical staff who are part of the same arm of the trial. In conventional randomised trials, particularly of non-pharmacological treatments, the effect of an intervention can be diluted when there is contamination across arms of the study. For example, in the study by Courneya (2003) of an exercise intervention for colorectal cancer patients the control group initiated exercise due to a contamination effect from the intervention group.

One disadvantage of this approach is that it is crucial to account for cluster randomisation in the calculation of sample size since much larger samples are required than for conventional randomised controlled trials (Kerry and Bland, 1998). This and other factors mean that cluster randomised trials are expensive to run and require considerable resources in terms of

research expertise. There were not the financial resources available to conduct a multicentre cluster randomised trial for the evaluation of the stem cell transplant rehabilitation programme. However, it should also be noted that even if resources had been available this would have been a very problematic approach to employ. The reason for this is that the research was conducted at the request of the unit which had designed the health profession led programme. It would have been unpalatable to many staff on the unit to agree to a study design whereby the unit risked being randomly allocated to the control arm of a trial.

It has been argued that randomised controlled trials can be self defeating if the intervention being tested requires participants to engage with their allocated treatment (Black 1996). The concept of resentful demoralisation, whereby patients who do not receive their preferred treatment have a poorer outcome, is an important concern (Torgerson and Sibbald, 1998). This was an area of concern in this study since the extent to which participants engaged with the programmes was likely to have impacted on the benefit gained from taking part.

A potential solution to the problems associated with trials of this kind is to use a patient preference trial (Torgerson and Sibbald, 1998). In patient preference trials all patients are asked about both their preference for treatment and their willingness to be randomised. Patients who have no preference and who are therefore happy to be randomised form one group. Patients who have a preference but are still willing to be randomised form a second group. Patients who have a strong preference and are not willing to be randomised form a third group and receive their treatment of choice. It can be argued that the results of this type of trial are more generalisable since many participants who would normally not consent to taking part in a

trial are included. The disadvantages of this approach are that the analysis of such trials is uncertain and the design increases the size and cost of trials (Torgerson and Sibbald, 1998).

The most appropriate way to assess the impact of patient preference on an intervention is to assess patient preference prior to randomisation, to randomise all participants, and then to test for an interaction effect between preference and outcome in the analysis of findings (Torgerson & Sibbald 1998). This was the approach taken in the present study. However, this approach is not unproblematic ethically or methodologically. Ethically, it can be argued that asking about a patients' preferences and then ignoring them may be more distressing for the patient than not asking. Methodologically, interaction tests often lack sufficient power to detect an interaction effect.

Given the difficulties involved in using an experimental approach, the greater use of well designed observational studies has been advocated (Black 1998). A prospective observational design charting the recovery of stem cell transplant patients before and after the introduction of the rehabilitation programme would have been an alternative design for this study. Possible benefits to this approach might have been a higher level of participation, since patients would not have been required to consent to randomisation. Furthermore, it can be argued that the results would be more generalisable since strict inclusion and exclusion criterion would not have been necessary. An observational approach might not have impacted on the health profession led programme in the way that the trial was argued to have done. Therefore it may have enabled the observation of a fully working intervention. However, the clear disadvantage of this approach would have been that since it is not possible to know the impact

of unknown confounding variables, any findings that indicated the effectiveness of the health profession led programme could be artifactual.

### **Strengths and limitations of the qualitative data**

The qualitative interviews conducted as part of this study provided an insight into the experiences of staff and participants. As with the other aspects of the study it is important to consider the strengths and limitations of the approach employed.

Due to the limited size of the research team the same researcher conducted the qualitative interviews as had managed the quantitative trial. Through the process of recruiting participants to the main trial and of collecting the quantitative outcome measures I had developed a rapport with participants. The advantage of this was that participants felt comfortable in my company and were at ease in the interviews. The disadvantage of this was that the participants clearly associated me with both the rehabilitation programmes and with the trial which may have moderated the opinions that they were willing to express when discussing their participation. It can be argued that in an ideal world a new researcher with no prior contact with the trial would have conducted the interviews. This would help to allay any fears that participants felt obliged to present a particular viewpoint in the interviews. However, the fact that participants did not provide a very favourable account of the programmes suggests that in this study participants were comfortable to express their opinions even if they were critical of the trial.

Given the useful information that was generated from the interviews with participants and staff it is important to consider if a solely qualitative

approach would have been an appropriate way to evaluate the health profession led programme. The qualitative data that was gathered as part of this study was very important in exploring the perspectives of participants and staff. This information aided the understanding of what went wrong in this trial, and even if the trial had been successful, having a qualitative view on the health profession led programme would still have been invaluable. Could the health profession led programme have been evaluated just using a qualitative approach? It is possible to argue that it could; providing answers to such questions as, was the programme acceptable to patients? Did patients engage with the programme? Did the programme improve patients' perceptions of their recovery after transplant? All these questions are very important but unfortunately a purely qualitative approach is unable to answer the question: did the health profession led programme actually improve patients' recovery after stem cell transplantation? If this is a key question then a purely qualitative approach is not able to provide a sufficient answer.

### **Conclusions from the discussion of methodology**

Whilst there are undoubtedly practical difficulties with using randomised controlled trials to evaluate complex interventions it remains the gold standard by which evidence of effectiveness is judged. Therefore the use of randomised controlled trials in the evaluation of complex interventions should be encouraged. However, randomised controlled trials are expensive, and, by definition, the more complex the intervention being evaluated the more considerable the resource implications.

With regard to the complex intervention in this study, the most appropriate approach to assessing its efficacy might be to conduct a multicentre cluster

randomised controlled trial accompanied by a qualitative evaluation of the programme. Multiple centres would provide access to a greater number of potential participants. Randomising the centre rather than the individuals taking part would reduce the problems of contamination and resentful demoralisation. As with the present study a qualitative component would enable the evaluation of different individuals experiences of the programme and provide depth and context to the quantitative data. Furthermore, future research on this topic might benefit from investigating, not the impact of a set rehabilitation programme, at a set point in patients' recovery, but the impact of having a rehabilitation service available to patients when they require it. Unfortunately, the cost of such an investigation would be considerable and may prove prohibitive.

### **6.3 Implications for practice**

This research was initiated in the clinical environment in response to the staff's recognition of the fact that there was insufficient evidence as to the efficacy of rehabilitation interventions for patients recovering after stem cell transplantation. The research was designed to provide guidance to staff involved in clinical practice in how they should proceed in providing rehabilitation following stem cell transplantation. If the research had demonstrated that the health profession led programme was more effective than the self managed programme then this would have provided evidence with which to pursue clinical support and long term financing for that programme to be provided routinely. However, no difference in any outcome measure was observed between the modes of rehabilitation precluding this eventuality.

Due to the problems with recruitment the study was underpowered.

Underpowered studies are liable to type II errors since it is possible for a

true difference to exist that cannot be observed in the small volume of data. Therefore, despite no differences being observed between the two modes of rehabilitation it is not possible to conclude that the two programmes are equal. Evidence for equivalence can only be generated from equivalence trials that require much larger samples (Jones et al., 1996). Therefore there was no evidence to support the self managed programme being implemented as routine care for patients recovering after stem cell transplantation.

The literature review conducted for this thesis, the experiences of staff and patients expressed in the interviews and the comparison of the SF-36 data from this study with UK population norms all underline the importance of rehabilitation for individuals recovering after stem cell transplantation. Clinical colleagues are keen to continue to provide a rehabilitation intervention for patients recovering after stem cell transplantation. However, it is difficult to know exactly how to proceed from this point.

It was clear from the interview data from staff and patients that continuing with the health profession led programme in the format trialled in this study was not appropriate. This was supported by the poor attendance rates at the programme. Furthermore, the self managed programme was not well received by the majority of patients with the exception of those who were unable or unwilling to attend a programme based at the hospital.

Having stated that neither programme was ideal in the format in which it was trialled in this study it is important to recognise that there were elements from the programmes that were well evaluated by staff and patients. Furthermore, the comments and reflections of patients and staff

enabled a number of suggestions to be developed as to how a rehabilitation intervention for this patient group could be improved.

With regard to the potential content of a rehabilitation programme to be implemented in clinical practice the following findings are relevant.

Rehabilitation with an exercise component is appropriate and acceptable to patients following stem cell transplantation. This is consistent with previous research (Oldervoll et al., 2003, Courneya et al., 2000, Dimeo, 2000).

Patients value apposite information (Tarzian et al., 1999, Mills and Sullivan, 1999) and an information component is of merit in a rehabilitation intervention. Group support and the chance to engage with fellow patients and members of staff can be perceived as very beneficial in promoting psychosocial recovery after cancer treatment (Feigin et al., 2000), particularly within the context of an activity based programme (Adamsen et al., 2001, Emslie et al., 2007). The value of including relaxation exercises in a rehabilitation programme can be questioned and may be more appropriate for in-patient care (Fife et al., 2000).

With regard to the potential format for a rehabilitation intervention this study highlighted that any intervention for this patient group needs to be flexible allowing for the different needs of different patients. No evaluations of other rehabilitation programmes providing exercise, information and social support have been identified for patients recovering after stem cell transplantation. However, other studies with this patient group have emphasised the need for flexibility in order to meet the needs of individuals (Tarzian et al., 1999).

Patient choice and flexibility are central to the success of programmes which rely on patient engagement. However, this can be problematic within

the constraints of the National Health Service. Choice and flexibility must be balanced with cost-effectiveness and meeting the needs of as many patients as possible. One potential approach for providing a flexible, patient centred rehabilitation service may be for staff and individual patients to work together, selecting from a series of specified options a programme with the appropriate content and duration to meet that individual's requirements. This would allow someone who is confident of their ability to exercise and who does not feel the need for any additional support and information to exercise unsupervised at home. Alternatively, a person with more complex needs could attend a supervised programme weekly to build their confidence in exercising. Similarly, the provision of information and support could be directed towards those individuals who require it. Furthermore it may be appropriate to offer this service to anyone who has had a stem cell transplant regardless of the time since their transplant. To assume that all transplant related complications will be apparent shortly after transplantation is simplistic. The needs of patients could be more fully served with an open service available when it is required.

It is envisaged that the findings of this study in relation to the components and structure of potential rehabilitation programmes will assist clinical colleagues with the ongoing development of appropriate interventions aimed at addressing the known biopsychosocial side effects of stem cell transplantation. However it must be reiterated that, whilst these findings are based on the experiences of patients and staff and should therefore lead to the development of programmes with a greater degree of patient satisfaction than was identified in this study, the efficacy of providing a rehabilitation intervention following stem cell transplantation remains unproven.

At the centre where the research was carried out a new rehabilitation programme has been developed which is now being provided as part of routine care after stem cell transplantation. Early attendance and attrition rates for the new programme suggest that it now has a greater degree of acceptability with patients. However, no formal qualitative or quantitative evaluation of the new programme has yet been initiated.

## **6.4 Conclusions**

Stem cell transplantation is an aggressive treatment associated with numerous negative biopsychosocial sequelae (Edman et al., 2001, Frick et al., 2004, Hacker and Ferrans, 2003). The impact of stem cell transplantation can be prolonged supporting the need for rehabilitation to promote optimum physical and psychological recovery after treatment (Bush et al., 1995, Whedon and Ferrell, 1994).

This study aimed to assess the efficacy of a health profession led rehabilitation programme for patients who have had a stem cell transplant. The outcome measures in this trial included a range of biopsychosocial outcomes measured at both three and six months after randomisation. The 95% confidence intervals for all outcomes included zero indicating that there was no evidence of any difference in any aspect of recovery between the health profession led and self managed rehabilitation groups. However the confidence interval around the estimated difference in the primary outcome measure of physical functioning could not exclude differences of up to 10 points in either direction. In all dimensions of the SF-36 scale the patients from this trial had poorer mean scores than found in the general population indicating that recovery after transplantation can be protracted and endorsing the concept of rehabilitation for this patient group.

Qualitative evaluation of the programmes highlighted that important elements of a rehabilitation programme are exercise, information and social support. However, individual patients have differing needs and preferences and therefore flexibility is required in the provision of rehabilitation. Evidence as to the efficacy of rehabilitation for this patient group remains scant.

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## **Appendix A - Rehabilitation Leaflets**

(The actual leaflets given to patients were A5 in size, with the exception of booklet 8 which was A4 with the medications table in the centre across two pages.)

## **After Your Bone Marrow-Transplant**

**Book 1 of 8**

# **Exercising after your Bone Marrow Transplant**

## **Exercising after your Bone Marrow Transplant**

This information leaflet is to help you as you recover from your bone marrow transplant. Exercise can help you regain the strength and mobility that you will have lost during your time in hospital.

At the moment your joints may feel stiff and you may feel tired very easily. This is normal and is due to your muscles not being worked whilst you have been in bed.

You have probably lost weight whilst in hospital. You will have lost a combination of fat and muscle. It is easier to regain the fat you have lost than it is to regain the muscle. So even if you put weight back on, you will not regain your muscle bulk and strength unless you are exercising.

This booklet will give you information about how, why and when to exercise and a programme of exercises that you can try at home. There is also a section for you to write down how you get on when you exercise. This should help you monitor your progress.

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**Please read all of this booklet before you do any exercise.**

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### **Why should I exercise?**

- Exercise helps you regain strength in your muscles
- Exercise gives you more energy to do the things you enjoy
- Exercise can help reduce the feeling of fatigue
- Exercise helps you feel fit and healthy
- Exercise can improve your confidence
- Exercise reduces the risk of other diseases such as, heart disease, stroke and osteoporosis (brittle bones)

## **How much exercise should I be doing?**

Everyone is an individual. The right level of exercise will be different for each person. How much exercise you are able to do will depend on:

- how long you were in hospital for
- what condition you were diagnosed with
- the type of transplant you received
- your strength and mobility prior to diagnosis

Pushing yourself too hard, too quickly will not mean that you get better faster. It will tire you out and may discourage you.

You should very gradually increase the amount that you do.

You should be aiming to do some form of exercise 3-5 times a week.

At first you may get tired very easily, as your muscles are not used to having to work hard.

You should be able to talk whilst exercising. If you are too short of breath to talk, you are exercising too hard and need to reduce the intensity.

Doing too much or too little exercise may make any fatigue you might be experiencing worse. The leaflet 'managing fatigue after a bone marrow transplant' gives more details about how to find the right level of activity.

## **What sort of exercise should I be doing?**

You should choose a form of exercise that:

- you can do
- you enjoy doing
- you will want to keep doing
- will exercise your whole body.

Types of exercise you could try are:

- walking
- cycling
- gentle jogging
- circuit exercises

Included in this leaflet are some suitable exercises that you can complete at home.

### **Important guidelines**

It is important to increase your fitness very gradually. This can be achieved by:

- increasing the number of times a week you exercise.
- increasing how long you exercise for in each session.
- increasing how hard you work for in each session.

For example:

walking faster

increasing the number of exercise repetitions

adding a weight to the exercise

**When you can easily do your current exercises, increase the amount you are doing by a small amount. Never make large changes.**

### **Take care when you exercise**

- Always start and finish slowly. This will give muscles time to warm up and cool down reducing the risk of injury.
- If the weather is cold or wet, either make sure you have suitable clothing on, or do some exercise inside.
- Allow 2 hours after eating before you exercise, to ensure that food is fully digested.
- If you feel unwell reduce your usual level of exercise until you feel well again.

- It is normal to feel some slight muscle soreness after exercising. Sharp pain or pains lasting more than 24hours suggest that you need to reduce the amount of exercise you are doing.
- If any of the following occur whilst exercising, stop immediately.

Chest pains or increased chest tightness

Severe joint or muscle pain

Dizziness or feeling faint

Excessive shortness of breath. You should be able to breathe normally within 3-4 minutes after stopping exercise.

Do not restart until you have seen a doctor at clinic.

### The Borg scale of perceived exertion

The Borg scale can be used as a guide to make sure you are exercising at the right intensity. The scale is graded from 6-20 as shown below. You should use the scale to rate how hard you feel you are exerting yourself when doing your exercises.

When exercising, you should be working at a level which gives you a Borg rating of between 12 and 15.

The Borg scale of perceived exertion

6	very very light
7	
8	very light
9	
10	light
11	
12	somewhat hard
13	
14	hard
15	
16	very hard
17	
18	very very hard
19	
20	

Aim to exercise at a level which gives you a Borg rating of between 12 and 15.

## Exercising

We have included an exercise programme, consisting of ten exercises that are suitable for you to complete at home. We suggest that you try to do the exercises three to five times a week.

You should get ready to exercise by:

- making sure that you are wearing comfy loose fitting clothes and flat shoes
- reading the exercise programme through from start to finish
- gathering together the equipment you will need – this should include
  - a drink and biscuit for when you finish
  - music to listen to whilst you exercise (optional)
  - a pen to write down how you get on
  - two weights or tins of beans (optional)
  - a short pole or stick (for exercise 5)

Before you start the exercises on the sheet you should walk on the spot for about a minute to warm up your muscles and get you ready for exercise.

After warming up you should do each exercise on the sheet in turn. Repeat each exercise several times before moving on to the next one. Count how many times you repeat the exercise and write it down on the exercise sheets.

Gradually increase the number of repetitions that you do. Another way to make the exercises harder is to add a weight. You don't need to buy gym weights, a tin of beans will work equally well. If you find the exercises very hard you should reduce the number of repetitions that you do.

When you first start these exercises you may need to stop and rest between exercises. Don't worry if you need to sit and have a rest or walk slowly on the spot until you feel ready to start again.

If you get any feeling of discomfort make sure you take some time to recover before continuing.

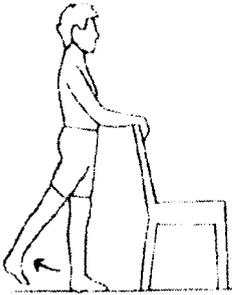
When you have finished the exercises on the sheet walk on the spot, slowly reducing your pace for about a minute. Make sure you have your drink and biscuit, then take a well-deserved rest.

If you keep exercising you will soon start to see an improvement in what you can achieve.

Use the exercise diary sheets to record both how you get on with the exercises and how much other activity such as walking you are doing each day. By recording how you are getting on you can look back and see how much you have improved.

## Exercise Programme

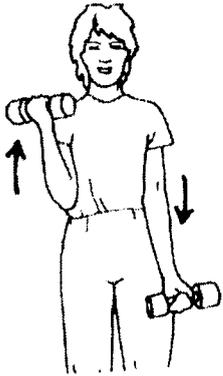
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### Exercise 1

Stand straight holding onto a chair.  
Bring your leg backwards keeping your knee straight. Do not lean forwards.  
Repeat with your other leg.

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### Exercise 2

Stand with arms hanging down, either with or without weights, i.e. tin of beans or water in a bottle.  
Bend alternate elbows briskly.  
Repeat.

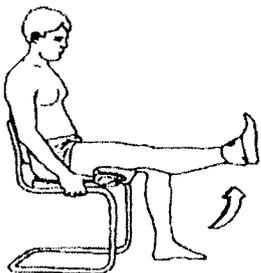
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### Exercise 3

Sit or stand holding your hands on your chest.  
Start with no weights, but progress if required to a small weight in each hand, i.e. tin of beans.  
Alternating arms lift your hands with or without the weights from your chest straight up and down.  
Repeat.

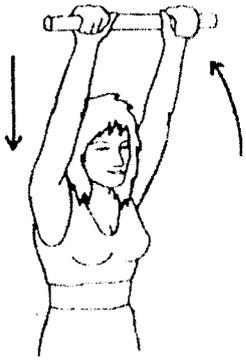
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### Exercise 4

Sit on a chair with a cushion under your knee.  
Pull your toes up, tighten the front of your thigh muscle and straighten your knee slowly. Hold for approximately five seconds.  
Change legs and repeat.

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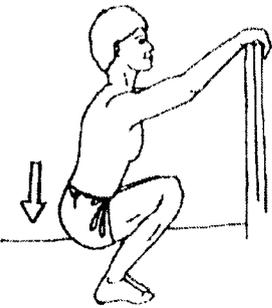
### Exercise 5

Stand or sit holding a pole or stick with your arms down and in front of you.

Lift arms straight up and then lower the stick behind your neck. Lift arms up and return to starting position.

Repeat.

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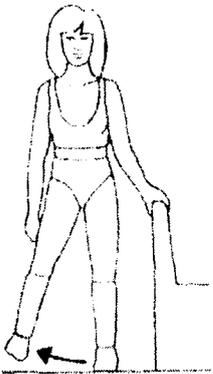
### Exercise 6

Stand in front of a table or chair holding on to the support with both hands.

Slowly crouch down as far as you can reasonably go. Keeping your back straight and heels on the floor. Stay down for approximately five seconds. Use arms to pull yourself up a little and then push up through your legs.

Repeat.

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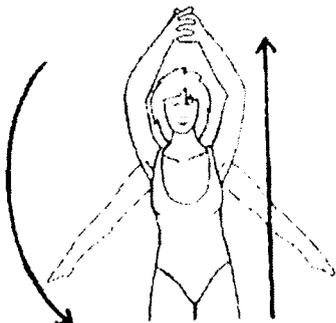
### Exercise 7

Stand straight holding onto a support.

Lift your leg sideways, keeping your trunk straight throughout the exercise.

Repeat.

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### Exercise 8

Standing with hands clasped in front of you.

Lift both arms straight forward over your head.

Separate your arms sideways and take them back to the starting position.

Repeat.

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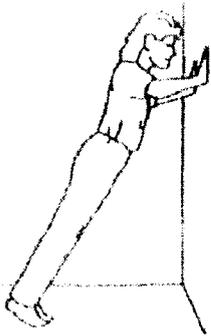


### **Exercise 9**

Stand in front of a step/bottom step on a flight of stairs.

Step up ten times with one leg leading and then repeat with the other leg leading.

Ensure your knee stays in line with your toes.



### **Exercise 10**

Stand facing a wall with your arms straight and hands on the wall.

Do push-ups against the wall keeping your body in a straight line.

Repeat.



Walking is an excellent form of exercise. Try to get out of the house and go for a walk most days. But remember you may be very weak and you should start with just a short walk. You can then gradually increase how far you go.



Climbing stairs is also good exercise.

**Exercise Diary:** how many times can you repeat each exercise?

Put today's date in the first row, and then underneath record how many times you completed each exercise.

<b>Date→</b>									
<b>Exercise↓</b>									
<b>1</b>									
<b>2</b>									
<b>3</b>									
<b>4</b>									
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## **After Your Bone Marrow Transplant**

**Book 2 of 8**

# **Eating after your Bone Marrow Transplant**

## **Eating after your Bone Marrow Transplant**

After you have had a bone marrow transplant it is common to experience some difficulty with eating. This leaflet suggests ways to help overcome some common food related problems associated with having had a bone marrow transplant.

### **Clean diets**

On discharge from hospital you will have been told that you need to follow a clean or neutropenic diet. This is because you are immunocompromised. Therefore you are at risk of picking up a stomach bug from foods that you would normally be able to eat. It is most important that you follow this advice whilst your white cell count is below 1.0.

To reduce the risk of getting a stomach bug you should:

- store your food according to the instructions.
- ensure that the food is within the best before or use by date.
- cook your food according to the instructions.
- only eat dairy products that have been pasteurised.
- avoid re-heating food.
- avoid soft or blue veined cheeses, raw meat, raw fish, raw eggs, and live or bio yoghurts.

Take care when eating food you have not prepared yourself. Avoid buying take-aways if the company cannot guarantee that your order will be cooked fresh. Kebabs and other foods that are kept warm should be avoided. It is also very important that rice has been freshly cooked as reheated rice is a major cause of food poisoning. If you want to eat out in a restaurant the same principles apply. Always ensure you are eating somewhere with a good reputation for freshly prepared food.

If you microwave food, make sure that all the food is piping hot and stir the food well as microwaves don't always cook foods evenly.

## **Taste changes**

Taste changes can last for a while after your treatment but your taste should return to normal with time. Taste changes affect different people in different ways. You will need to experiment and find out what works for you.

Many people find that tea and coffee taste unpleasant. If you stop drinking tea and coffee it is important that you replace them with other fluids. You should aim to drink about 2 litres per day. Many people find that pineapple juice tastes good and it can help to restore your normal taste palate.

Food may taste bland, sweet or sour. You may find that marinating meat with wine or sherry may help. Or you could try serving it with a sweet and sour or BBQ sauce. It may also be helpful to add extra spices or herbs to your foods. If things taste sour, try eating more sweet foods.

Some people add extra salt to their food to improve the flavour. If this helps you then in the short term it won't do any harm. But remember that salt is not good for your health. Once your taste improves it is very important to reduce your salt again.

Keep trying different food as you may find you enjoy food that you don't normally like and you will find that your taste changes over time.

## **Poor appetite**

If you have a poor appetite it is important that you try to eat well even if you don't feel like it. Don't try and eat too much at once. Instead of having three normal size meals a day you may find it helpful to eat more often but to eat less on each occasion.

A small glass of alcohol before meals can help your appetite. Try to get some fresh air before eating and avoid the smell of food while it is cooking. The smell of certain foods, often steamed vegetables,

may affect you strongly as you may associate them with times during the treatment when you were feeling nauseous. This should reduce with time.

## **Dry mouth**

Having a dry mouth is a side effect of the treatment you have had. This along with so many other things will gradually return to normal. Whilst you are recovering you may find the following things help you to cope with the problem.

- Try tart foods such as lemon or pineapple.
- Try drinking pineapple juice or chewing pineapple chunks.
- Eat moist soft foods.
- Have a drink with meals

Some people say that bread and potato feel like cotton wool in their mouth and are too difficult to eat. If this is true for you try replacing them with cereal, rice and pasta. Alternatively you could try serving them with a sauce e.g. beans on toast, or adding butter/cream to moisten potatoes.

## **Weight loss**

It is very likely that you have lost weight during or after your treatment. If you continue to lose weight this will have an impact on your recovery by affecting your energy levels. There are several things you could try in order to maximise your food intake.

- Don't push yourself to eat more than you want but eat more often.
- Have snacks between meals. This could be crisps or biscuits, eat whatever appeals to you.
- Add butter, cream and cheese to meals, for example mash potatoes with cream and butter rather than milk.
- Don't buy low fat foods and change your milk and other dairy products to full fat.
- You could try supplementary drinks such as build-up or complan, which are available in most supermarkets or chemists.

## **Nausea (feeling sick)**

It is often helpful to eat a little food more often if you are suffering with nausea because if you go too long between meals the feeling gets worse.

Try flat fizzy drinks and plain dry foods such as biscuits and toast if you are having trouble tolerating normal food.

Some people find that foods flavoured with ginger and arrowroot help.

If nausea is an ongoing problem talk to your doctor. They will review your medication as there are lots of different anti sickness drugs you can try.

## **Diarrhoea**

Diarrhoea can be a problem at times. If you have had diarrhoea, you should always mention it to the doctor when you go to clinic. It is very important to take extra fluids if you have diarrhoea to make sure that you don't get dehydrated.

You may also need to temporarily reduce the fibre content of your diet. To do this you could cut down on white bread, plain cereals, fruit (especially dried), vegetables and nuts.

## **Healthy eating**

Once you are eating as normal, with a healthy weight, it is important that you ensure your diet is healthy.

This means watching your intake of sugar, salt and fatty foods.

It is also important to have a good intake of fibre in your diet and to aim to eat at least five portions of fruit and vegetables a day.

A portion is an apple, banana, orange, two plums or kiwis, dessert bowl of salad, glass of fruit juice or two tablespoons of cooked vegetables.

If you have any concerns about any of the things discussed in this leaflet please remember to ask for some advice at clinic.

## **After Your Bone Marrow Transplant**

**Book 3 of 8**

# **Coping with stress after your Bone Marrow Transplant**

## **Coping with stress after your Bone Marrow Transplant**

Stress is very difficult to define. It is how we react when we are in situations that stretch our ability to cope. The effects of stress may be physical and/or emotional.

There are numerous emotional effects of stress. Stress may make you feel that you are:

- always rushing
- impatient with others
- keyed up
- often tired
- experiencing strange pains
- often worried
- frustrated

The physical effects of stress are caused when your body produces adrenaline which makes you feel that your:

- heart is pounding
- muscles are tense
- breathing is fast/shallow
- mouth is dry
- hands are clammy
- head aches.

### **Coping with stress**

It can be very difficult to cope with stress and no one solution will suit everyone as people cope in different ways. Below are some suggestions that may help you to cope with stress.

### **Exercise**

When we exercise chemicals are released called endorphins. These act on the brain and are associated with feeling positive and energetic. Exercising regularly will help you to feel positive and to cope with the stresses

that you are facing. Use the advice in the leaflet 'Exercising after your BMT' to plan an exercise routine that will help improve both your physical and mental health.

### **Leisure pursuits and socialising**

Talking to friends can reduce your stress and help you feel more positive, but seeing people can also be stressful. Don't let socialising add to your stress. Decide who you feel comfortable seeing and how long you think you can cope with seeing them for.

You may find that you are spending more time at home than you have ever done before and you may get bored very easily. Being bored will increase your stress levels so try to find activities to keep your mind busy. You could try reading, puzzles or listening to music.

**Relaxation** can be seen as 'doing nothing' but when we are stressed our bodies and minds find it difficult to unwind. Just because we are sitting 'doing nothing' our minds may be racing preventing us from getting the rest that we need. Specific relaxation techniques can help to relieve tension and reduce stress. Below are some brief explanations of some common relaxation techniques. Have a go at finding out what works for you. If you want more information there are many books available, most local libraries have a selection, or you could ask for some advice when you come to clinic.

Tensing and relaxing each part of your body in turn - Start with one part of your body, for example your left hand and try to tense the muscles, pause and then relax the muscles. Then move on and think about another part such as your left arm. Work your way systematically round your body slowly and deliberately tensing and relaxing your muscles.

Breathing exercises – When we are stressed our pattern of breathing can become very fast and shallow. It can be very effective to focus on deliberately changing your breathing pattern to control your stress. By breathing slowly and deeply you will feel calmer and better able to cope. You should breathe in through your nose a long slow breath, pause and then slowly release the breath out through your mouth.

Imagery exercises – There are lots of different imagery exercises. One exercise involves shutting your eyes and thinking of a special place where you feel safe and happy. It might be an actual memory of a place you have visited or it might be an imaginary place. Spend time imagining you are there, try to feel what it would be like. Think about what you might be able to hear, see, smell and touch.

Relaxation tapes – most local libraries have relaxation tapes and they are available in shops and on the internet. There are a variety of different types of tapes available. Some provide exercises to follow, usually to music, others are simply a recording of natural sounds such as rippling streams or whale song. You can put these on, shut your eyes and drift away to a relaxing place.

## **Sleep**

Getting enough sleep will help you cope with stress. Below are some tips that will help you get a good nights rest.

- Try to go to bed and get up at the same time each day. This will help your body to establish a regular sleep pattern.
- Have a light snack and a drink such as warm milk before going to bed. If you are hungry in the night it will disturb your sleep.
- Avoid stimulants such as cola drinks, coffee, tea and chocolate especially in the evening.

- Limit your intake of alcohol. Alcohol might help you fall asleep quickly but your sleep is likely to be disturbed.
- Try to do some exercise each day but avoid exercising just before going to bed.

A more detailed booklet on sleeping well can be obtained from the Royal College of Psychiatrists by phoning 020 7235 2351 or from their website - [www.repsych.ac.uk](http://www.repsych.ac.uk)

## **Talking**

Some people find it helps to talk about their feelings and emotions to a good friend. If you want to talk to someone try to find a friend who you trust and who is good at listening.

You may want to talk about things that you don't feel comfortable speaking to a friend about. A variety of organisations offer telephone support services where you can ring and talk to someone about how you are feeling.

You could ring the Macmillan Cancer Relief telephone line or the Cancer Backup telephone service. They will be happy to talk with you and can recommend other cancer support services in your area. The Cancer Counselling Trust offers a confidential telephone counselling service to individuals, couples or families affected by cancer.

If you are stressed and you feel that you are not coping, please ask for some advice next time you visit clinic.

**Macmillan Cancer Relief  
89 Albert Embankment  
London  
SE1 7UQ**

**Freephone:  
0808 808 2020  
E-mail:  
cancerline@macmillan.org.uk  
Website:  
www.macmillan.org.uk**

**Cancer Bacup Information Centre  
Nottingham City Hospital  
Hucknall Road  
Nottingham  
0115 840 2650  
Freephone: 0808 800 1234  
Website:www.cancerbacup.org.uk**

**Cancer Counselling Trust  
1 Noel Road  
London  
N1 8HQ**

**Tel: 020 7704 1137  
Fax: 020 7704 1783  
Email: support@cctrust.org.uk  
Website: www.cctrust.org.uk**

**After Your Bone Marrow Transplant**

**Book 4 of 8**

**Managing fatigue after your  
Bone Marrow Transplant**

# **Managing fatigue after your Bone Marrow Transplant**

## **What is fatigue?**

- Fatigue is a feeling of excessive tiredness or exhaustion that may occur some or all of the time.
- Fatigue is when the feeling of tiredness does not go away even if you have lots of sleep and get plenty of rest.
- Fatigue can affect you physically, psychologically and emotionally.

## **What causes fatigue?**

- There are many causes of fatigue
- We do not always know why one person becomes fatigued and another does not.
- Chemotherapy and radiotherapy can cause fatigue.
- Fatigue can also be caused by anaemia, which is when you have reduced levels of red blood cells.

## **What can be done to help reduce fatigue?**

After your bone marrow transplant you will have regular blood tests and if your red cell count is very low you may be given a blood transfusion. Alternatively you may be given a regular subcutaneous (under the skin) injection of a red cell growth factor that should increase your red cell count.

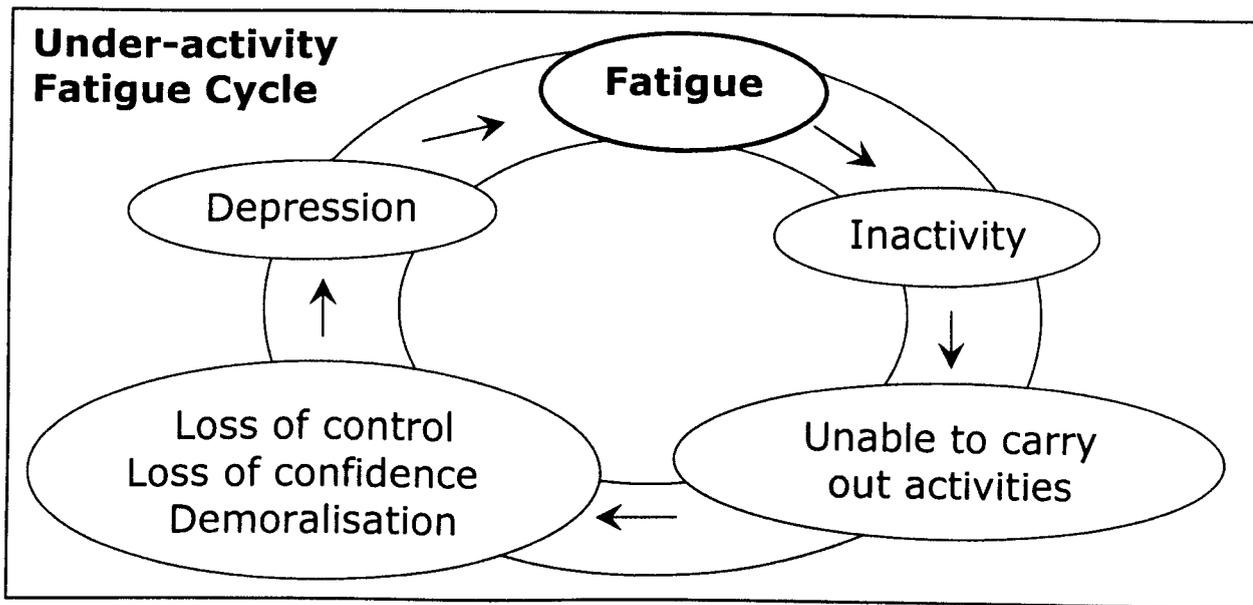
If anaemia is not the cause of your fatigue a blood transfusion or injections of growth factors will not help and you need to find other ways to manage your fatigue until it resolves.

There is lots of advice about how to manage fatigue but no plan suits everyone. You will need to find out what works for you. In this leaflet we explain two common problems, how you can avoid them and what positive steps you can take to cope with your fatigue.

### **Under-activity fatigue cycle.**

Many people try and deal with fatigue by resting and sleeping. If you avoid activity and rest continuously you can become more fatigued rather than less. It might help you to think of this as an under-activity fatigue cycle.

A lack of activity will cause further physical weakness. You may feel unable to do the things you want to do, and this can leave you feeling demoralised. You may lose confidence or you may feel you are losing control. All of these things can then make you feel worried, depressed or anxious which in turn reduces your energy levels, your fatigue increases and the cycle begins again.

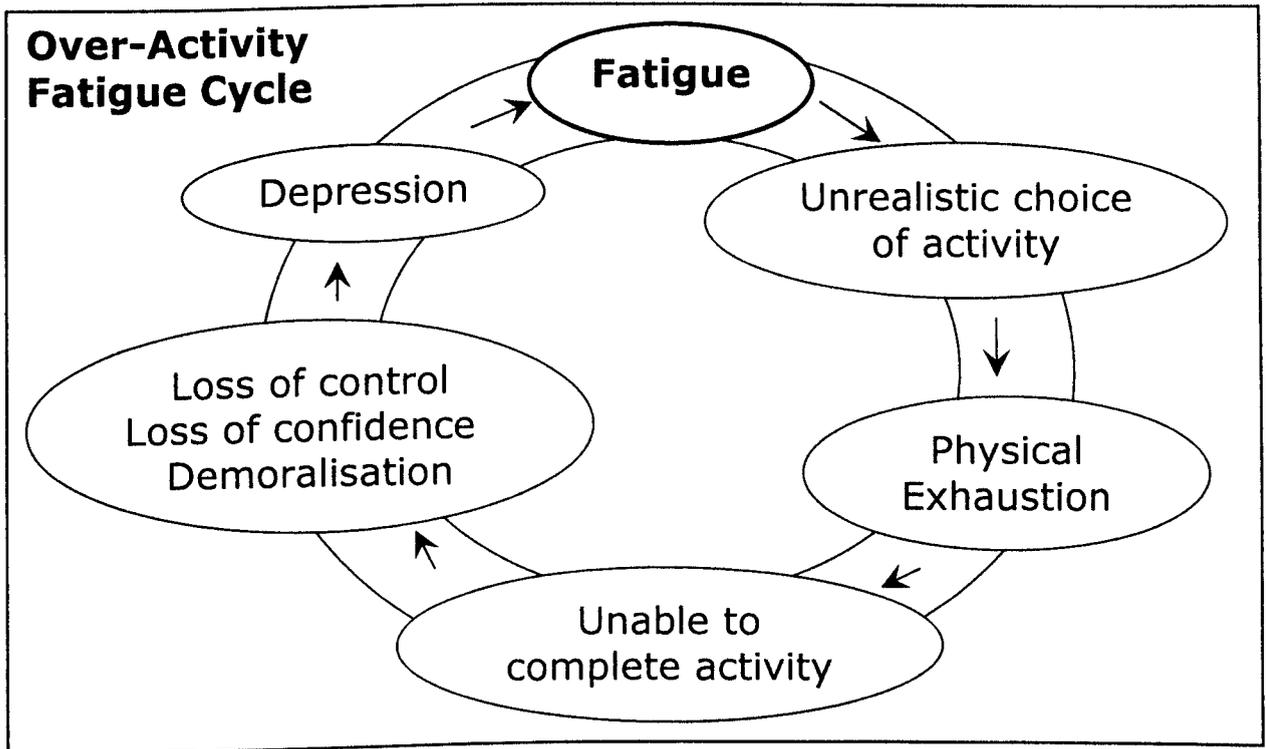


In order to reduce fatigue it is important to break this cycle. The best place to do that is at the inactivity point. Increasing your activity a small amount will help you to increase your muscle strength enabling you to complete an activity that you want to achieve. This increases your confidence, reduces the risk of depression and should prevent increased fatigue. The negative cycle is broken and a new positive cycle of improving health begins.

There is more information later in this leaflet about how you can gradually increase your activity levels when you have fatigue.

## Over-activity fatigue cycle.

Rather than doing nothing, some people experiencing fatigue try to deal with the problem by doing too much. Trying to do too much when you are fatigued will result in increased not decreased levels of fatigue. You may find it helpful to think of this as an over-activity fatigue cycle.



In order to reduce fatigue it is important to break this cycle. The place to do this is at the over-activity point. Choosing an activity that you can realistically complete is very important. By gradually increasing your activity levels and choosing realistic tasks you can rebuild your strength, increase your confidence, reduce the risk of depression and your levels of fatigue will slowly reduce.

It is completely normal when faced with fatigue to fall into one or other of these cycles. It is not uncommon for people to yo-yo between the two, not able to find the right level of activity. The rest of this leaflet suggests some guidelines for finding the right level of activity for you.

## **Finding the right level of activity.**

When coping with fatigue you need to look for a balance in the amount you try and achieve. The following tips may help you to avoid getting stuck in a cycle of increasing fatigue.

- Pace your activities. Doing activities throughout the day interspersed with periods of rest will help you to conserve energy.
- Take a break before you need it so you are able to maintain a certain level of activity day after day and avoid over tiredness.
- Be aware that your limits will fluctuate from day to day.
- Do not take on more than you can manage.
- Stop when you feel tired. 'Listen to your body'.
- Take frequent rests both before and after completing a task. Many short rest periods are better than a few long ones.
- Set actual time limits and stick to them, especially on good days when you may feel you can do more.

Learn when in the day you have the most energy and plan activities accordingly.

On bad days make sure you do a little activity.

- Learn relaxation techniques to ensure proper rest is achieved. Some basic relaxation techniques are outlined in the leaflet 'Coping with stress after your BMT'.
- Have a routine sleep pattern by going to bed and waking at the same time every day.

- Consider the tasks you do during each day. Usually there are ways of making each task easier to do:

Can the task be broken down into smaller tasks?

Can any part of a task be eliminated?

Can someone else help with the task?

### **Coping with fatigue is not easy.**

There are no quick fix solutions and your improvement will be gradual. This leaflet is just an introduction to the issue of fatigue. If you want more information and support you could:

- Speak to your doctor at clinic. This is especially important if you feel that you are becoming depressed. It is very common to feel this way after treatment for cancer and it is important that you are honest with your doctor. If you don't tell them how you are feeling they can't help you.
- Contact Cancer Bacup and ask for a free copy of their 'coping with fatigue' leaflet.

Cancer Bacup Information Centre  
Nottingham City Hospital  
Hucknall Road  
Nottingham  
0115 840 2650

Freephone: 0808 800 1234

Website: [www.cancerbacup.org.uk](http://www.cancerbacup.org.uk)

- Phone Social Services on 0115 969 1169 ext. 46573. If your fatigue means that you need help with personal care and assistance at home a social worker may be able to arrange for you to have some short term assistance. Many social workers are also trained counsellors, if your fatigue is getting you down you may want to talk to them about how you are feeling.

**After Your Bone Marrow Transplant**

**Book 5 of 8**

**Financial support after your  
Bone Marrow Transplant**

# **Financial Support after your Bone Marrow Transplant**

## **Are you receiving the benefits you are entitled to?**

The Benefits Agency publish booklets which outline the benefits that are available and who is entitled to them. You can ask for the relevant booklets to be sent to you by phoning the Benefit Enquiry Line.

Alternatively you can contact Social Services. You can arrange to speak to a social worker who will check that you are getting the correct benefits. This is especially important if you did not see a social worker before you were discharged from hospital. There may well be benefits that you are unaware of, that you are entitled to.

## **Do you need some help with personal care at home?**

## **Do you need help with managing your house and shopping?**

## **Are you struggling with food preparation?**

Help is available for these problems. If you would like to find out more then you need to speak to a social worker. You can contact Social Services on the number listed on page 5.

## **Would you like to apply for a one off grant to help with a particular expense such as a holiday?**

Macmillan Cancer Relief provide grants to help people living with cancer. You can find out more by phoning their advice line; the number is listed below.

Social Services can also provide you with information about applying for grants.

## **Would you like to talk to a trained counsellor?**

Many social workers are also trained counsellors. If you feel that you would benefit from seeing a counsellor contact social services on the number below.

Several charities also provide advice and counselling for people affected by cancer. Macmillan Cancer Relief or Cancer Bacup can give you more information.

**If you think you need any further information about the services mentioned in this booklet, then contact any of the organisations shown below:**

- Benefit Enquiry Line                      0800 882200
- Macmillan Cancer Relief                0808 808 2020
- Social Services                            0115 969 1169 ext. 46573
- Cancer Bacup                              0115 840 2650

## **After Your Bone Marrow Transplant**

**Book 6 of 8**

**"My life after a Bone Marrow  
Transplant"  
by someone who has been through it**

## **"My life after a Bone Marrow Transplant" by someone who has been through it**

Welcome to my true-life story. I am 39 years old and I feel very fit and healthy. My children are growing up fast around me and I have a fulfilling and happy relationship with my partner. I am employed and I also volunteer for a cancer charity. I am proud to be where I am today.

For me the last few years have been a journey and the ride has not always been a comfortable one. I have written about my experiences and emotions. You may or may not be experiencing similar feelings. The aim of writing this is to reassure you that you too can get your life back on track and to let you know that you are not alone.

At the age of 31, I was diagnosed with Chronic Myeloid Leukaemia (CML). At this stage in my life I was a healthy, fit, football playing man with everything to live for. My symptoms started with feeling really tired so I went to visit my local doctors. After 3 months of investigations I was diagnosed and was admitted the next day.

From March to May I was cared for at the Derbyshire Royal Infirmary, but then my Leukaemia went into a myeloblastic form and then the battle really began. I remember this day very well - it was my 32<sup>nd</sup> birthday. I was then admitted to Nottingham City Hospital, where I received all my treatment prior to, and all the care after, my transplant. It wasn't until December that I was finally able to go home and try to get back to a normal life.

After my discharge, appointments had been set up for me on a weekly basis but still I felt isolated and frightened, as I really didn't know what to expect. If I got an ache or pain did this mean my leukaemia was back? If life in the outside world was too much who would I turn to? My family had been through enough; I didn't want to worry them any more than I had to.

My transplant had been a success, so medically I was fit for discharge. What hadn't been addressed was what to expect physically, mentally, emotionally, when facing the outside world again. I'd gone into hospital looking relatively fit, yet here I was now looking and feeling somewhat different.

After all the different types of treatment I'd received I came out of hospital bald, thin, blotted in the face. One person said, "you look like a hamster, who's storing its food in its mouth". Now I can smile, but then it really brought it home to me what I looked like and it hurt. People have no idea the battering your body has undergone to get you back on the road to recovery.

My complexion was quite dark, grey with a tinge of yellow, not looking like my old self from before. Basically the way you look is the last things on your mind. But to people who haven't seen you since your treatment started it's somewhat disturbing and embarrassing. You need to remember what your body has been through and know that in time it will correct itself.

On the path to recovery there will be lots of visits to the day case unit for blood checks, transfusions, platelets, and other forms of healthy top-ups. There could also be other barriers to test you. You may find yourself battling infections. You might find these physically and mentally tiring. Patience and stamina are required through these stages of recovery, just keep thinking of where you want to get to, back in a normal and healthy life style.

My own rehabilitation appeared to go in stages and cycles depending on my body's strength at the time to deal with these changes. Patience, time and understanding is required here and slowly but surely month by month you will get things under control with the help of the after care clinics. Battling leukaemia is like running a marathon not a sprint. Something to bear in mind at all times.

There will be lots of feelings running through your mind when you return home, some nice and some not so nice.

You may feel lonely after your stay in hospital surrounded by other patients and nursing staff. You may feel anxiety, depression, tiredness and other pressures of coping again in the outside world. Again feelings of 'how do I cope', and 'will I ever get back my normal life?'

On the opposite side to the negative emotions you may feel, there will always be positive feelings. Good friends, family and other acquaintances will send you letters and get well cards. I also had one or two local churches saying prayers for me. Friends who could not visit in hospital will start coming round to see you. Once again this can be an emotional time but you need to take heart and draw on the support being offered by others.

Remember you should feel extremely proud and positive, you have just battled with a life threatening disease and you are on the road to a fit and healthy life again.

Below are some tips from my experience.

- I really feel that good support is vital whether it be from family, friends, or carers, especially for the first few months because believe me you are not at your best!
- Exercise. This word feels like a swear word in the first few weeks after returning home but the sooner you start the better you will start to feel, being careful not to over exceed your limits. You'll quickly find your stamina improves and your energy levels increase as you build up your exercise time.
- Force yourself to eat as much as you can. "Little and often" was always a good tip as your taste buds will not hold the pleasure they used to. But they will get better.
- Avoid crowds and anyone with a cold or flu, always remembering your immune system is back in it's infancy stage. You must give yourself the space your body needs after the hammering its taken through chemotherapy and radiotherapy.

- Set yourself mini goals, strive for these as it helps with the time on your hands between appointments and gives you something to focus on. It is very rewarding too and gives you a lot of satisfaction, as when you succeed it helps boost your moral.
- Fear is a very strong emotion in that it can take all your energy. Communicating is definitely the key to this. You need to find somebody, it can be a family member, friend, neighbour, who ever it is don't bottle up your emotions, talk. You'll find it of great benefit and it helps eradicate a lot of problems. You'll also receive guidance so you know when you need to seek expert advice. If you have a question seek advice and ask it, don't let it eat you up inside.
- What is essential is to keep warm. I felt the cold like never before but clothes were ill fitting due to the amount of weight I'd lost. It's essential to wear comfortable warm clothes in order to feel comfortable, what I looked like at this stage wasn't even an issue. Obviously if you don't feel like going out buying clothes other people can do this for you, just to keep you ticking over until you do feel like shopping. If you haven't access to this, don't worry. You can shop as easily at home now-a-days with catalogues and over the Internet, you just have to use the services that are available to you.
- My only other tip that worked for me was positive thinking. This includes relaxation and visualising your body healing, though this will take time and require plenty of rest.

If you would like to get in touch to ask any questions my email address is [lifefterbmt@hotmail.co.uk](mailto:lifefterbmt@hotmail.co.uk)

I would be very happy to hear from you.

**After Your Bone Marrow Transplant**

**Book 7 of 8**

**Relationships after your  
Bone Marrow Transplant**

## Relationships after your Bone Marrow Transplant

This leaflet contains a collection of opinions expressed by people who have had a bone marrow transplant and by the family and friends of someone who has had a bone marrow transplant.

There is no normal or correct way to feel after you have had a bone marrow transplant. You may find that some of the things expressed in this leaflet voice exactly how you are feeling at the moment. You might read others and think 'I can't imagine ever feeling like that'.

You and the important people in your life might find it helpful to discuss how the process of a transplant has affected your lives by looking together at what other people have said.

If you are feeling particularly worried or anxious about the issues raised in this booklet or any other aspect of your recovery it's a good idea to talk to someone about how you are feeling. At the back of this leaflet is a list of some of the places you can go to get support and advice.

If you have any concerns please speak to a doctor or nurse next time you come to clinic.

### Worries and Anxieties

" I couldn't get it across to people that this was as major as having a heart transplant... If I'd had a heart transplant they wouldn't be expecting me to be running around... back to normal, but a bone marrow transplant, a lot of people really felt... it's not very major, because you don't get cut open I think..."

Patient

"It was a relief to see him back in his own home but we were so fearful of visiting and passing on colds."

Sibling

"Whilst my partner was going through the transplant process all I can remember is being so scared and worried. " What if it does not work?"

Partner

"I've watched the effect of it when she was coming in and being all brave and smiling away and going home and crying all night."

Patient speaking about the effect on his partner

"We were always anxious for news."

Sibling

"I was afraid of the phone ringing, in case it was bad news."

Friend

"Emotions were very high with a feeling of hopelessness, nothing we could do to help but be there."

Parent

"I thought a lot about why and how this happened."

Friend

## Keeping Positive

"I always tried to keep positive but it was very hard especially when visiting."

Friend

"It was also hard because the closeness you had as a couple takes a long time to come back. I felt very lonely at times. This does come back but it just takes time."

Partner

"It brought all of our relationships closer and stronger."

Sibling

"I tried to keep my friend positive by reflecting on our happy times and trying to look forward to the future."

Friend

"I have time with my child and my wife... I mean I never used to see my wife... but now I try and spend more time with her and my son."

Patient

## Ways of Coping.

"When my partner returned home from hospital it was so hard to cope with the mood swings and of course you're the closest person to them so you get the worst of it. You've got to remember it's the medication and that they don't mean to upset you."

Partner

"We took each day, a day at a time."

Parents

"Talk to the doctors and nurses ask them anything you are unsure about."

Partner

"Talk to people about how you are feeling. I bottled everything up trying to cope, trying to be brave. Not really wanting my partner to know how I was feeling. You need help as well. My family used to ask me if I was okay and I'd say I'm fine! But I wasn't! I should have been more honest about how I was feeling."

Partner

"I think life means a lot more to you when you have had a serious illness... it puts a different light on life... well it does for me anyway, like you... don't take things for granted any more."

Patient

"a friend of mine ... went through a very bad experience where she had a very bad divorce and then got re married really quickly and I was concerned and she said she wasn't going to live her life in fear... I've really hung onto it, I wasn't going to live my life in fear."

Patient

## **Where can I go for more help and advice?**

If you would like to talk to someone about any of the issues raised in this leaflet there are several places you could go for further advice and support.

- You could speak to the doctor or nurse next time you are at clinic.
- The hospital has support staff from different faiths and religions who would be happy to talk with you. You can find out more by ringing 0115 969 1169 ext 46616.
- Cancer Bacup have a cancer information and support centre at the City Hospital, Nottingham, where you can get advice and support from a specialist cancer nurse. For more information ring 0115 8402650 or go to [www.cancerbacup.org.uk](http://www.cancerbacup.org.uk).
- You could contact the Cancer Counselling Trust on 020 7704 1137. The Cancer Counselling Trust offer a confidential telephone counselling service to individuals, couples or families affected by cancer.
- You could ring the Macmillan Cancer Relief telephone line. They will be happy to talk with you and can recommend other cancer support services in your area. You can contact Macmillan Cancer Relief on the following Freephone number 0808 808 2020.
- You could ring Social Services on 0115 969 1169 ext. 46573. Many social workers are also trained counsellors.

## **After Your Bone Marrow Transplant**

**Book 8 of 8**

# **Medicines after your Bone Marrow Transplant**

## **Medicines after your Bone Marrow Transplant**

This leaflet will explain what you need to know about the most common medicines that your doctor may prescribe for you after your bone marrow transplant.

You can look up the medicine that you have been prescribed in the table and find out, why each medicine is used, how long you might expect to need it for, how to take it and any side effects that can occur when you take the medication. You will not be prescribed all of the medications in the table. Which medicines you have been prescribed will be affected by several factors including the type of transplant you have had.

It is important to take your medication regularly and to make sure you don't miss doses – this is especially important with antibiotics and ciclosporin.

Always read the labels and leaflets that come with your medication.

The doses in this booklet are only a guide. There are many reasons why your doctor may have prescribed you a different dose. For example you may be prescribed a lower dose in order to reduce the side effects or if you have kidney or liver problems.

### **What to do if you experience the side effects of your medication**

With all medicines if you notice side effects report them to a nurse, doctor or pharmacist. You should mention any minor concerns that you have when you come to clinic. If you feel that you are experiencing problematic side effects or you want some advice about your medications you can phone

Lynn Watson (Bone marrow transplant co-ordinator) 0115 969 1169  
ext. 45702

Haematology Day-Case Unit 0115 969 1169  
ext. 34263

Fletcher ward 0115 969 1169  
ext. 34687

### **What to do if you think you are allergic to your medication**

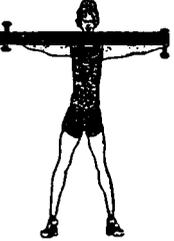
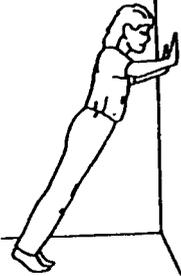
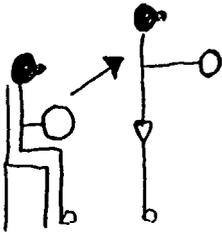
Some people can have an allergic reaction to a medication that they have been prescribed however this is very unusual. The following symptoms can occur if you are allergic to a medication;

- sudden wheezing or difficulty breathing;
- swelling of the eyelids, face or lips;
- skin lumps or hives (raised red or white itchy patches of skin).

It is very important that if you experience any of these symptoms you seek urgent medical advice.

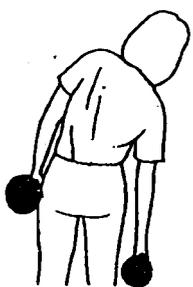
<b>Drug Name</b>	<b>Dose</b>	<b>What does it do?</b>	<b>How long must I take it for?</b>	<b>Special Instructions</b>	<b>Possible Side Effects</b>
<b>Aciclovir</b>	400mg or 800mg four times daily if you have had an allogeneic transplant.  200mg if you have had an autologous transplant.	It is an antiviral which protects against CMV (cytomegalovirus) infection, and other herpes infections.	6 months or more if you are also taking steroids or if you develop GVHD - allogeneic transplant patients only.  1 month if you have had an autologous transplant.	You should space the doses evenly throughout the day Best taken with food Can be dissolved in water	Skin rash, stomach irritation, dizziness, confusion, headaches.
<b>Ciclosporin (Neoral)</b>	The dose you are prescribed will alter according to your blood levels and your weight. Ciclosporin is usually prescribed as a liquid. The strength of the liquid is 100mg per 1ml. If you cannot tolerate the liquid you may be prescribed capsules. The capsules come in the following strengths - 25mg, 50mg, 100mg	Reduces the body's immune reaction. This is important because it protects against GVHD (Graft Versus Host Disease).  Only needed by allogeneic transplant patients.	Approximately 6 months	If you are taking the liquid-dose it must be measured in a syringe. For improved taste, dilute with orange/apple juice, squash, or water (Do not dilute with grapefruit juice). When your blood levels are going to be checked wait until after your blood test to take this medicine.	Increased blood pressure, tremor, headache, or facial hair growth. Some people experience kidney problems. The doctors will check how well your kidneys are coping with the medicine by taking regular blood tests.
<b>Ciprofloxacin</b>	250mg - 500mg twice daily.	It is an antibiotic which protects against lung infections.	For as long as your blood counts are low.	Swallow whole with water. You should take it just before, with or just after food. You should avoid drinking milk for 1 hour before taking your medication and for 4 hours after you have taken it. Space doses evenly throughout the day	Diarrhoea, sickness, headaches, dizziness, or painful tendons.
<b>Co-trimoxazole (Septrin)</b>	960mg (2 tablets) twice daily on Mondays and Thursdays	It is an antibiotic which protects against lung infections	1 month if you have had an autologous transplant. 6 months if you have had allogeneic transplant.	Best taken with food and drink You should space the doses evenly throughout the day	Nausea, vomiting.
<b>Fluconazole</b>	50mg - 200mg once daily.	It protects your body against fungal infections. It will also treat any infections that you pick up.	For as long as your blood counts are low.	There are no special instructions for taking this medicine.	Nausea, stomach discomfort, diarrhoea, wind, rash, headache.
<b>Foscarnet</b>	By injection twice daily for 2 weeks then once daily. Can be given as an infusion over 1 hour on the ward or in day case	It stops the CMV (cytomegalovirus) virus reproducing. It is used to try and prevent infection with CMV and to treat CMV disease if infection occurs.	Up to 4 weeks but may be repeated if needed.	There are no special instructions for taking this medicine.	Tingling, numbness, headaches, dizziness. Your dose may need to be reduced if your kidneys are sensitive
<b>Ganciclovir</b>	By injection twice daily for 2 weeks then once daily. Can be given as an infusion over 1 hour on the ward or in daycase.	It stops the CMV (cytomegalovirus) virus reproducing. It is used to try and prevent infection with CMV and to treat CMV disease if infection occurs.	Up to 4 weeks in total but may be repeated if CMV (cytomegalovirus) reoccurs	There are no special instructions for taking this medicine.	Chills, itchy skin, rash, muscle pain, blood pressure changes. Your dose may be reduced if your kidneys are sensitive. Treatment can reduce your white and red cell count.
<b>Itraconazole</b>	100mg twice daily	It protects your body against fungal infections, and treats any infections you pick up.	For as long as your blood counts are low.	You should space doses evenly throughout the day	Headaches, dizziness, nausea, abdominal pain or constipation.
<b>Penicillin V</b>	250mg twice daily	It is an antibiotic which protects against pneumonia.	1 month if you have had an autologous transplant. 6 months if you have had allogeneic transplant.	You should space doses evenly throughout the day After taking penicillin v you should wait for at least 30mins before eating any food	Sickness, rash, wheezing, swelling, of the lips, face or eyelids.
<b>Valganciclovir</b>	Tablets twice daily for 3 weeks then once daily	It stops the CMV (cytomegalovirus) virus reproducing. It is used to try and prevent infection with CMV and to treat CMV disease if infection occurs.	Up to 4 weeks but may be repeated if needed	There are no special instructions for taking this medicine.	Tingling, numbness, headaches, dizziness. Your dose may need to be reduced if your kidneys are sensitive.
<b>Voriconazole</b>	200mg twice daily.	It protects your body against fungal infections and treats any infections you pick up.	For as long as your blood counts are low.	You should space doses evenly throughout the day.	Headaches, dizziness, nausea, abdominal pain or constipation. It may have an effect on your liver tests.

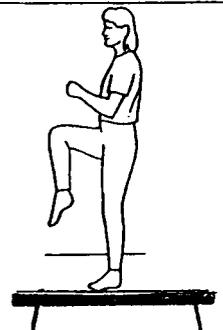
## **Appendix B - HPL Programme Exercise Sheets**

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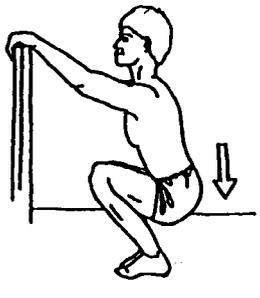
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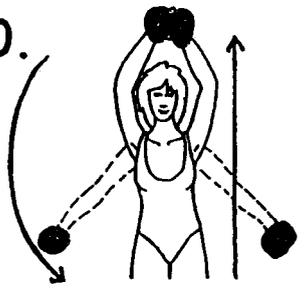
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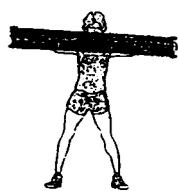
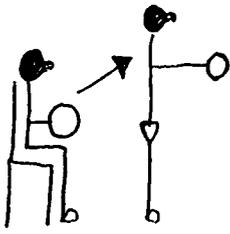
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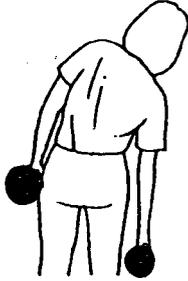
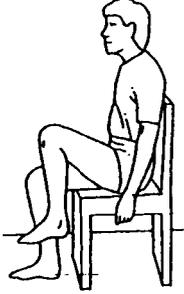
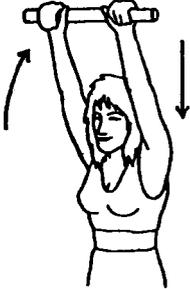
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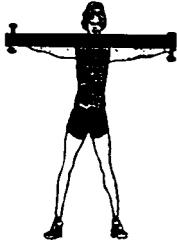
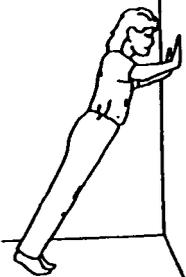
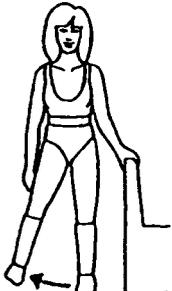
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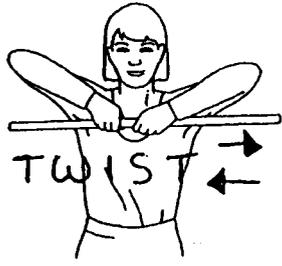
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## **Appendix C - Approach Letters and Information Sheets**

Nottingham City Hospital  
Hucknall Road  
Nottingham  
NG5 1PB

Tel: [REDACTED]

Email: [REDACTED]

Date

Dear

We would like to invite you to take part in a research trial which is investigating the effects of rehabilitation on recovery after bone marrow or peripheral stem cell transplantation.

This is a randomised controlled trial, which means that, if you agree to take part, you will be randomly assigned to one of two groups.

One group will be asked to complete a health profession led rehabilitation programme. This will involve attending the City Hospital in Nottingham, once a week for 10 weeks. Each week a physiotherapist will assist you to complete an exercise and relaxation programme – lasting about 1 hour and 20 minutes. This will be followed by a support/information session. This session is on a different topic each week and will be led by a relevant health professional. Topics that will be covered include fatigue, stress, nutrition and financial support. This discussion time will last about 40 minutes. The total time that the programme takes each week is 2 hours.

The other group will be asked to complete a self managed rehabilitation programme. This can be completed at home and therefore does not require additional visits to hospital. The programme provides advice on exercise and includes a selection of exercises that can be completed at home without specialist equipment. This programme also provides information booklets on the same topics as covered in the health profession-led programme.

If you agree to take part there is a one in two (i.e. 50%) chance of you being assigned to each group.

Please feel reassured that if you decide not to take part this will not affect your future treatment in any way.

If you would like more information about the study please feel free to speak to either [REDACTED], [REDACTED] or [REDACTED]. Contact details are listed on the attached information sheet.

With best wishes

[REDACTED]  
Clinical Haematology

## **The Macmillan Bone Marrow Transplant Rehabilitation Programme**

### **A randomised controlled trial investigating the effects of rehabilitation on recovery after bone marrow or peripheral stem cell transplantation.**

You are being invited to take part in a randomised controlled trial. Before you decide if you would like to take part, it is important for you to understand why we are undertaking the study and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

#### **The purpose of the study**

Bone marrow or stem cell transplants are an increasingly common treatment for many cancers of the blood. However, recovering after a bone marrow or stem cell transplant can be difficult and frustrating. This is because treatment with a transplant has many side effects. The extent and type of side effects that people experience vary. Common problems include fatigue, reduced ability to carry out physical tasks, and weight loss.

We are investigating ways of supporting people who have had a bone marrow or stem cell transplant. Two different rehabilitation programmes have been devised which provide information on how to cope with the common side effects experienced after a bone marrow or stem cell transplant. We want to compare these two programmes, so we are inviting people who have had bone marrow or stem cell transplants to take part in this study. People who choose to take part will be asked to complete one or other of the programmes.

#### **What do the two programmes consist of?**

One programme is a health profession led rehabilitation programme. Participants assigned to this programme will be asked to attend the City Hospital in Nottingham once a week for 10 weeks. Each week participants will take part in a series of group activities. A physiotherapist will assist participants to complete a group exercise and relaxation programme. This will be followed by a group support/information session. This session will be on a different topic each week and will be led by a relevant health professional. Topics that will be covered include fatigue, stress, nutrition and financial support. The total time that the programme takes each week is 2 hours.

The other programme is a self-managed rehabilitation programme. This draws together the information and advice that is available to patients after a transplant into an information pack that can be read at home. The programme provides advice on exercise and includes a selection of exercises that can be completed at home without specialist equipment.

## **How do the two programmes compare with the usual care patients receive after a bone marrow transplant?**

Currently patients recovering after a bone marrow or stem cell transplant are given advice about coping at home before they are discharged from hospital, they are then seen regularly, initially once a week, at an outpatient clinic. There are also a large number of resources that patients can access to find out more information about coping after a transplant, for example the hospital has a Cancer Bacup Information Centre where anyone affected by cancer can get information and advice. Regardless of whether or not someone takes part in this study they will receive this care and the usual support systems will be available to them.

## **Can I choose which programme I would like to complete?**

If you agree to take part in the study you will be assigned to one or other of these two programmes. Participants are randomly assigned to one or other of the groups by a computer that does not have any information about the individual – ie. by chance.

The fact that assignment to each group is random means that you cannot choose which group you would like to be part of. None of the staff involved in this trial or in your routine care have any control over the group to which you are assigned. If you decide to take part there is a one in two (i.e. 50%) chance of you being assigned to each group.

## **Why have I been chosen?**

As you have already undergone a bone marrow/stem cell transplant we would like to invite you to take part in this study.

## **Do I have to take part?**

It is entirely up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and you will be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

## **What would I have to do?**

As well as completing the programme assigned to them, participants from both groups will be asked to complete three questionnaires on three separate occasions; at the start of the trial, at the end of the rehabilitation programme; and after six months. Participants will be asked to complete these questionnaires when attending a routine clinic appointment. The questionnaires should only take about 25 minutes to complete.

Your exercise capacity will also be assessed at the start of the trial, after the end of the rehabilitation programme and after six months. This assessment will take place when you come for a routine clinic appointment and should take about 20 minutes to complete.

Some patients will also be invited to take part in an interview with a researcher at the end of the trial. This can take place whilst you are visiting for a clinic appointment or we can arrange for a researcher to visit you at home. The interview will take approximately 1 hour and if you give permission an audio

recording of the interview will be made. If you agree to take part in an interview but find that talking about your experiences is distressing, the interview can be stopped at any time. This is the same whether you are interviewed at clinic or in your own home. The person conducting the interviews is a trained nurse and they will seek to minimise the potential for distress.

If you find any part of this research distressing you can contact either [REDACTED] who can provide further support and advice. The contact numbers for [REDACTED] are at the end of this information sheet.

There will be no other restrictions imposed on you, and you should continue with your usual activities as normal.

### **What are the risks and disadvantages of taking part?**

We do not believe that by being involved in the programme you will be taking any personal risk. The exercise components of the programme have been designed to meet individuals needs and capabilities.

### **What are the possible benefits of taking part?**

We hope that undertaking either programme will be of benefit to you, however we cannot guarantee this. The information from this study may help us to improve the care given to future patients recovering following a bone marrow/stem cell transplant.

### **What if something goes wrong?**

If taking part in this study harms you, there are no special compensation arrangements. If you are harmed due to someone's' negligence, then you may have grounds for legal action but you may have to pay for it. If you wish to complain about any aspects of the way you have been approached or treated during the course of this study, you can contact [REDACTED] works for the University of Nottingham but is completely independent of this research. His contact details are provided at the end of this information sheet.

### **Will my taking part in this study be kept confidential?**

All information collected about you during the course of the study will be kept strictly confidential. Any information about you which leaves the hospital will have your name and address removed so that you cannot be recognised from it.

If you decide to take part we will be informing your GP of your participation in this trial.

### **What will happen to the results of the study?**

We do not anticipate producing any results of the research until the two-year programme has been completed. Your identity will remain anonymous upon publication of the results.

Once the results have been analysed you will be invited to an informal meeting at the City Hospital, Nottingham so that you can find out how the study went. A brief written report will also be sent to you.

**Who is organising and funding the project?**

The study is being organised by a team from the School of Nursing at the University of Nottingham, working with the Haematology team at Nottingham City Hospital.

The programme has been funded with a grant from Macmillan Cancer Relief.

None of the team will be financially rewarded by your taking part in this study.

Finally we would like to thank you for reading this. If you have any more questions please contact a member of the team who will be happy to discuss the study with you.

**Contact names and numbers.**

For information and support please contact

Details removed to maintain confidentiality

## **Participant Information Sheet**

### **The Macmillan Bone Marrow Transplant Rehabilitation Programme Trial.**

We would like to invite you to be interviewed about your involvement in the rehabilitation after bone marrow or peripheral stem cell transplantation research trial. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish.

Ask if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

#### **What is the purpose of the study?**

We are conducting a number of interviews with doctors, nurses and allied health professionals as part of a larger study investigating recovery after bone marrow or stem cell transplantation. It is anticipated that the interviews with these staff will provide an opportunity to explore the thoughts and opinions of staff about recovery after bone marrow or stem cell transplantation and the Macmillan Bone Marrow Transplant Rehabilitation Trial.

#### **Why have I been chosen?**

You have been chosen to be invited to take part in an interview because you have been involved in the rehabilitation trial.

#### **Do I have to take part?**

No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason

#### **What will happen to me if I take part?**

If you decide to take part we will arrange a time and location for an interview which is convenient for you. This will be during work time and the interview will take place in a quiet room in the clinic or office areas. It is not expected that interviews will last for longer than 1 hour.

#### **Will my taking part in the study be kept confidential?**

Yes. All the information about your participation in this study will be kept confidential. Your identity will remain anonymous in any publications of the results.

#### **What if I have a complaint about the study?**

If you have a concern about any aspect of this study, you should ask to speak with the primary researcher who will do their best to answer your questions (██████████). If you remain unhappy and wish to complain formally, you can do (██████████).

this through the NHS Complaints Procedure. Details can be obtained from the hospital.

**What will happen to the results of the research study?**

Once the results have been analysed you will be invited to an informal meeting at the City Hospital, Nottingham so that you can find out how the study went. A brief written report will also be sent to you.

**Who is organising and funding the project?**

The study is being organised by a team from the School of Nursing at the University of Nottingham. The programme has been funded with a grant from Macmillan Cancer Relief.

For further information about the study please contact



***Thank you for taking the time to read this information sheet.***

## **Appendix D – Trial Paperwork**

Consent forms, GP information letter, consultant referral form & randomisation letters

**CONSENT FORM**

**A randomised control trial investigating the effects of rehabilitation on recovery after bone marrow or peripheral stem cell transplantation.**

Nottingham City Hospital

Department of Clinical Haematology and the University of Nottingham

Please initial box

I confirm that I have read & understood the patient information sheet

I confirm that I have had opportunity to ask questions & discuss the study and my questions have been answered satisfactorily

I understand that my participation is voluntary and I am free to withdraw at any time, without giving a reason, without my medical care or legal rights being affected.

I understand that sections of any of my medical notes may be looked at by the researcher from the University of Nottingham or from regulatory authorities where it is relevant to my taking part on this research. I give permission for these individuals to have access to my records.

I give permission for my GP to be informed that I am taking part on this research.

I agree to take part in the above study.

\_\_\_\_\_  
Name of Patient

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Name of person taking consent  
(if different to researcher)

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Researcher

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

**CONSENT FORM for interview participation.**

**A randomised control trial investigating the effects of rehabilitation on recovery after bone marrow or peripheral stem cell transplantation.**

Nottingham City Hospital

Department of Clinical Haematology and the University of Nottingham

Please initial box

I agree to being interviewed about my experience of recovering after a BM/SCT

I agree to the interview being recorded with audio equipment

I understand that anonymous quotations from this interview may be used in publications about this research

I understand that I am free to stop the interview at any time, without giving a reason and without my future care or legal rights being affected.

\_\_\_\_\_  
Name of Patient

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Name of person taking consent  
(if different to researcher)

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Researcher

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

**CONSENT FORM for interview participation.**

**A randomised control trial investigating the effects of rehabilitation on recovery after bone marrow or peripheral stem cell transplantation (BM/SCT).**

Nottingham City Hospital

Department of Clinical Haematology and the University of Nottingham

Please initial box

I agree to being interviewed about my involvement in the BM/SCT rehabilitation trial.

I agree to the interview being recorded with audio equipment

I understand that anonymous quotations from this interview may be used in publications about this research

I understand that I am free to stop the interview at any time, without giving a reason and without my employment and legal right being affected.

\_\_\_\_\_  
Name of Participant

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Name of person taking consent  
(if different to researcher)

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Researcher

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

## **The Macmillan Bone Marrow Transplant Rehabilitation Programme Trial.**

**A randomised controlled trial investigating the effects of rehabilitation on recovery after bone marrow or peripheral stem cell transplantation.**

GP Information Letter

Name of Patient .....

Hospital Number .....

We are writing to inform you that the above patient has agreed to take part in the Macmillan Bone Marrow Transplant trial. Some information regarding this study is included below but if you would like further information please contact Lydia Bird on 9249924 ext 42462.

Signature

Date

### **The purpose of the study**

It is estimated that world-wide approximately 100000 people are 5 year survivors of bone marrow/peripheral blood stem cell transplant (BM/SCT). This once experimental procedure is now the treatment of choice for many patients diagnosed with haematological malignancies. However the enormous impact that diagnosis and subsequent treatment with BM/SCT has on an individual should not be underestimated. Whilst this process does now offer the chance of cure from previously fatal diseases, it is still a high risk treatment which is associated with significant short and long term side effects that have a considerable impact on patients' quality of life. Common complications include infection, bleeding, malaise, nausea, pain, reduced physical functioning and fatigue.

This study aims to investigate physical and psychosocial recovery after BM/SCT. A randomised controlled study design has been chosen to evaluate different programmes aimed at providing support and information to patients who have undergone a BM/SCT. Participants are randomly allocated to one or other of the rehabilitation programmes.

### **What do the two programmes consist of?**

One programme is a health profession led rehabilitation programme. Participants assigned to this programme will be asked to attend the City Hospital in Nottingham once a week for 10 weeks. Each week participants will take part in a series of group activities. A physiotherapist will assist participants to complete a group exercise and relaxation programme. This will be followed by a group support/information session. This session will be on a different topic each week and will be led by a relevant health professional. Topics that will be covered include fatigue, stress, nutrition and financial support. The total time that the programme takes each week is 2 hours.

The other programme is a self-managed rehabilitation programme. This draws together the information and advice that is usually given to patients after a transplant into an information pack that can be read at home. The programme provides advice on exercise and includes a selection of exercises that can be completed at home without specialist equipment.

### **How do the two programmes compare with the usual care patients receive after a bone marrow transplant?**

Currently patients recovering after a bone marrow or stem cell transplant are given advice about coping at home before they are discharged from hospital, they are then seen regularly, initially once a week, at an outpatient clinic. There are also a large number of resources that patients can access to find out more information about coping after a transplant. Regardless of whether or not someone takes part in this study they will receive this care and the usual support systems will be available to them.

### **What are participants asked to do?**

As well as completing the programme assigned to them, participants from both groups will be asked to complete three questionnaires on three separate occasions; at the start of the trial, at the end of the rehabilitation programme; and after six months. Participants will be asked to complete these questionnaires when attending a routine clinic appointment.

Participants exercise capacity will also be assessed at the start of the trial, after the end of the rehabilitation programme and after six months.

Some patients will also be invited to take part in an interview with a researcher at the end of the trial.

### **Who is organising and funding the project?**

The study is being organised by a team from the School of Nursing at the University of Nottingham, working with the Haematology team at Nottingham City Hospital.

The programme has been funded with a grant from Macmillan Cancer Relief.

### **For further information about the study please contact**



**The Macmillan Bone Marrow Transplant Programme Trial.**

**Consultant Referral**

Name of Patient .....

Hospital Number .....

Date of Transplant .....

Type of Transplant .....

I am in agreement with the above patient taking part in the Macmillan Bone Marrow Transplant programme trial. I have assessed the above and their blood counts and confirm that they are physically able to take part in the programme.

Signature of Doctor

Date

0 [REDACTED] 7

[REDACTED]

Date

Dear

Thank you for agreeing to take part in the Macmillan Bone Marrow Transplant Rehabilitation Trial. You have been randomly allocated to the Health Profession Led Rehabilitation Programme.

This will involve attending the City Hospital in Nottingham, once a week for 10 weeks. Each week a physiotherapist will assist you to complete an exercise programme. The exercise programme will be tailored to your current level of health. The exercise session is followed by a relaxation time which will usually consist of a hand, foot or shoulder massage. This will be followed by a support/information session. This information session is on a different topic each week and will be led by a relevant health professional. Topics that will be covered include fatigue, stress, nutrition and financial support. The total time that the programme takes each week is approximately 2 hours.

The first rehabilitation session that you should attend will be held on

You need to arrive by **12pm** and report to the **Physiotherapy Main Department Gym**.

Please wear comfortable loose fitting clothes and flat shoes. You do not need to wear sports clothing and trainer shoes. You might also like to bring a warm jumper or jacket as you may feel cold when you finish exercising.

If you would like more information please feel free to speak to [REDACTED]

[REDACTED].

With best wishes

The BMT Rehabilitation Trial Team.

Nottingham City Hospital  
Hucknall Road  
Nottingham  
NG5 1PB

[REDACTED]

[REDACTED]

Date

Dear

Thank you for agreeing to take part in the Macmillan Bone Marrow Transplant Rehabilitation Trial. You have been randomly allocated to the Self Managed Rehabilitation Programme.

With this letter you will be given a information pack that has been written specifically for people who have just had a bone marrow or stem cell transplant. The pack contains advice and information on eight different topics. One of these is exercise. As well as providing guidance on exercising safely the leaflet suggests a programme of exercises for you to complete at home.

Please take these leaflets home with you and read them carefully. You can ask any questions, you may have, relating to the information in the leaflets on any visit to clinic. In approximately 12 weeks time you will be asked to complete the same questionnaires as you have completed today. We will also ask you to complete them again in 6 months time.

If you would like more information please feel free to speak to [REDACTED]  
[REDACTED].

With best wishes  
The BMT Rehabilitation Trial Team.

## **Appendix E - Data Collection Questionnaires**

## Your Health and Well-Being

---

**This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. Thank you for completing this survey!**

**For each of the following questions, please tick the one box that best describes your answer.**

**1. In general, would you say your health is:**

Excellent	Very good	Good	Fair	Poor
▼	▼	▼	▼	▼
<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	<input type="checkbox"/> <sub>5</sub>

**2. Compared to one year ago, how would you rate your health in general now?**

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago
▼	▼	▼	▼	▼
<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	<input type="checkbox"/> <sub>5</sub>

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, limited a lot ▼	Yes, limited a little ▼	No, not limited at all ▼
a. <u>Vigorous activities</u> , such as running, lifting heavy objects, participating in strenuous sports.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
b. <u>Moderate activities</u> , such as moving a table, pushing a vacuum cleaner, bowling, or playing golf.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
c. Lifting or carrying groceries .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
d. Climbing <u>several</u> flights of stairs.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
e. Climbing <u>one</u> flight of stairs.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
f. Bending, kneeling, or stooping.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
g. Walking <u>more than a mile</u> .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
h. Walking <u>several hundred yards</u> .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
i. Walking <u>one hundred yards</u> .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3
j. Bathing or dressing yourself.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3

4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time ▼	Most of the time ▼	Some of the time ▼	A little of the time ▼	None of the time ▼
a. Cut down on the <u>amount of time</u> you spent on work or other activities .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
b. <u>Accomplished less</u> than you would like.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
c. Were limited in the <u>kind</u> of work or other activities.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
d. Had <u>difficulty</u> performing the work or other activities (for example, it took extra effort).....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

5. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Cut down on the <u>amount of time</u> you spent on work or other activities .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
b. <u>Accomplished less</u> than you would like .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
c. Did work or other activities <u>less carefully than usual</u> .....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?

Not at all	Slightly	Moderately	Quite a bit	Extremely
<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

7. How much bodily pain have you had during the past 4 weeks?

None	Very mild	Mild	Moderate	Severe	Very severe
<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/> 6

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely
▼	▼	▼	▼	▼
<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	<input type="checkbox"/> <sub>5</sub>

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks...

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
	▼	▼	▼	▼	▼

a	Did you feel full of life? .....	<input type="checkbox"/> <sub>1</sub>	.....	<input type="checkbox"/> <sub>2</sub>	.....	<input type="checkbox"/> <sub>3</sub>	.....	<input type="checkbox"/> <sub>4</sub>	.....	<input type="checkbox"/> <sub>5</sub>
b	Have you been very nervous? .....	<input type="checkbox"/> <sub>1</sub>	.....	<input type="checkbox"/> <sub>2</sub>	.....	<input type="checkbox"/> <sub>3</sub>	.....	<input type="checkbox"/> <sub>4</sub>	.....	<input type="checkbox"/> <sub>5</sub>
c	Have you felt so down in the dumps that nothing could cheer you up? .....	<input type="checkbox"/> <sub>1</sub>	.....	<input type="checkbox"/> <sub>2</sub>	.....	<input type="checkbox"/> <sub>3</sub>	.....	<input type="checkbox"/> <sub>4</sub>	.....	<input type="checkbox"/> <sub>5</sub>
d	Have you felt calm and peaceful? .....	<input type="checkbox"/> <sub>1</sub>	.....	<input type="checkbox"/> <sub>2</sub>	.....	<input type="checkbox"/> <sub>3</sub>	.....	<input type="checkbox"/> <sub>4</sub>	.....	<input type="checkbox"/> <sub>5</sub>
e	Did you have a lot of energy? .....	<input type="checkbox"/> <sub>1</sub>	.....	<input type="checkbox"/> <sub>2</sub>	.....	<input type="checkbox"/> <sub>3</sub>	.....	<input type="checkbox"/> <sub>4</sub>	.....	<input type="checkbox"/> <sub>5</sub>
f	Have you felt downhearted and low? .....	<input type="checkbox"/> <sub>1</sub>	.....	<input type="checkbox"/> <sub>2</sub>	.....	<input type="checkbox"/> <sub>3</sub>	.....	<input type="checkbox"/> <sub>4</sub>	.....	<input type="checkbox"/> <sub>5</sub>
g	Did you feel worn out? .....	<input type="checkbox"/> <sub>1</sub>	.....	<input type="checkbox"/> <sub>2</sub>	.....	<input type="checkbox"/> <sub>3</sub>	.....	<input type="checkbox"/> <sub>4</sub>	.....	<input type="checkbox"/> <sub>5</sub>
h	Have you been happy? .....	<input type="checkbox"/> <sub>1</sub>	.....	<input type="checkbox"/> <sub>2</sub>	.....	<input type="checkbox"/> <sub>3</sub>	.....	<input type="checkbox"/> <sub>4</sub>	.....	<input type="checkbox"/> <sub>5</sub>
i	Did you feel tired? .....	<input type="checkbox"/> <sub>1</sub>	.....	<input type="checkbox"/> <sub>2</sub>	.....	<input type="checkbox"/> <sub>3</sub>	.....	<input type="checkbox"/> <sub>4</sub>	.....	<input type="checkbox"/> <sub>5</sub>

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
▼	▼	▼	▼	▼
<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	<input type="checkbox"/> <sub>5</sub>

11. How TRUE or FALSE is each of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
	▼	▼	▼	▼	▼
a. I seem to get ill more easily than other people.....	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	<input type="checkbox"/> <sub>5</sub>
b. I am as healthy as anybody I know.....	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	<input type="checkbox"/> <sub>5</sub>
c. I expect my health to get worse.....	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	<input type="checkbox"/> <sub>5</sub>
d. My health is excellent.....	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>	<input type="checkbox"/> <sub>3</sub>	<input type="checkbox"/> <sub>4</sub>	<input type="checkbox"/> <sub>5</sub>

*Thank you for completing these questions!*

Study Number:  
Today's date:  
Date of Birth:

# General Health Questionnaire

(GHQ-12)

**Please read this carefully.**

We should like to know if you have had any medical complaints and how your health has been in general, over the last few weeks. Please answer ALL the questions simply by underlining the answer which you think most nearly applies to you. Remember that we want to know about present and recent complaints, not those that you had in the past.

It is important that you try to answer ALL the questions.

Thank you very much for your co-operation.

Have you recently . . .

1. been able to concentrate on whatever you're doing?	Better than usual	Same as usual	Less than usual	Much less than usual
2. lost much sleep over worry?	Not at all	No more than usual	Rather more than usual	Much more than usual
3. felt that you are playing a useful part in things?	More so than usual	Same as usual	Less useful than usual	Much less useful
4. felt capable of making decisions about things?	More so than usual	Same as usual	Less so than usual	Much less than usual
5. felt constantly under strain?	Not at all	No more than usual	Rather more than usual	Much more than usual
6. felt you couldn't overcome your difficulties?	Not at all	No more than usual	Rather more than usual	Much more than usual
7. been able to enjoy your normal day-to-day activities?	More so than usual	Same as usual	Less so than usual	Much less than usual
8. been able to face up to your problems?	More so than usual	Same as usual	Less so than usual	Much less able
9. been feeling unhappy and depressed?	Not at all	No more than usual	Rather more than usual	Much more than usual
10. been losing confidence in yourself?	Not at all	No more than usual	Rather more than usual	Much more than usual
11. been thinking of yourself as a worthless person?	Not at all	No more than usual	Rather more than usual	Much more than usual
12. been feeling reasonably happy, all things considered?	More so than usual	About same as usual	Less so than usual	Much less than usual

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Study Number:  
Today's Date:  
Date of Birth:

## **The Graham and Longman Two Question Quality of Life Scale.** (Graham and Longman 1987).

- How would you rate your current quality of life?

(poor) 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 (excellent)

- How satisfied are you with your current quality of life?

(not satisfied at all) 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 (very satisfied)

Thank you for taking the time to answer these questions.

**Name** \_\_\_\_\_

**Date** \_\_\_\_\_

**Which Rehabilitation Programme would you prefer to complete?**

**Self Managed / Health Profession Led / No preference**

Please be aware that your choice will not affect which group you are allocated to.

**The Macmillan Bone Marrow Transplant Programme**  
**Patient Demographic Information**

Name of Patient -----  
 Hospital Number -----  
 Disease Type -----  
 Date of Diagnosis -----  
 Date of Birth -----  
 Gender Male/Female  
 Height -----  
 Weight -----  
 Type of Treatment:  
     Conditioning protocol -----  
     Type of Transplant -----  
     Source of Cells -----  
     Date of Transplant -----  
     Disease status (time of transplant) -----  
     Current Disease Status -----

Most Recent Blood Count Results:  
     Haemoglobin -----  
     Platelets -----  
     White cells -----  
     Neutrophils -----

CMV status:  
     Donor -----  
     Recipient -----

GVHD:  
     Grade -----  
     Site -----  
     Acute/Chronic

Social Circumstances, patient lives:  
     Alone Yes/No  
     With NOK Yes/No  
     With dependants Yes/No

## **Appendix F - Interview Schedules**

## Interview Guide - HPL

Thank you for agreeing to see me. Please feel free to say exactly what you want. I am interested in your story and your views. What you tell me will be treated in the strictest confidence.

I have come to talk to you today about the rehabilitation trial that you have taken part in over the last 6 months.

Now that you are at the end of the trial how do you feel about having taken part?

---

How did you feel about the fact that the allocation of the rehabilitation programmes was done randomly?

Did you receive the programme that you most preferred?

At the time how did that make you feel?

Looking back now do you still feel the same way?

---

Can you tell me about the rehabilitation programme that you received?

Was the programme what you expected?

How did you find the exercise component of the rehab?

Was it helpful?

Would you change anything about the exercise sessions?

Did you use the structured exercises that were described in the leaflet?

How did you find them?

Do you use the exercise diary?

Are you still doing them?

---

How did you find the information sessions?

Which ones were you able to attend?

Were you given information that was new / helpful?

What stands out in your memory about the information sessions?

Would you change anything about the information sessions?

What about the other information leaflets?

Were they helpful?

What stands out in your memory about the leaflets?

Would you change anything about the information leaflets?

---

Did you find the relaxation exercises helpful?

---

How did you find being in a group with other people who had also had bone marrow or stem cell transplants?

How important or unimportant was this aspect of the programme for you?

---

How did you find the questionnaires that you were asked to fill in?

How did you find the walking test?

Were these a bother to complete? Did you find that they caused any problems with your visit to clinic?

Did you have to make an extra trip to hospital to complete them?

---

If you could step back in time would you change any of the decisions you made in relation to the trial?

Is there anything that you think should be changed about the trial?

Is there anything else you would like to share with me about either the trial or the rehab programme?

### General Probes:

Could you tell me a bit more about that  
How did you find that experience

What do you mean by...  
How did that make you feel

What could have been done different  
Why do you think that happened

## Interview Guide – SM

Thank you for agreeing to see me. Please feel free to say exactly what you want. I am interested in your story and your views. What you tell me will be treated in the strictest confidence.

I have come to talk to you today about the rehabilitation trial that you have taken part in over the last 6 months.

Now that you are at the end of the trial how do you feel about having taken part?

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How did you feel about the fact that the allocation of the rehabilitation programmes was done randomly?

Did you receive the programme that you most preferred?

At the time how did that make you feel?

Looking back now do you still feel the same way?

---

Can you tell me about the rehabilitation programme that you received?

Was the programme what you expected?

How did you find the exercise component of the rehab?

Did you use the structured exercises that were described in the leaflet?

How did you find them?

Do you use the exercise diary?

Are you still doing the exercises?

---

What about the other leaflets?

Were they helpful?

Did they contain information that was new to you?

What stands out in your memory about the leaflets?

Would you change anything about the information leaflets?

---

How did you feel about not being in a group with other people who had also had bone marrow or stem cell transplants?

---

How did you find the questionnaires that you were asked to fill in?

How did you find the walking test?

Where these a bother to complete? Did you find that they caused any problems with your visit to clinic?

Did you have to make an extra trip to hospital to complete them?

---

If you could step back in time would you change any of the decisions you made in relation to the trial?

Is there anything that you think should be changed about the trial?

Is there anything else you would like to share with me about either the trial or the rehab programme?

### General Probes:

Could you tell me a bit more about that  
How did you find that experience

What do you mean by...  
How did that make you feel

What could have been done differen  
Why do you think that happened

## **Staff interviews – Nursing and Physio staff**

Thanks for agreeing to be interviewed.

Can you start by telling me about the work that you do with BMT patients as part of your regular clinical role?

Can you tell me about your involvement in the BMT rehab trial?  
Design, Set up, Running, Recruiting

And what about the HPL programme in particular?

Which elements of the programme did you think were particularly important?

How did you find your involvement in the trial?  
What was positive/negative?

How did you feel about the trial being run in the department?

Did you have any concerns about the trial?

As you will be aware the trial did not recruit as many patients as would have been ideal. Did this surprise you?

Where you involved in speaking to patients about the trial?

How did you find this?

Do you have any ideas about how recruitment and retention could have been increased?

From your experience of working with patients who have had BMT what do you think are the key barriers to engagement with rehab services? And what do you think promotes engagement?

In both this study and others, where patients have been interviewed retrospectively about their illness many patients suggest that they would have liked more rehab. Yet engagement with the intervention in this trial was low. Do you have any ideas why that is?

What do you think should happen to the programmes now that the trial has finished?  
HPL/SM

Is there anything you think should be done differently if the trial was starting over again?

Can you tell me what you hoped the trial would achieve? Do you think this happened?

## **Staff interviews – Doctors**

Thanks for agreeing to be interviewed.

How did you feel about the trial being run in the department?

Did you have any concerns about the trial?

As you will be aware the trial did not recruit as many patients as would have been ideal. Did this surprise you?

Where you involved in speaking to patients about the trial?

Did patients ever speak to you/seek advice from you in relation to the trial?

Do you have any ideas about how recruitment and retention could have been increased?

From your experience of working with patients who have had BMT what do you think are the key barriers to engagement with rehab services? And what do you think promotes engagement?

In both this study and others, where patients have been interviewed retrospectively about their illness many patients suggest that they would have liked more rehab. Yet engagement with the intervention in this trial was low. Do you have any ideas why that is?

What do you think should happen to the programmes now that the trial has finished?  
HPL/SM

Is there anything you think should be done differently if the trial was starting over again?

Can you tell me what you thought the trial would achieve? Do you think this happened?

## **Appendix G – Power Calculation**

Power Calculation to determine sample size.

The following formula (Pocock, 1983) was used to calculate the sample size required for the trial.

$$n = \frac{2\sigma^2}{(v_2 - v_1)^2} \times f(\alpha, \beta)$$

$\sigma$  = the standard deviation of the mean change obtained from the pilot data

$v_2 - v_1$  = expected change in mean response

$f(\alpha, \beta)$  = Value for power and significance obtained from Pocock (1983) where alpha=0.05 and beta=0.2.

$$n = \frac{2 \times 18.92^2}{10^2} \times 7.9$$

$$n = 56.6$$

$$2n = 114$$

Aim to recruit 132 to allow for 15% attrition.