PSYCHOLOGICAL RESPONSES TO BONE-MARROW-TRANSPLANTATION

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ABSTRACT OF THESIS

This thesis contains two studies; the main study investigating psychological consequences of Bone Marow Transplantation for patients and a study investigating the difficulties experienced by the 'significant other' close to the patient investigated.

Study into Psychological Consequences of Bone Marrow Transplantation

The aim of this study was to investigate the feelings of anxiety, depression, quality of life and mental adjustment to cancer in a group of patients undergoing Bone Marrow Transplantation at the Royal Marsden Hospital and the Royal Free Hospital. It was hoped that the findings, as well as offering a contribution to knowledge, would provide a basis for improving the care of patients, and that a fuller understanding of their changing feelings during the period of treatment would enable medical staff to respond more effectively to their needs.

To this end the main study follows a group of patients from their decision for transplant as a treatment option to a year post-transplant. Assessment of the patients' psychological states was done at fixed points at the end of evaluated stages. These stages were evaluated according to findings from literature and the observation of past research that the psychological well-being of these patients closely follows their medical procedure.

Seven sequential stages were evaluated for this study and patients were assessed at the end of each stage. Furthermore, 3 non-sequential assessments were added. These were at the time of discharge, first rehospitalization following transplant and if the patient relapsed.

At each assessment patients' psychological state was assessed by a number of established questionnaires with regards to their levels of anxiety, depression, quality of life and mental adjustment to cancer. In addition a semi-structured interview was used to evaluate issues around the patient's decision for transplant, the patients' expectations, stressful events and available support throughout the transplant period.

It was hypothesised that the variables investigated do not remain constant during the treatment but are influenced by the changes in the treatment during the different stages.

The result shows that patients' emotional well-being changes with changing stages. The obtained results confirm hypotheses that patients' emotional well-being does not remain consistent throughout the transplant period, but tended to change during different stages depending on treatment procedures and events happening during the assessed stage.

However patients' expectations regarding the outcome of this treatment tend to remain stable throughout.

Responses Of The Patient's Relative

The aim of the study of the patient's significant other was to investigate the psychological responses of the 'significant other' to the patient's medical and psychological experiences during the medical procedure. This was done by one interview. The interview sought to discover the information provided to them about the procedure, the distress they experienced from their close contact with the patient, and what kind of support they needed and found. To this end, relatives of surviving patients were interviewed once at three months post-transplant by a questionnaire designed by the author and based on observations on the ward.

The results of these interviews indicated that the relatives were generally well informed about the medical procedure and its physical side effects, but that they felt ill-prepared and unsupported in dealing with the unexpected side effects of the treatment. Patients in pain and feeling hopeless and low caused most distress to the involved relatives.

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1.1.1 Background

Bone Marrow Transplantation (BMT) is a treatment for haematological disorders. It is a relatively new medical procedure and has been used in clinical settings for approximately 25 years. (Kamani & August, 1984). The objective of this treatment is to replace the patient's own malignant, defective or absent cells with normal haematopoietic cells, (ibid).

BMT has been made possible by scientific advances in the following three areas:

1. the area of histocompatability;

2. the area of chemotherapy and radiotherapy allowing:

    a) eradication of diseased cells,
    b) an immunosuppressive state;
    c) a space for the transplanted marrow to grow;

3. the area of general medicine, allowing medical support for the patient without immunity during the period following eradication of the patient's own marrow until successful engraftment of the transplanted marrow.

Initially BMT was only performed on patients who had donors with an identical human leukocyte antigen (HLA) complex, found in genetically identical twins. Transplants in which donor and recipients are identical twins are called syngeneic transplants. Later BMT was expanded to patient-donor pairs with non-identical but matched HLA complex but who were related, mostly siblings, and to unrelated patient-donor pairs with HLA matched complex. These transplants are called allogeneic transplants. However, an HLA matched donor is found for only 35-40% of patients (O'Reilly, 1983) and the majority of patients remains without a suitable donor. In cases without a suitable donor, the patient's own, previously harvested marrow, collected in remission, has become the third alternative to related and unrelated donors. This form of transplant is called autologous transplant.

Many clinicians consider BMT as "the treatment of choice" for severe Aplastic Anaemia and congenital disorders such as Franconis Anaemia and Gaucher Disease, (O'Reilly, 1983; Kamani & August, 1984; Deeg, 1988; Lesko, 1990).

In the early stages of this new treatment, syngeneic and allogeneic transplants were used for end-stage patients only. In the last 20 years the application of BMT has been expanded. BMT is now the preferred treatment for Aplastic Anaemia and Congenital Disorders, and an experimental treatment for the Leukaemias, Lymphoma, tumours such as breast carcinomas, testicular cancer, AIDS and Hodgkin's Disease.

BMT is a potentially life saving treatment but at the same time the procedure can be fatal. The patient is prepared, or "conditioned", for transplant with high doses of chemotherapy and radiotherapy. However, this conditioning procedure is more toxic than any other intensive chemotherapy used in the conventional treatment of cancer (Philipps, 1988).

As Klingemann (1988) explained:

> "Conditioning regimes produce considerable morbidity, and at least contribute to the high mortality rate observed early after transplantation ", (p 85).

When BMT was introduced into clinical practice, it was applied to patients who did not respond to conventional treatment such as chemotherapy, or for whom all available treatment options had been exhausted. Mortality among this group of patients was high. (Thomas et al., 1983; Barrett, 1987; Kanfer, 1988). In subsequent applications of BMT it was shown that the survival rate increased if this treatment was performed in the early stages of the patient's disease. (Thomas et al., 1983; Barrett, 1987; Kanfer, 1988; Gale & Butturini, 1989).

Treatment outcome is also influenced by additional factors such as disease stage, the patient's age, the patient's overall medical condition, histocompatability of the donated marrow and the donor's age and sex, although the effect of the latter two factors on outcome are not altogether clear. (Klingemann et al, 1986; Barret, 1987; Burnett, 1988; Working Party on Leukaemia, European Group for BMT, 1988).

During the last 10 years the USA and Europe has witnessed the expansion of experimental BMT. In 1981 fewer than 200 Bone-Marrow-Transplantations were

performed per year world-wide. In 1991 no less than 143 teams in 20 European countries performed 4234 Bone-Marrow-Transplantations. (Gratwohl 1991).

However, in a recent analysis by the "Working Party on Leukaemia European Group for BMT " (1988) it was concluded that the percentage of leukaemia-free patients surviving the BMT procedure has not changed since 1979.

1.1.2 The Timing Of The Treatment:

More patients survived and they survived longer when transplanted earlier; that is during the chronic stage in the chronic Leukaemias; during first remission instead of third remission in the acute Leukaemias, or in the un-transfused patient with Aplastic Anaemia. The state of remission in patients with acute Leukaemias treated by chemotherapy can be defined as a condition in which the number of leukaemic cells falls to "less than 4% of the bone marrow. " and " the Leukaemia is usually undetectable or in remission". (Hoffbrand & Pettit, 1980).

This has been confirmed by Barrett (1987):

> "Best results (BMT) are achieved when BMT is carried out as an elective procedure and the worst results are obtained when the treatment is used for disease that is relapsed and resistant to standard chemo-and radiotherapy".

1.1.3 The Optimal Patient For The Treatment

The better the physical state of the patients, the better they are able to tolerate the pre-transplant conditioning. (Klingeman, 1986). Although there appears to exist a consensus that increasing age in patients correlates with an increased risk of post-transplant complications and increasing mortality (O'Reilly, 1983; Kamani, 1984; Klingemann 1986; Kanfer, 1988) the practice of transplanting increasingly older patients indicates a reverse trend. The Working Party on Leukaemia for Europe reports in its 1988 assessment a "clear trend in recent years to do transplants in older patients" despite the less good results.

1.1.4 The Transplant Procedure

The BMT procedure can be divided into several sequential stages. They are as follows: (See Table 1.1.4)

Table: 1.1.4 Timetable of the Medical Procedure and Stages

Days	Periods	Events	Stages	Assessments
	(Period I)	DECISION FOR TRANSPLANT	1	Baseline
-10		ADMISSION		
		CONDITIONING		
		Time spent in Isolation		
0		TRANSPLANT		
+1	Period II)		2	assessed
	Start of immediate Post-Transplant period with the possibility of acute GvHD			
7			3	assessed
14			3a	assessed
21			3b	assessed
28			3c	assessed
30+		END OF ISOLATION	4	assessed
		DISCHARGE	1	Assessment within 7 days
42	Onset of somnolence period for patients treated with TBI		5	assessed
70				
		REHOSPITALISATION	11	Assessment within 7 days
	(Period III)			
100	Start of late post-transplant period with possibility of chronic GvHD		6	assessed
		RELAPSE*	III	Assessment of relapsed patients
360	a year	post-transplant	7	assessed

* Relapse can occur earlier or later, but was more likely to occur after days 100+

TIME AS OUT-PATIENT | TIME AS IN-PATIENT | TIME IN ISOLATION

1.1.6 Decision For Transplant

Prior to hospitalisation for transplant and after the original diagnosis of the disease, BMT is introduced to the patient as a possible treatment option. There will be discussions between the physician and the patient. However, the extent of the discussion varies from country to country. In the USA where an informed consent prior to transplant is a legal requirement the discussion will include side effects and risks of this treatment to the patient and to the donor, as well as alternative treatment options. In the UK where no such requirements exist the extent of information provided depends on the hospital as well as on the consultant presenting the treatment to the patient. Discussions may include the family and the potential donor depending on the hospital.

Prior to hospitalisation for transplant, the issue of availability of a matched donor will be investigated through extended in vitro blood tests and blood reactions between the recipient and the potential donor. The results of these tests will determine the type of transplant opted for.

The patient may already be attached to a hospital providing BMT. The majority however will be referred from their local hospital to a teaching hospital with an appropriate BMT unit.

It is at this stage that the patient's general physical health is thoroughly investigated. This includes organ function as well as confirmation of the original disease and disease status. It is essential that the patient is in remission with the number of leukaemic cells less than 4% when transplantation takes place.

1.1.7 Hospitalisation

The procedure commences with the patient's admission to hospital some 10 days prior to transplant. The length of this period may vary slightly from hospital to hospital. This period is used for the "conditioning," of the patient for transplant itself, (this is described in detail below). The transplant-marrow is infused on day "0" at the end of conditioning. This is followed by a period of engraftment lasting anything between 2-5 weeks and up to 3 months. "Engraftment" is the process when transplanted donor cells start to replicate and start to appear in the peripheral blood. The patient spends this time in isolation. Days 0-100 encompass the immediate post-transplant period. The late transplant or "convalescence" phase lasts approximately from day 100 to day 360. It takes at least a year for the patient to recover physically and psychologically. (Lesko, 1990).

1.1.8 Conditioning

The first step towards conditioning is the insertion of a Hickman-Line or central line into the right external jugular vein under local or general anaesthetic, unless the patient has one already in place. This allows easy access to the vein for the purpose of drawing of blood samples and infusions of blood products and medication over an extended period of time.

During BMT, readily available and safe venous access is necessary for daily blood checks, for the infusions of blood products, chemotherapeutic agents and other intravenous medication. Venous access in these patients may be difficult due to prior damage by chemotherapeutic agents, intensive use and/or small fragile veins.

The standard conditioning regime, as it prepares the patient for transplant, consists of a course of intensive chemotherapy combined with Total Body Irradiation (TBI). There are, however, regimes which use a combination of chemotherapeutic agents only.

Conditioning has a threefold purpose:

1. Immunosuppression in the recipient. This allows engraftment and the avoidance of a host-versus-graft reaction which can result in the rejection of the transplanted graft.

2. To eradicate the abnormal cell population (usually malignant). Successful eradication remains one of the major problems in this treatment.

3. To create a "space" for the transplanted stem cells to "relocate and proliferate". (Philipps, 1988).

The combination of conditioning agents vary according to the type of transplant (allogeneic vs. autologous), the type of disease and the on-going research in a unit. In the majority of conditioning regimes, multiple agents are used since the "tolerable doses for most single agents provide only marginal immunosuppression". (Philipps ibid). Therefore additional agents are required. The most frequently used combinations are:

Cyclophosphomide and TBI; Cyclophosphomide and Busulfan; Melphalan and TBI.

Doses of TBI range between 800 to 1,000 rads. Applied on its own, it is lethal. (Lesko,1989). Its administration entails either a single dose or fractionated doses given over several days.

These agents are highly toxic and produce a number of reversible and irreversible side effects but still they are not necessarily totally successful in achieving the three aims outlined above. In order to achieve these aims, even higher doses of these agents are required. However, the increase of these drugs is limited as Barrett (1987) explains:

> "the limitations to escalating chemotherapy and radiotherapy ... is that of toxicity to other tissues, notably the lungs, liver, gastrointestinal tracts and nervous system".

1.1.9 The Transplant

Bone marrow is harvested from the anaesthetised donor prior to transplant (in allogeneic transplant) or from the patient him/herself during remission. Between 500-800 ccm marrow is harvested by multiple aspirations from the anterior or posterior iliac crest. The marrow is heparinized, pooled and filtered. In some centres, the marrow is treated by T-cell depletion. In the case of an autologeous transplant, the harvested marrow is frozen at -90' Celsius and stored. At the time of transplant the marrow is rapidly thawed and immediately infused.

This is done through the central venous catheter or the Hickman line. The transplant itself takes 2-4 hours and is a relatively easy procedure.

1.1.10 Immediate Post-Transplant Phase

One of the three aims of conditioning is to produce an immunosuppressive state in the patient to enable the transplanted marrow to engraft. This can be a potentially dangerous condition, leaving the patient vulnerable to bacterial, viral and fungal infections. To protect the patient from infections he/she will spend the next few weeks in isolation until such time as the transplanted graft is producing enough white cells to allow some immunity against infections. The form and degree of isolation varies from centre to centre. There are, however, some common aspects. In all centres access to the patient is limited. Staff and visitors dealing with patients in isolation are required to dress in protective clothing consisting of a sterile cap, mask, gown, gloves and /or an apron. In some centres all items are required, in others one or two (e.g. gloves and mask). All objects brought into isolation are sterilised. Visitors are, in many cases, discouraged. In any case they are limited and/or restricted.

The concept of isolation is based on two basic designs. The first is the "Life Island", consisting of a bed surrounded by a plastic tent. The other is a cubicle or room with a laminar air flow. Both contain toilet facilities.

The immediate period following transplant is characterised by high morbidity and high mortality. (Barrett, 1987; Burnett, 1988). It is during the isolation period that the patient will experience the early complicating side-effects of the conditioning treatment. The most common ones are as follows.

Oral complications are frequent and tend to occur during the first two weeks after conditioning. Gastro-enteritis and diarrhoea are produced by "muscosal damage throughout the gastrointestinal tract". (Klingeman, 1988). Haemorrhagic cystitis usually occurs within the two week period after the administration of Cyclophosphomide and is known to be extremely painful. (Klingeman, 1988). Hepatitic damage is due to conditioning and tends to be more severe in older patients. (Klingeman, 1988). Cardiotoxicity is also influenced and accentuated by increasing age. Interstitial pneumonitis is a syndrome observed after TBI. (Philips, 1988). Although related lung problems decrease over time, some patients develop obstructive pulmonary problems during the late post-transplant phase. (Klingeman, 1988). Skin rash and hairloss are reversible complications during the period immediately after transplant. (Philips, 1988).

During the late post-transplant phase, additional medical side effects may appear. These include damage to the eyes and/or secondary malignancies. (Kolb & Bender-Goetze, 1990). In many cases, the conditioning leads to symptoms of menopause in women and sexual problems in both, men and women. A survey has shown that 90% of women treated with BMT are amenorrheic and only 8% menstruate after BMT. (Klingeman, 1988). A recent study by Benjamin & Baruch (1991) of sexual functioning in male survivors of BMT reveals post-transplant sexual dysfunctioning. In their study, 49% of men reported sexual problems. However, this very first study only assessed a small number of patients.

1.1.11 Engraftment Versus Non-Engraftment

In an "uncomplicated" transplant, the graft settles and proliferates to produce healthy blood cells. When the number of produced blood cells reaches an acceptable level of white blood cells, the patient is allowed to leave protective isolation and hospital. Until the successful engraftment and full functioning of the graft is achieved, the patient is dependent on transfusions of red blood cells and platelets. Engraftment is not usually evident before the second week after transplant. (Kamani & August, 1984).

Despite intensive immunosuppressive therapy, the patient's own surviving immunity may cause graft rejection or engraftment failure after initial signs of engraftment. In both conditions, the patient is left with a depleted bone-marrow and will require bone marrow rescue with his own stored marrow. The latter has been routinely harvested and stored for emergency situations as described above.

1.1.12 Graft-versus-Host-Disease (GvHD)

> "Presumably all transplants other than autologous or syngeneic result in a graft-versus-host reaction".
> (Deeg, Klingemann & Philipps, 1988).

In the case of successful engraftment, healthy donor cells replace diseased or absent ones. The graft "invades" the recipient's body with the "donor derived immune system." (Deeg, 1988). In cases of imperfect HLA- matching, the "invading" donor derived T-cells react against the host cells. This interaction may lead to potentially serious complications. "Complications are those of a reaction of donor derived cells against recipients tissue and organs". (Deeg, Klingemann & Philips, 1988). Tissue and organ damage in the recipient include especially those of the skin, the liver and intestinal tract. The observed syndrome caused by this graft versus host reaction is called Graft-versus-Host-Disease (GvHD). GvHD is associated with a high morbidity and mortality. GvHD also impairs and delays the reconstitution of the patient's immune system following transplantation. (Deeg, 1988).

Tissue and organ damage due to GvHD may take the form of skin-rash. In a mild form the rash may only appear localised on palms and soles. In a severe reaction the rash may involve the entire body and affect the organs such as the liver. In the case of the latter the rash appears like a total body burn. The rash may be accompanied or followed by a rise of bilirubin and serum alkaline phosphatase and aspartate aminotransferase. Depending on the severity of GvHD, the patient may experience nausea and vomiting with watery and bloody diarrhoea and abdominal pain. Five to ten percent of patients developing acute GvHD will die of associated complications, particularly infections. (Deeg, 1988).

Medicine distinguishes between acute and chronic GvHD. This distinction depends on the timing of the onset as well as symptoms of GvHD

Acute GvHD refers to the observed reaction within the first 100 days post-transplant, usually developing 2-10 weeks after transplant. (Kamani & August, 1984; Klingeman,1988). The number of patients developing the acute form of the syndrome following allogeneic transplant are 30 - 70%. On the other hand chronic GvHD is developed after the first 100 days, that is, during the late post-transplant period.

Chronic GvHD is often an extension of acute GvHD. However, 20 - 30 % of patients develop it for the first time after the 100 day period. Chronic GvHD manifests itself in the skin, liver, eyes , salivary glands, gastrointestinal tract, gut and lungs. (Klingemann, 1988).

The discharged patient with a fully functioning graft will continue to need careful monitoring of his/her health and blood-count during the first 100 days post-transplant. Regular visits to the out-patient department are required during this period. In most cases the patient will need further transfusions of blood and platelets during these early months. Recovery will take at least a year. (Lesko, 1990).

1.1.12 Relapse

Relapse at any time of the original disease remains one of the major problems in BMT. The number of relapsed patients varies. Percentages given are as low as 10% and as high as 50% of all surviving patients. The following examples illustrate these divergent findings:

> Santos, 1984: 30-50%; Bostrom et al: 12-21%; Tutschka et al, 1987: 10 - 40 % ; Kanfer, 1988: 20- 33 % ;

At present there is no explanation for these divergent findings.

1.2 PSYCHOLOGICAL ASPECTS OF BMT
A Review of the Literature

1.2.1 Introduction

Systematic research into the psychological aspects of BMT is in its infancy, although publications on the subject date back to 1976. The early literature is based mainly on clinical observations of patients during the treatment procedure. These observations were written by physicians, nurses and psychiatrists involved in the patient's care, and often take the form of case-reports. (Popkin et al., 1977; Brown & Kelly, 1976). Nonetheless, these early papers form the basis for later publications to which authors have tended to add further clinical impressions. (Lesko, 1986; Haberman, 1988).

BMT patients are not only confronted with a potentially life-threatening disease but also with a potentially life-threatening treatment which is not true for other cancer patients. It has been well documented that cancer and its treatment can cause considerable distress among cancer patients. (Derogatis et al., 1983). The emotional distress is mainly in the form of anxiety and depression. (Kardinal and Cupper, 1977; Silberfarb et al., 1980; Hopwood, 1984). Moorey et al. (1991) reported that "the most common emotional disorders in medical patients are anxiety and depression" and they stressed that these two disorders frequently coexist. However, the degree of distress experienced is influenced by a number of factors. These can be physical, psychological or social.

It is known that in other diagnostic groups psychological morbidity can be high. Derogatis et al. (1983), found a prevalence of psychiatric disorder of no less than 47% among a group of 215 newly admitted cancer patients. This is three times the incidence rate of psychiatric disorders in the general population which stands at 15%. Kardinal and Cupper, (1977), found that among cancer patients depression was a dominant early reaction which " all patients experienced to some degree". This was confirmed by Silberfarb et al. (1980) who found when assessing 146 breast cancer patients, that, besides depression, anxiety was the most frequently reported emotional disturbance.

The genesis of BMT research emerged mainly from work with childhood leukaemia. Small sample numbers and descriptive rather than analytic data characterised research findings. (Pfefferbaum et al., 1977; Magni et al., 1986). To date, the majority of publications remain the prerogative of paediatricians and

related professionals. There are, however, some periods and events during BMT which have received more detailed attention. For example, the patient in isolation and the long-term survivor have been looked at most extensively (Koehle et al., 1970; Holland et al., 1976). A few authors have attempted to assess psychological responses retrospectively, using interviews with long-term survivors. (Hengelveld et al., 1988; Jenkins et al., 1991).

To date, there are no prospective studies that assess psychological morbidity in adult patients receiving BMT.

Thus, existing research has failed, so far, to provide clear answers to the following questions:

1. Are there specific events and critical periods during BMT which affect psychological morbidity?

2. What proportion of patients experience adverse psychological reactions during the different phases of BMT?

3. Are stressful events common to all patients or are they experienced by more vulnerable patients. (i.e. patients showing high levels of anxiety and depression)?

Two early publications on psychological aspects of BMT base themselves on daily psychiatric observations of patients undergoing BMT. Popkin & Moldow, (1977) and Popkin et al., (1977).

The authors outline the multiple stressors observed during BMT and the most frequent responses. They group these stressors into the following areas:

Psychological - the decision for transplant and the proximity to death;

Physical - major weight loss, fever and sepsis, bleeding, abcess formation , alopoecia, lassitude, sleep dysfunction and anorexia;

Environmental - isolation. Some of these stressors are linked to specific events and procedures such as the transplant itself.

Responses include "high anxiety, phobic preoccupations (i.e. concern with "germs" and "viruses"), intrusive thoughts and feelings, regressive behaviours, and emotional lability, episodes of despondency, guilt and depression, the re-emergence of denial and ritualised obsessional patterns". (Popkin & Moldow, 1973).

Responses also include preoccupation with the white blood cell count, and mood responses fluctuate with the ups and downs of this very count. (Popkin et al., 1977).

In reviewing the stressors described in the literature I shall follow the chronological order of the medical events, since other authors have stressed, too, that psychological states closely follow the medical stages as described in the medical procedure. (Brown & Kelly, 1976; Farkas-Patenaude et al., 1979; Lesko & Holland, 1988; Lesko, 1989).

1.2.2 The Decision For Transplant

The decision for or against transplant is considered by Popkin & Moldow (1977) as the initial stressor in the BMT treatment. In the discussions about the treatment, its side effects and the factors speaking for or against BMT preceding the decision, patients are confronted with the critical nature of their illness. This confrontation comes at a time when they show no clinical symptoms of the disease and are, indeed, in remission. Haberman (1988) argues that the most distressing aspect of this decision making is the uncertainty of treatment which can be potentially life saving but at the same time is potentially fatal. This decision is often made quickly due to the actual and anticipated changing medical status of the patient e.g. the threat of relapse, the availability of a bed on the ward, and the issue of a suitable and available donor. (Lesko, 1985; 1989; 1993). Moreover, the decision is a joint one involving both patient and the medical team. On the one hand, the latter has to assess whether BMT is the best treatment option for a particular patient, and on the other hand patients must decide whether the treatment offered is the right one for them. (DeCuir Whalley, 1985). Patients cannot draw on previous experience since there is no comparable procedure in medicine. Unlike heart and liver transplant patients, those undergoing BMT are not at this particular point end-stage patients. Rather, they are in remission with the hope and apparent prospect of a good quality of life ahead. Furthermore, the former is reliant on the organ of a dead donor, whereas the latter depends on a replaceable product of a living donor. Therefore, the decision making of the groups happens against diverse backgrounds. It cannot be taken for granted, therefore, that the psychological outcomes of organ recipients and bone-marrow recipients will be similar.

The argument presented in favour of transplant is based on the observation that conventional treatment with chemotherapy alone does not offer a long-term "cure", while BMT does. (Haberman, 1988; Lesko,1989). Hope for this "cure" is a decisive factor in making the decision for transplant. Several writers quote patients as saying that transplant is their "last and only hope". (Pfefferbaum, 1977; Popkin et al., 1977). This sentiment is verified in the work of several other authors who agree that without the hope neither patients nor their families would agree to the procedure. (Artenian, 1976; Gardner et al., 1977; Haberman, 1988).

If hope for a cure is one side of the coin, despair about a possible failure and fear of death should be the other. How do patients deal with the potential threat of death as a result of treatment? Haberman (1988) found the most common way of dealing with the threat was to discount or minimise " the significance of estimates *of low*

percentages [1]of survival" presented to the patient by some medical teams. Her observations of leukaemia patients have allowed her to conclude that "patients redefine statistics in their own favour to inflate their chances of survival". However, this coping strategy is not restricted to patients. Doctors are also believed to give a higher possibility of survival than actual survival rates indicate. (Pfefferbaum, 1977; Popkin et al., 1977). Farkas-Patenaude et al. (1986) acknowledge the difficulties for the physician in explaining and interpreting the variety, sheer scale and seriousness of known side-effects to the patient in view of the "physician's own commitment to this field and his personal belief in the efficacy of transplantation". (Farkas-Patenaude et al., 1986).

A similar caution is voiced by Philipps (1988) who advises medical colleagues:

> " Although it is very unlikely that a member of the transplant team would deliberately mislead a patient, the mere fact of his or her enthusiasm for marrow transplantation might subtly influence a patient to accept marrow transplantation rather than more conventional therapy." p 26

In addition to inflated hope, denial is seen as a typical coping strategy by Cohen et al. (1977). Data have shown that patients with acute leukaemia who are in remission, also deny the gravity of their physical state. One study showed that adult leukaemia patients in remission reported that denial allowed these patients to cope with the ever underlying fear of relapse and the possibility of death (Sanders, 1977). It could be argued that the patient who is deciding to undergo BMT has accepted the diagnosis of the disease but has denied its prognosis.

The decision for transplant has been quoted as stressful and difficult. There is, however, no formal evidence as to what psychological symptoms are experienced as a result. However, "unrealistic hope" and "denial" are quoted as the most frequently observed coping strategies.

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[1] Italic: Author's addition

1.2.3 Admission For Treatment

Admission to hospital for BMT has attracted surprisingly little attention. It has been treated in passing in studies dealing with the whole procedure and its psychosocial consequences. (Farkas-Patenaude et al., 1979; DeCuir Whalley, 1985; Haberman, 1988; Lesko, 1989; Pot-Mees, 1989). Nonetheless, knowledge based on clinical experience gives some indication that admission can be a major stressor.

While many of the quoted authors see admission into the hospital as the end of the worry of waiting for the transplant, other authors make the point that the uncertainty of undergoing the procedures leading up to the prospective BMT is a major time of stress. These procedures include a period of tests to identify a possible donor and the resulting transplant type i.e. allogeneic or autologous. It also includes the waiting for an available bed in the transplant unit. (Haberman, 1988; Pot-Mees, 1989). Pot-Mees (1987) concludes from her experience with paediatric patients that families tend to arrange their life around the expected admission time. For many there exists a sense of urgency due to the possible change in the medical condition of the patient and the fear that this change may lead to a postponement of the planned transplant. Haberman (1988) writes in her observations that the waiting is experienced as a "race against time", while Pot-Mees (1987) observed that the existing feeling of ambivalence towards the treatment increased with increasing waiting time.

For many patients, admission to a unit means geographic "dislocation" (this term has been introduced by Farkas-Patenaude et al., 1979, to reflect the geographical change for families) and general upheaval with loss of the usual support systems available to the family, separation of the family, and, disruption of professional, social and school life. (Cohen et al., 1977; Pfefferbaum et al., 1977). Admission includes a confrontation with a new place, new people and an enormous amount of new information. (DeCuir Whalley, 1985). This information covers transplant techniques and the teaching of self-care as well as information and warning of the possible treatment complications that may arise. Haberman (1988) believes that this confrontation with information at the time of admission leads to a renewed confrontation with the disease and in some cases to an acceptance of the possibility of non-survival. She has observed patients saying "good-bye" to their families and making funeral arrangements. She argues that despite the imparting of important information to patients, they will use "denial" and it remains difficult for patients " to construct a clear mental image of the upcoming transplantation experience".

The observed responses among the patients during admission range from initial relief (Pot-Mees, 1987) to anger and frustration (Haberman, 1988). This anger is seen to lead to confrontations with the medical staff. The above authors noted that "anxious anticipation", "anxiety", "frustration" and "anger" are the most frequently observed responses to the stressors on admission and the period preceding admission.

1.2.4 Conditioning For Transplant

Popkin & Moldow (1977) condense the conditioning period preceding transplant into an "interval and ordeal to be bridged in order to reach hope", but do not consider it a major stressor. There exists a paucity of information on the psychological side effects of intense chemotherapy and radiotherapy endured during the conditioning treatment. Despite the considerable number of papers based on observations of patients, very few refer to the psychological side-effects of chemotherapy. Most bridge this interval by concentrating on the physical side effects. (I shall follow the authors' outline of stressors as they tend to occur chronologically in the published literature). (Cohen et al., 1977; Gardner et al., 1977; Farkas-Patenaude et al., 1979; McGahan Hutchinson & Hubbard King, 1983; Lesko, 1986, 1989).

TBI receives slightly more attention. Haberman (1988) considers that for patients it is a new and frightening experience. Brown & Kelly (1976) report that "The possible psychiatric (and neurological) effects of central nervous system irradiation do not appear to be marked". However, a recent study by Andrykowski et al. (in press) into the cognitive function of long-term survivors contradicts the latter statement. The authors found a positive relationship between the dose of TBI and degree of mild to moderate cognitive dysfunctioning primarily in the form of "slowed cognitive processing, difficulties with reasoning, attention/concentration, and perhaps, short-term memory".

In a retrospective assessment of 17 long-term survivors, Hengelveld et al. (1988) noted that chemotherapy and TBI "were considered to be a burden and did not fit in with the expectations of more than half the patients". Retrospective studies of this kind are invalid in that a considerable number of patients cannot voice their opinion since they did not survive the treatment. This makes it difficult to assess the accuracy of the recall of what has been considered a "frightening experience." (Farkas-Patenaude et al., 1979). One aspect mentioned is the resurgence of doubt about the treatment (Farkas-Patenaude et al., 1979; Haberman, 1988). Brown & Kelly (1976) illustrate this with the following quotation:

> "(we) begin to wonder why they (the patients) agree to the procedure in the first place".

It appears that information about possible side effects must be derived from literature in the areas of radiotherapy and chemotherapy in other cancer groups in

order to identify possible psychological reactions to treatment for BMT patients. Silberfarb et al. (1980) provide information about some possible responses by pointing out that "by its very nature, radiation therapy may augment cancer patients' already weakened sense of control and mastery over their illness" and Peck & Bolund (1977) consider radiotherapy a "strong challenge to the individual's ability to cope with stress". In their prospective study with 50 patients, the observed anxiety and depression increased during radiotherapy. Seventy-four to eighty percent of all observed patients showed signs of mild to moderate anxiety and depression. Holland et al. (1979) come to a similar conclusion after assessing 20 female patients prior to and during radiotherapy. They report an overall increase in depression and anger over time, but a decrease in overall anxiety. The latter did not reach statistical significance. Forester et al. (1978) consider radiotherapy "another trauma" added to the distress of having cancer. They found a high incidence rate of both anxiety and depression among their sample of 200 patients treated with radiotherapy but found a difference between patients treated with a linear and betatron accelerator, and argue that the loud noise made by the betatron may be responsible for additional distress. A later study by King et al (1985) observed a degree of fatigue among their 96 patients receiving radiotherapy, a state which lasted for well over a three month period.

Increased emotional morbidity in the form of anxiety states and depressive illness is also reported by Maguire et al. (1980) in a prospective comparative study looking at the impact of chemotherapy among breast cancer patients. The drugs mentioned by the authors include a combination of cyclophosphomide, methotraxate, 5-fluoroucil (CMF) and melphalan, the very drugs used in conditioning in BMT. The CMF combination was associated with increased emotional morbidity. Meyerowitz et al. (1979) studied a group of 50 women undergoing chemotherapy with CMF and found adverse changes such as disruption in family and sexual relationships. In addition, psychological distress was observed but did not correlate with the physical side-effects of treatment suggesting that the latter does not account for all the distress experienced by the study group. Silberfarb (1983) reports that the commonly used chemotherapeutic agents can and do lead to cognitive deficits, for example impairment of "thinking" and intellectual functioning particularly when used in combination with radiotherapy. This impairment is reported to take the form of "mental changes", "hallucinations", "confusion" and "delirium".

At the conclusion of the conditioning treatment the BMT patient is without immunity and unable to survive without medical support. Patients who have reached this

point cannot change their mind about the treatment but can only go forward. They have nothing to fall back on. Several writers call this "the point of no return" (Brown & Kelly, 1976; Pot-Mees, 1987; Haberman, 1988).

1.2.6 The Transplant

Transplant itself is an uncomplicated and brief transfusion of marrow into the recipient's blood stream. Popkin & Moldow (1977) acknowledge the simplicity of this procedure and argue that the transplant of bone-marrow is quite distinct from other organ transplants. This "simplicity" "belies the drama for the patient" (ibid) and does not indicate the subsequent severe medical problems which may endanger the patient's survival. For these reasons transplant itself is seen by them as a major stressor. This has been reiterated by other writers (Lesko, 1986; Pot-Mees, 1987). Pot-Mees points out that transplant is considered an anti-climax after the intense conditioning. Gluckman et al. (1979) report that BMT patients cannot accept this "simple" procedure. Patients talk about missing the anticipated "change" in themselves and its tangible signs on their body after transplant. Thus the ensuing anxiety that the graft may be lost is experienced by many. In contrast, half of Hengelveld et al.'s (1988) long-term survivors, retrospectively interviewed, report that they experienced the infusion of the graft as a "dramatic event" and highly "intense moment" and fully realised the importance of this event at the time.

These are very conflicting findings. They may arise from the timing of assessment in the patients' career. While transplant may be experienced as anticlimax after conditioning, it may assume greater importance and dramatic effect when looked at retrospectively by long-term survivors.

Transplant itself leads to a period of protracted waiting for the infused graft to take. The waiting stage is one of uncertainty. The marrow may take or fail to engraft. This is a stage in the patient's transplant during which the patient will experience the "emotional proximity to death". (Popkin & Moldow, 1977).

1.2.7 Protective Isolation

The patient in protective isolation has been extensively researched and there exists a considerable body of publications revolving around this procedure. The majority deal with paediatric patients and their immediate and delayed psychosocial and developmental problems. (Drotar et al., 1976; Freedman et al., 1976 ; Smedler et al., 1990).

Historically isolation was introduced for the vulnerable leukaemia patient in treatment, and therefore the majority of publications deal with this group. (Holland et al., 1971; Koehle et al., 1971; Gordon, 1975; Powazek et al., 1978; Meehan, 1980; Foester, 1984). Only a handful report on BMT patients in isolation. (Watson et al., 1977; Peterson et al., 1987). The concept of isolation is based on two basic designs. The first is the "Life Island", consisting of a bed surrounded by a plastic tent. The other is a cubicle or room with a laminar air flow. Both contain toilet facilities and both restrict access from the outside.

For example Popkin and Moldow (1977) name this protective isolation as an important environmental stressor over a prolonged period of time. This procedure restricts physical contact and requires intense nursing care. Most patients are not allowed to leave protective isolation during their treatment. This is known to lead to extreme dependency on medical and nursing staff. "All basic activities require participation of a staff member", writes Gordon, (1975) after repeatedly interviewing 10 adult leukaemia patients in isolation over an extended period of time. This pressure towards dependency has been confirmed as stressful by several other authors (Koehle et al., 1971; Cohen et al., 1977; Foester, 1984) and leads, in Foester's experience (op. cit.), to a loss of the ability of self-government, exacerbated by helplessness. (Rooyman et al., 1979).

Overdependence coupled with helplessness has also been observed by Garner et al. (1977) among a group of paediatric patients in isolation. Koehle et al. (1971) talk about an "aggressive dependency" produced by this environment. Furthermore it is an environment in which motor activity and free movement are severely restricted.

The patient depends for all basic activities on the help of the staff. Access to the patient is however not straightforward and simple. All who intend to enter isolation are required to put on protective clothing. Mask, gown and gloves are worn and hygienic precautions such as hand washing with special soaps are strictly

observed. Entering isolation for the staff thus becomes awkward and time consuming. Furthermore most units limit the number of visitors to one or two for each patient. It is therefore not surprising that a number of authors name separation, social isolation and particularly the loss of human touch as particularly stressful for the patient. (Koehle et al., 1971; Cohen et al., 1977; Holland et al., 1977; Foester, 1984). Gorden (1975) did not however report a perception of social isolation, but agrees that among the many losses experienced by this group, the loss of human touch was most missed. Several writers argue that monotony and boredom make isolation more difficult to tolerate for the patient. (Holland et al., 1977; Popkin et al., 1977; Watson et al., 1977).

Emotional morbidity has been frequently observed, mainly in the form of anxiety and depression. (Gordon, 1975; Gardner et al., 1977; Gluckmann et al., 1979; Foester, 1984; Pot-Mees, 1987). Anxiety frequently takes the form of panic attacks, particularly at the start of isolation. Gordon (1975) recorded panic attacks in 20% of his patients entering isolation, but observed that anxiety decreased and tolerance of isolation increased with increasing time spent in isolation. Anxiety, however, tends to return at times of physical deterioration. Depression is frequent among patients and is often associated with withdrawal and refusal to cooperate. Other severe psychological problems mentioned are hallucinations (Popkin & Moldow,1977); cognitive impairment and paranoid ideas about being poisoned, (Koehle et al., 1971).

A paper by Holland et al. (1977) contradicts the above findings. In a group of 52 adult patients, no depression or anxiety appeared to manifest itself. Instead this sample maintained emotional stability throughout their time in isolation. The authors attribute this result to the special care of the nursing staff who had themselves carried out the daily assessments filling out a "specially adapted nurse observation form" at the end of their working shift. (Holland et al., 1977). This form is based on patients' behaviour and includes such items as 'ability to interact', 'cooperation in treatment' and 'participation in care'.

The majority of authors see psychological disorders as a consequence of medical complications such as high temperatures and not of isolation per se; and argue that psychological and psychiatric conditions are most strongly influenced by patients' somatic conditions (Fine et al., 1974; Koehle et al., 1971; Holland et al., 1977; Gluckman et al., 1979; Gordon 1975).

The number of publications concerning BMT patients in isolation compared to leukaemia patients in isolation is too small to allow for comparisons and assessments as to whether BMT patients react differently from leukaemia patients. Certainly two authors report differing conclusions. Lesko (1986), assessing isolation for BMT, writes that "isolation is contributing little to the patient's tolerating the transplant procedure - more have lasting psychological side effects", while Watson (1977) concludes after assessing paediatric leukaemia patients that "isolation in paediatric practice was found highly acceptable to both patients and staff". This difference may be due to a variety of factors, such as patient population, method of research or to the researchers themselves. While Lesko has a well established record of research in BMT, the Watson team originates from the Department of Bacteriology at the Westminster Children's Hospital. The difference of objectives may have contributed to the differences in research findings. The Watson study was looking at the acceptability of isolation to the patient, family and staff, while Lesko described the psychological impact of isolation upon the patient.

Factors contributing to easing isolation include the support provided by fellow patients in isolation. (Holland et al., 1977; Rooymans et al., 1979; Farkas Patenaude & Rappeport , 1982). Patenaude & Rappeport (op. cit.) report that relationships developed between fellow patients help to diminish feelings of isolation in patients. This has been confirmed by Rooymans et al. (1979) who present the case history of one patient during isolation. This patient had felt that talks with other patients provide a great deal of support because these other patients " are going through the same thing or having at least comparable experiences". Patients looked for similarities with other patients. The close feelings subsequently developing with fellow patients were compared to feelings of "kinship" (Holland et al., 1977) and the fellow patient in the other bed was referred to as "best friend", (Patenaude & Rappeport, 1982).

When the patient in the other bed dies patients are very upset. The death of a fellow patient was quoted by patients as the most difficult time during isolation. (Patenaude & Rappeport, 1982). The death of a fellow patient reawakened the fear of their own death and they responded with withdrawal from staff, depression, increased anxiety, denial of sadness and the guilt of being a survivor. (Patenaude & Rappeport, 1982).

Another factor contributing to easing the isolation experience is the support provided by the family of the patient. Popkin et al. (1977) talk about a patient who became despondent whenever his wife was away.

How much do personality factors influence emotional tolerance of isolation? Not much has been written on this factor. Gluckmann et al. (1974) argue that no patient is similar to another and each patient is treated differently by the staff. This implies that there is no common denominator for comparison. However, Rooymans et al. (1979) argue that the "patient's personality structure, coping mechanism and personal circumstances" influence the patient's emotional equilibrium during isolation. Gordon (1975) found in his sample of patients that women adapted better than men, and Brown and Kelly (1976) report that toleration of isolation was easier for the passive intellectually oriented patient than the active type of patient.

Personality has been looked at with regard to management, survival and emotional morbidity during transplant. Neuser (1988) tested the association between personality factors such as 'achievement oriented' and 'strive for recognition and help' and survival time. He reports that survival time was influenced "by the degree to which patients strive for recognition and help". He argues that patients are highly dependent on the support of others during and after BMT and those who strive for help do get more help. Furthermore, patients' survival depends also on compliance with the medical procedure, such as oral hygiene and taking medication. He argues that the patient striving for recognition and help is a more compliant patient than patients with other personality factors.

Alby (1991) and Gordon (1975) link personality factors to the management of patients in isolation. Alby (1991) argues that very anxious and obsessional personalities cannot adjust to the demands of BMT. Gordon voices similar constraints saying that patients with psychotic illness are difficult to manage, and Lesko (1993) states that patients with a past history of psychiatric illness are at high risk of a recurrence of that illness during BMT.

Questions such as " whether personality factors influence emotional morbidity during transplant?" and "what are these factors?" have only been touched on. Brown and Kelly (1976) report that during isolation patients' existing personality features are usually intensified. Obsessive patients became more obsessive and needed more detailed explanations and greater control of their care, while inhibited patients became progressively withdrawn.

At the end of isolation the patient is ambivalent, pleased to leave and worried about the unprotective "outside world" and lack of medical supervision. Anxiety may increase prior to termination of isolation. (Holland et al., 1977). This led one team

(Alby, 1991) to a gradual transition by opening curtains further each day. Alby (op. cit.) identifies some of the fears present. These are fear of functioning without the availability of skilled staff; fear of facing a changed body image and fear of infections. Patients discharged "feel as though they are in a vacuum" (Rooymans et al., 1979), they now must stand on their own feet, they feel unprotected without the staff's support.

1.2.8 The First 100 Days: Immediate Post-Transplant Period

It takes at least seven days before the first signs of an early engraftment after infusion manifest themselves. Engraftment or non-engraftment means life or death to the patient. For patients of allogeneic transplant the desired engraftment may produce the life threatening syndrome GvHD. Treatment of GvHD includes more drugs which themselves have been shown to induce psychological morbidity. For example, cyclosporin can produce visual hallucinations causing great psychological distress, (Noll & Kulkarni,1984). Steroids are also used to treat GvHD and they too can produce severe psychiatric reactions with affective symptoms i.e. depression or mild euphoria and/or psychotic symptoms i.e. delirium, disturbances in reality or changes in psychomotor activity. (Lewis & Smith, 1983).

Successful engraftment means termination of isolation and ultimately discharge from hospital. This time is viewed with mixed feelings. Pot-Mees (1987) observed that patients look forward to a normal life at home. However, Freund et al. (1985) and Freund & Siegel (1986) report feelings of ambivalence in the patient at the time of discharge. Eighty-three patients who had completed treatment and returned home, talked about their loss of support from medical staff and their attachment to them. Furthermore, patients experienced unique stressors during this time involving self-care, including hygienic care of the Hickman line and the fear of relapse and infections. Patients are aware that infections may lead to rehospitalization. Stream (1983) found that patients attending the out-patient clinic after BMT viewed readmission as a major set-back. An anxious preoccupation about physical states and recovery which in turn caused psychological morbidity was observed. (Popkin et al., 1977; Freund et al., 1985; Freund & Siegel, 1986).

Freund and Siegel (1986) stress that among the "unrealistic expectations" in patients and their families was a transition without difficulties and a perception that discharge can be seen as cure. They write:

> "All patients and their families are vulnerable to a profound sense of disappointment later if they expect return to normalcy faster than is likely."

Indeed, a retrospective study which looked at the long-term survivors (Hengelveld et al., 1988) reported that the period of discharge was similar to "falling into a vacuum". Not only does the future bring with it a fear of relapse and infection but survivors must re-establish their family, social and professional life.

1.2.9 Between Days 100-360: The Late Post-Transplant Period

It is difficult to draw valid conclusions from the existing literature about emotional problems occurring during the three to twelve month period, although there is a considerable body of published work about the long term survivor. (Wolcott et al., 1986; Hengelveld et al., 1988; Andrykowski et al., 1989; Andrykowski et al., in print).

The above authors do not have a consensus as to what constitutes "long-term". It can be three months to five years (Andrykowski et al., 1989). This is in contrast to guidelines published by Ochs & Mulhern (1988) who argue that a patient had to be off treatment for at least two years to qualify as long-term survivor. The authors agree that long-term adjustment poses a great challenge to the BMT survivor (Freund & Siegel, 1986; Andrykowski et al., 1989). Patients report a change in personality and that they were simply, no longer "the same". (Alby et al.; unpublished paper; Farkas-Patenaude et al., 1986). Andrykowski et al. (1989) report that the quality of life of "long-term survivors" of BMT compares less favourably to survivors of lung cancer and testicular cancer. BMT survivors suffer greater mood disturbances. The authors conclude that "emotional readjustment may pose a greater challenge for BMT survivors than is currently recognised". This is confirmed by Wolcott et al. (1986) who found "significant emotional distress, low self-esteem and less-than-optimal life satisfaction" in 15-25% of a group of long-term survivors. Alby et al. (unpublished paper) found that the fear of relapse was ever present in long-term survivors and relapse does indeed occur.

1.2.10 Relapse

Between 20% to 60%[2] of all patients survive BMT relapse. (Tutschka et al., 1987; Kanfer, 1988; Santos, 1984;). Although the fear of relapse experienced by long-term survivors has been mentioned (by Andrykowski et al., 1989 and Alby et al., unpublished paper) there exists no literature which looks at the psychological and social impact that relapse may have on the lives of the long-term survivors.

Relapse of cancer has been identified in other cancers as an extremely stressful event. Silberfarb et al. (1980) looked at three groups of breast cancer patients. Each group represented one stage in the disease process; that is, primary, recurrent and terminal disease. The first recurrence of the breast cancer was the most disturbing and stressful time for the patient. Relapse of the original disease led to an increase in psychological distress, particularly in the form of anxiety and depression. Psychological distress was paired with a negative attitude towards the primary physician.

[2] The author has no explanation for the discrepancy in percentages quoted in the literature.

CHAPTER Two: THE THEORY OF STAGES

2.1 Stages Described By Brown And Kelly

As the above literature documents, stressors and patients' responses during BMT are not static, nor are they repetitive but tend to run parallel to the medical treatment procedure.

Brown & Kelly (1976) were the first authors to acknowledge the "somewhat predictable pattern of psychological reactions to stress in various stages of the procedure" and to divide the whole BMT-procedure into stages. They delineated eight distinct stages and based these on observations made during their intensive work as part of a multidisciplinary team caring for BMT patients. Their paper describes this work with six adolescents and one adult patient during the transplant period.

This early report has been extensively used as a reference for later research and publications such as:

> Pfefferbaum et al., 1977; Popkin & Moldow, 1977; Popkin et al., 1977; Farkas-Patenaude et al., 1979; Gluckman et al., 1979; King et al., 1985; Hengelveld et al., 1988; Lesko & Holland, 1988; Jenkins & Roberts, 1991.

It has been used as a basis for later authors to propose a stage division of the procedure (Farkas-Patenaude et al., 1979; Haberman, 1988; Lesko & Holland, 1988; Lesko,1989).

This outline of the eight stages follows the medical procedure. At the same time the emotional impact of each stage appears to relate to a particular psychological theme; for example stage five encompasses the engraftment process with graft rejection or take and the emotional theme is "waiting". The authors explain the medical procedures particular to a stage and the emotional issues arising for the patient in this situation.

The eight stages outlined by Brown and Kelly are described in chronological order and give the medical procedure followed by the psychological/emotional "theme".

There are no psychological/emotional "themes" for stages four, six, seven and eight.:

Stage 1 : The decision to accept treatment:- "Anticipation",

Stage 2: Initial admission evaluation and care planning - "Preparation",

Stage 3: Immunosuppression and entry into isolation - "The Point of No Return",

Stage 4: Transplant itself (Day 0),

Stage 5: Graft rejection or take:-"Waiting" (approximately days 6 to 35),

Stage 6: Graft-versus-Host Disease (approximately days 6-100),

Stage 7: Preparation for discharge,

Stage 8: Adaptation out of hospital.

Although fairly comprehensive, the stages have some shortcomings. The period between transplant itself on day 0 and the stage covering engraftment commencing with day 6 is not covered. However, this is a period which is characterised by high morbidity and mortality. (Barrett, 1987; Burnett, 1988). It is during these first days after transplant that the patient will experience the first wave of side effects to the conditioning treatment. One could expect some psychological responses to this particular stressor, thereby justifying attention to this period.

The following stage, commencing with day 6 and ending with successful engraftment, is introduced by the authors with : "Unless there are problems with infections or haemorrhage, patients are generally well during this period". As their study was linked to a small sample and confined to only one treatment centre and has not been supported elsewhere, the effect fails to generalise.
There are other limitations to Brown & Kelly's model. One is the very small sample number. At the onset of treatment the sample comprises eight patients, by stage eight the authors inform us that " only about one-third of the already small number make it this far". (Brown & Kelly, 1976).

A more serious limitation to the findings of Brown and Kelly is the source of these findings. Psychological statements are not based on the use and application of established questionnaires, interviews or records but exclusively on clinical observations of the two authors. The authors did not provide any data on reliability of their clinical observations.

It is however important to note that psychological issues and problems appear to be stage specific. Brown & Kelly's findings are outlined as followed: Stage one was seen as potentially threatening, when patients are confronted with the critical nature of their illness causing anxiety and helplessness. The predominant responses to this threat were denial and displacement. Emotional morbidity was observed during stages three, five and six. In stage three it took the form of obsession, withdrawal, psychotic reactions and refusal to cooperate. Morbidity was not permanent but transient. In stage five, dreams and nightmares about the procedure were particularly bothersome to patients in this sample. In stage six, morbidity took the form of anger and depression. Depression was often deepened by prolonged isolation.

2.2 Stages

Stages have certain characteristics. A stage can be a period of time, a part or a phase of a process or a section of a larger piece. A stage does not stand unconnected on its own. It is always a part of a larger unit and is either preceded, followed or both preceded and followed by other stages. Stages are successive and sequential. Only when the lowest stage is completed can the second stage commence. The development of a succession of stages follows a logical sequence and consequence. Each stage has characteristics which tend to be stable.

Stages as outlined above have been used to describe phases in children's development. The most notable example is Piaget's theory of stages in the development of cognitive abilities in children. Piaget spent a lifetime researching the changes and development in children's perception and intelligence. (Boden,1979). His research and observations led to his formulation of a theory of stages in cognitive development. According to his theory children have to pass through certain stages in their development before they can perform certain tasks. All children pass through the outlined stages in the same order, and all children must go through the first stage before they can move into the second stage.

Piaget's theory of stages has distinct attributes. These attributes are as follows:

a) The order of the stages remains always the same. Stages have therefore a definite sequence which is predictable and invariable.

b) Completion of one stage leads to the next stage. Each progression from one stage to the next higher stage depends on the completion of the previous stage.

c) A stage is irreversible.

d) Stages are qualitatively and quantitatively different from each other.

e) A child is either in a stage or out of a stage.

Although there has been some critique by Flavell (1977), Donaldson (1978) and Bower (1976) regarding the content and boundaries of stages the attributes of stages as outlined have been accepted.

Any theoretical model using a stage division applied to the whole of the medical BMT procedure must contain the attributes outlined by Piaget's theory of stages.

Stages must have definite, predictable and invariable sequences. Stages must progress distinctively - completion of one stage leads to the next. Progression depends on the completion of the previous stage.

Stages are irreversible, and quantitatively and qualitatively different from each other. In regards to BMT patients are either in or out of a stage.

The emerging questions are: Is Piaget's stage model of cognitive development applicable to the medical procedure of BMT in the way Brown and Kelly attempted? Although a theory of stages offers itself as extremely useful to the psychological researcher in the field of BMT, we must remember that with leukaemic patients the stages are imposed from the outside, by the medical procedure they have elected to undergo. They are not the gradual accumulation of skills and abilities acquired by a child during the process of healthy development. If it is, do all patients proceed through the same medical stages in the same order?

The argument for the adaptation of Piaget's stage model to BMT is that medical treatment as it has been outlined above clearly follows a stage pattern. It is not a repetitive treatment with a cyclical pattern. This is particularly evident in the stages of conditioning, transplant and engraftment. All patients have to pass through the stage of "medical conditioning" for transplant before the marrow can be transplanted. Conditioning itself may vary but the order of conditioning followed by transplant cannot. The stage of "engraftment" has to follow the stage of "transplant" and cannot exist without transplant preceding it and without the earlier stage of "conditioning".

The sequence of stages does not vary from patient to patient nor from centre to centre; the sequence is definite and predictable. Progression of stages depends on the completion of the previous stage.

Stages in BMT are as irreversible as stages outlined by Piaget. Patients who completed conditioning cannot return to their pre-conditioning stage without completing the whole BMT procedure. Patients may relapse later after transplant and proceed to a second transplant, but they cannot return to a pre-conditioning state after completing the conditioning stage.

Stages in BMT are qualitatively and quantitatively different from each other. While the "conditioning" stage includes intensive treatment with chemotherapeutic agents over a ten day period, the stage of "transplant itself" lasts only one day and is characterised by a "simple" infusion of marrow.

Patients are either in or out of a stage. No patient goes through further conditioning, once the "conditioning" stage has been completed and the patient has moved on to the next stage of transplant itself.

Stages in BMT are definite, predictable, irreversible, and invariable in their order. They show a distinct progression and they apply to all patients.

2.3 Critique Of The Stages By Brown And Kelly

Stages one, two, three and four as defined by Brown and Kelly (1976) follow closely the medical procedure and show distinct boundaries and the attribute that the new stage cannot commence until the previous stage is completed. However, the next four stages show less definite boundaries and do overlap a great deal and may not merit the status of independent stages. Stage five covers the period from day 6 to day 35 post-transplant. The medical theme of stage five is "graft rejection or take"; the psychological theme is "waiting". To commence the stage at day 6 makes medical sense, since this is the earliest possible day for signs of engraftment to appear, and psychological sense since there is as yet no "waiting" before this day. Engraftment is usually not before the second week. (Kamani & August, 1984). This leaves the period between transplant day, day 0, and the commencement of stage five (starting day 6) uncovered. During this period however, important medical reactions take place. Patients experience their first wave of side effects due to the conditioning, and may have consequential psychological side effects.

Stages five and six again overlap. Stage six covers the period from day 6 - 100. The medical theme of this stage is potential complications of acute GvHD following successful engraftment. There is no psychological theme for this stage. GvHD is not the inevitable side effect of all successful engraftments. It does not apply to autologous transplant and to a varying percentage of allogeneic patients, depending on the treatment of the marrow prior to infusion. Not all patients who do develop GvHD develop it at the same time to the same degree. It may appear between days 10-100. (Kamani & August, 1984).

Stage seven has no time boundaries. Its theme is "preparation for discharge". Discharge may fall into the time scale of the two previous stages five and six. However, patients can only be discharged after successful engraftment.

For the last stage, stage eight, the theme is " adaptation out of hospital". There is neither a suggested time span nor an emotional theme.

Stages six, seven and eight have no psychological theme.
For the above reasons, (the confusion of boundaries, overlapping of stages, missing out of days 0-6) the following stages for this research are suggested:

2.4 Stages For This Research

Stages adopted from Brown and Kelly (1976) as well as the boundaries of new stages for this research are explained below. The first three stages suggested by Brown and Kelly (ibid) have been kept.

Stage four, "Transplant itself" however, has been left out. This stage has been left out for practical reasons, even though the medical procedure and its emotional impact have been documented and are recognised. Transplant itself is a very brief procedure (the marrow is infused into the patient's blood stream). This procedure needs nonetheless careful medical monitoring. Transplant follows immediately after conditioning when the patient is likely to feel ill. It is not practical to conduct a psychological assessment while medical activity is taking place.

Stages five, six , seven and eight have been changed for the reasons discussed earlier (the confusion of boundaries, overlapping of stages, missing out of days 0-6). (See section 2.3).

It has been reported that rehabilitation will take at least a year before patients physical and psychological states have recovered from the intensive treatment. (Haberman, 1988); Lesko,1989). Therefore, the last stage of this research will extend until a year (12 Months) post-transplant.

Stage 1 DECISION FOR TRANSPLANT

This stage covers the period leading up to the patient's decision for transplant. The decision can be taken anytime between a couple of months to two weeks prior to transplant depending on a variety of factors such as the state of the disease or the availability of a space in the transplant schedule of the transplant unit.

Stage 2 CONDITIONING

This stage covers the period from the decision for transplant until the conclusion of conditioning for transplant including transplant itself. Sometime during this period the patient will enter isolation.

Stage 3 FIRST SEVEN DAYS

This stage covers the first 7 days post-transplant when there is as yet no count of white blood cells indicating engraftment.

Stage 4 ISOLATION

This stage covers the period when the evidence of engraftment or non-engraftment appear. This period is spent in isolation. The stage commences at days 7 and concludes with the patients being able to leave isolation after successful engraftment.

Stage 5 SOMNOLENCE

Stage five was included following the suggestions by the consultant in charge (Dr. Powles) who observed that patients who had received Total Body Irradiation (TBI) developed severe somnolence and appeared to be depressed approximately six to ten weeks after TBI. This applied only to patients whose conditioning treatment included TBI.

Stage 6 THREE MONTHS

This stage covers the period from the end of isolation until three months, approximately 100 days, post-transplant. Acute GvHD can occur during the first 100 days.

Stage 7 TWELVE MONTHS

This stage covers the first year after transplant from day one.

Further Assessments

There are three further assessments included which are stage related but not applicable to all patients. These are:

Assessment I: This assessment will take place within the first 7 days after discharge from hospital.

Assessment II: This assessment will take place within the first week after the patient's first rehospitalization after discharge.

Assessment III: This assessment will take place if the patient does relapse.

All of these stages are summarised in Table 2.4 (see below)

Table 2.4

Stage/Assessment of expected stage progression	Events	Timing Of Assessment
Stage 1 (Baseline)	Decision For Transplant	2 Months To 2 Weeks Prior To Transplant
Stage 2	Conditioning Ending With Transplant (Isolation Starts)	1 Day Post-Transplant
Stage 3	First Week Post-Transplant	7-8 Days Post-Transplant
3a; 3b; 3c; Weekly Assessments	Period In Isolation	Days 14, 21. 28
Stage 4	Patients Leaves Isolation	At The End Of Isolation
Stage 5	Onset Of Somnolence For Patients Who Had TBI	Between 6-10 Weeks Post-Transplant
Stage 6	End Of Immediate Post-Transplant Period	3 Months Post-Transplant
Stage 7		12 Months Post-Transplant
Assessment of possible stages		
I	Discharge	Within The First 7 Days After Discharge
II	First Rehospitalization	Within 7 Days Of Rehospitalization
III	Relapse	If Patient Relapses A.s.a.p.

CHAPTER Three: HYPOTHESES TO BE TESTED

3.1 Hypotheses

On the basis of the stage model described above the following hypotheses are going to be tested.

1. The degree of Anxiety and Depression does not remain constant during the treatment. It is influenced by the changes in the medical treatment during the different stages.

2. The quality of life does not remain constant during the treatment. It is influenced by the changes in the treatment during the different stages.

3. The patient's attitude towards cancer does not remain constant during treatment. It is influenced by changes in the treatment during the different stages.

4. Perception of control does not remain constant during the treatment . It is influenced by the changes in the treatment during different stages.

5. Emotional problems and emotional morbidity are expected to be higher in some stages than in others.

6. Patient's expectation of treatment outcome does not remain constant. It changes over time and stages.

CHAPTER Four: M E T H O D

4.1 EXPERIMENTAL DESIGN

4.1.1 Timetable Of The Medical Procedure And Stages

The transplant period researched in this study covers approximately 14 months. (Table 4.1.1). It commences with the patient's decision to go ahead with Bone Marrow Transplant. The usual time for this decision is some 4-6 weeks prior to transplant. The study terminates 360 days after transplant when most of the surviving patients have become largely independent of close medical support.

This period was divided into 3 sections:

1. Time prior to transplant
   This includes the decision for transplant, conditioning and transplant itself.

2. The immediate post-transplant period
   This includes the time from transplant itself at day 0 until 100 days post-transplant.

3. Late post-transplant period
   This includes the time from Day 100 post to Day 360 a year post-transplant.

Patients usually make their decision to go ahead with BMT some weeks before transplant. Their first psychological assessment was done during this time. This assessment forms the baseline with which all later assessments will be compared to.

In some hospitals, e.g. the Royal Free, admission for conditioning is some 10 days prior to transplant. In other hospitals, e.g. the Royal Marsden Hospital, some of the conditioning is done on an out-patient basis and patients are admitted two or three days prior to transplant.

In both cases patients enter isolation by the time of transplantation of Bone Marrow at day 0. A day after transplant patients are assessed for their second assessment. This covers stage 2 (Conditioning). Patients remain in isolation until their white cell blood count reaches a certain number. This can vary from centre to centre. During the time in isolation patients were assessed on a weekly basis. These assessments came at stage 3 (7 days post-transplant), 3a (Week 2), 3b (Week 3), 3c (Week 4) until patients left isolation. The length spent in isolation varied from patient to patient, but was never earlier than 10 days post-transplant.

Discharge from hospital could follow very soon after the end of isolation or could be weeks later depending on the absence or presence of medical complications. In some cases patients who had developed Graft-versus-Host Disease did not leave hospital and died after a period of medical complications.

After discharge and during the period up to 100 days patients need careful medical monitoring and they are still very dependent on hospital support and medical treatment. Frequent visits to the hospital's out-patient unit for transfusions of blood products are the rule. Into this period also falls the somnolence period (days 42-70) for patients whose conditioning treatment included Total Body Irradiation (TBI).

First rehospitalization tends to occur for most patients somewhere in this period of the first 100 days. For those who received TBI rehospitalization often falls into the somnolence period.

The late post-transplant period falls between days 100 and 360. During this period a number of patients relapse. However, some patients in this study relapsed after day 360. They were still taken into this assessment.

Table: 4.1.1 Timetable of the Medical Procedure and Stages

Days	Periods	Events	Stages	Assessments
	(Period I)	DECISION FOR TRANSPLANT	I	Baseline
-10		ADMISSION		
		CONDITIONING		
		Time spent in Isolation		
0		TRANSPLANT		
+1	(Period II)		2	assessed
	Start of immediate Post-Transplant period with the possibility of acute GvHD			
7			3	assessed
14			3a	assessed
21			3b	assessed
28			3c	assessed
30+		END OF ISOLATION	4	assessed
		DISCHARGE	I	Assessment within 7 days
42	Onset of somnolence period for patients treated with TBI		5	assessed
70				
		REHOSPITALIZATION	II	Assessment within 7 days
	(Period III)			
100	Start of late post-transplant period with possibility of chronic GvHD		6	assessed
		RELAPSE*	III	Assessment of relapsed patients
360	a year post-transplant		7	assessed

* Relapse can occur earlier or later, but was more likely to occur after days 100+

TIME AS OUT-PATIENT	TIME AS IN-PATIENT	TIME IN ISOLATION

(Duplicate of Table 1.1.4)

4.1.1 Longitudinal Assessment

In this longitudinal study, patients were followed throughout their transplant procedure from the time following the decision to proceed with BMT until the point when they had completed the 12 months post-transplant period. Psychological functioning was assessed at the end of each of the stages outlined (see Figure 4.1.1). There were seven sequential assessments and three non-sequential assessments.

4.1.2 Possible Assessments Stages

The first assessment of patients formed the baseline, pre-treatment measure.

4.1.3 Additional Assessments

Initially there was no assessment planned between stages three (eight days after transplant) and four (end of isolation). However, it soon became evident that the time in isolation could vary from ten days to five weeks. It was, therefore, decided to assess patients at the end of each week spent in isolation (assessments 3a; 3b; 3c).

4.1.4 Subjects

A consecutive series of 80 patients admitted to the Royal Marsden Hospital in Sutton between January 1988 and March 1990 and to the Royal Free Hospital[3] between January 1989 and April 1990 who fulfilled the study entry criteria were approached and invited to participate in this research. These were patients treated on the hospitals' leukaemia wards, i.e. "Bud Flanagan" and "Compstom" respectively.

[3]A second series from the Royal Free Hospital, Hampstead, was included from January 1989 to increase the overall sample available to the study.

4.1.5 Selection Criteria

Inclusion criteria were as follows:

1. that patients were suffering from a possibly fatal disorder (they were all cancer patients) for which BMT was the treatment of choice;

2. that patients were aged eighteen years and over. No upper age limit was set; however, BMT is rarely performed on patients over fifty-five years of age.;

3. able to understand and read English;

4. no evidence of psychiatric disorders;

5. no evidence of serious cognitive impairment.

4.1.6 Recruitment Of Patients

Between January 1988 and March 1990 a total of eighty consecutive patients evaluated for BMT treatment in the Royal Marsden Hospital and the Royal Free Hospital were approached and invited to participate in this research. Out of these eighty patients seventy-five agreed to participate in the research. Five patients refused and the main reasons given for refusal were as follows:

(i) "The research was an intrusion into privacy (N=2);

(ii) patients were frightened and did not want to know and think about transplant (N=2);

(iii) patients were not interested in research" (N=1).

These patients did not differ from the study sample in terms of medical or sociographic characteristics.

4.2 MATERIALS

4.2.1 Selection Of Materials

Psychological factors known to influence the degree of morbidity are; patients' coping responses. (Watson et al. 1988), attitude and adjustment to the disease and perception of control. Perceived locus of control over the course of the disease is an important factor. Watson et al. (1990) defined locus of control as:

> "the perception that the cause of specific events will be attributed to personal (internal control) or situational (external control) elements".

Although perception of control over the course of the disease is associated with less emotional morbidity, control over emotions is not. Watson et al., (1990; 1991) found that increased emotional control is associated with fatalism and helplessness. Temoshok (1987) proposed that "chronically blocked expression of needs and feelings " may have an underlying belief that it is "useless to express one's needs." This in turn may lead to feelings of helplessness and fatalism. These factors may influence and be influenced by adjustment to the changed and changing demands on the cancer patients. Patients who are able to meet these new challenges and respond with positive adjustment to them, will feel more in control than those who don't. However, it remains somewhat contradictory which of the identified responses relate to greater vulnerability. (Watson et al., 1988).

The most commonly encountered psychological disorders among cancer patients are anxiety and depression. (Zigmond & Snaith, 1982; Moorey et al, 1991). There exist a number of well established and widely used tools for assessing anxiety and depression such as the General Health Questionnaire (GHQ), (Goldberg 1972), Beck's Depression Inventory (BDI), (Beck et al., 1961), Hamilton Rating Scale for Depression (HRSD), (Hamilton 1960). However, in assessing the presence and the degree of these two disorders in cancer patients, clinicians and researchers cannot rely on the usual guidelines and tools. These scales provide psychiatric guidelines for mood disorders. Symptoms like headaches, lack of energy, loss of libido, insomnia and anorexia play an important role in assessing these mood disorders. These somatic symptoms are likely to be found in cancer patients. They are frequently associated with the disease or the treatment itself. (Plumb & Holland, 1977; Moorey & Greer, 1989; Haes at al, 1990). It is therefore necessary, as Zigmond and Snaith stress, "to exclude symptoms which might equally arise from somatic as from mental disease" when assessing the presence and the

degree of psychological morbidity among cancer patients. However there is "no single scale available which adequately suits all purposes". (Watson et al ,1992).

4.2.2 Measures

The measures used:
(Copies of these measures are in Appendix I)

1. **The Hospital Anxiety and Depression (HAD) Scale (Zigmond & Snaith, 1982)**
2. **The Rotterdam Symptom Check List (RSCL) (de Haes et al ,1990)**
3. **The Mental Adjustment to Cancer (MAC) Scale (Watson et al., 1988)**
4. **The Cancer Locus of Control (CLOC) Scale (Watson, Pruyn, Greer & Van Den Borne, 1990)**
5. **A semi-structured interview**

4.2.3 BACKGROUND OF THE INDIVIDUAL MEASURES

1. The Hospital Anxiety And Depression (HAD)- Scale (Zigmond & Snaith, 1982)

In 1992 Watson et al. reported that the one of the most commonly used scales to measure anxiety and depression within oncology was the HAD-Scale. This scale was specifically designed for patients with physical illness. (Zigmond & Snaith, 1983). The aims of this self-assessment scale is to evaluate the "degree of distress" (Zigmond & Snaith, 1983) in patients in terms of anxiety and depression. It is the aim of this scale to provide a reliable screening instrument for clinically significant levels of anxiety and depression in patients.

The 14 items of this symptom checklist are based "solely on psychic symptoms of neurosis" (Zigmond & Snaith, 1983) excluding all physical symptoms. The checklist is divided into two sub-scales, one to measure anxiety, the other one to measure depression. Items chosen for each sub-scale should allow careful distinction between the two concepts of anxiety and depression. (Moorey et al., 1991). Items chosen for the anxiety sub-scale came from the appropriate section of the Present State Examination (Wing et al., 1974) and from personal research of Zigmond & Snaith (1983). Items forming the depression scale were based on the anhedonic state, which the authors considered the central psycho-pathological feature of a form of depression "which responds well to antidepressant drug treatment". Symptoms relating to severe mental disorders such as suicidal ideation or phobic limitations were excluded from the symptom checklist. The authors argued that these disorders were less common in medical patients.

The time required from the patient to fill out the questionnaire should take no more than five minutes.

The time span indicated for assessment on the HADS covers the last week prior to assessment.

Answers are on a four point Likert scale. Scoring ranges from 0-3. The anxiety and depression sub-scales are scored separately. The recommended threshold for indicating possible pathology is 8 or more (Zigmond & Snaith 1983). In this study the cut-off point for indicating cases was 8 points or more.

Moorey et al. (1991) reported the results of a factor analysis of HADS responses for 568 cancer patients. The authors confirmed two distinct stable but related factors which correspond to the sub-scales anxiety and depression.

Other research has looked at the validity of the HADS questionnaire, mainly by comparison with established scales. Notable here are the studies by Aylard et al. (1987); Barczak et al. (1988); Ibbotson et al. (1989); Razavi et al. (1990) confirming the HADS as a "simple, sensitive and specific tool for screening for psychiatric disorders in an oncology in-patient population". (Razavi et al 1990).

2. The Rotterdam Symptom Check-List (RSCL)
(de Haes et al ,1990)

The RSCL is a self-rating, Quality of Life measure developed "to measure the symptoms reported by cancer patients in clinical research". (De Haes et al., 1990).

Originally the RSCL was based on the following three checklists:

1. The Hopkins Symptom Checklist;

2. A Symptom Checklist used by Linssen et al., (1979), with breast cancer patients;

3. A Dutch version of the Symptom Distress Scale developed by McCorkle & Young, (1978).

The selection of items for the RSCL was based on factor loading and the relevance of these items to oncology judged by a group consensus. This led to the thirty item scale used in this research. There exist, however, various versions of the RSCL. (Watson et al., 1990). The thirty items cover psychological and physical distress experienced by oncology patients and are relevant to the disease and its treatment.

The checklist is divided into two sub-scales, one covering physical distress, the other one psychological distress.

The physical distress sub-scale comprises twenty-two items. Physical distress includes three factors:

1. distress relating to pain symptoms in various locations.;
(e.g. "headache" and "sore muscles");

2. symptoms relating to gastrointestinal distress ;
(e.g. "nausea" and "vomiting");

3. symptoms relating to the experience of fatigue and malaise;
(e.g. 'lack' of energy" and "tiredness")

The psychological distress sub-scale contains eight items and includes symptoms such as "worrying" and "feel desperate about the future". The authors stress that

this sub-scale contains "only purely psychological items" since "physical symptoms that usually accompany psychological morbidity have a different meaning for cancer patients. These symptoms are probably related to the disease or an effect of the cancer treatment".
(De Haes et al., 1990).

The presence of a dimension for psychological distress experienced by cancer patients has been found in all subsequent studies by De Haes et al. (1990), and the authors report that this dimension appears to be a stable element in the structure of the RSCL. Reliability was found to be consistently high. The authors also emphasise that "psychological symptoms do not automatically accompany physical distress". (de Haes et al., 1990).

The sub-scale physical distress appears to demonstrate a less stable pattern and the authors speculate that patients who are treated with chemotherapy experience distinct symptoms, such as constipation, diarrhoea and vomiting. Nonetheless, the authors reported that both the psychological and physical sub-scales could be distinguished empirically in the three studies executed and reported by the authors. Watson et al. (1990) reported that their data generally confirmed the original factor structure of 2 sub-scales. They also compared the RSCL to other scales and found the psychological symptoms sub-scale positively associated with similar measures. However, the combined physical symptoms sub-scale was also positively associated with the HADS measure of depression. They argued that some of this overlap may be accounted for by such physical symptoms in the sub-scale as 'lack of appetite' and 'lack of energy' which are sometimes evident in depressed patients. Further points of critique by Watson et al. (1992) were:

> (i) that the RSCL's psychological sub-scale does not distinguish anxiety from depression;
>
> (ii) that important aspects of patients' quality of life were not included (e.g. social, sexual and intellectual functioning).

The RSCL is a checklist which is easily understood by patients and it is easy to administer on a busy oncology ward. It takes about eight minutes to answer. (De Haes et al., 1990).

The Rotterdam Symptom Checklist not only assesses symptoms of distress but can also be used to "monitor the levels of a patient's anxiety and depression". (De

Haes et al., 1990). However, in this study it is primarily used to assess patients' level of physical symptoms. This has been confirmed by Trew & Maguire, (1982) who found the scale sensitive enough to detect the presence of psychological illness. Despite these statements there are no guide-lines for the interpretation of scores.

Patients are asked to report on the presence and degree of symptoms experienced during the preceding seven days. Each answer can be scored on a four point Likert rating scale ranging from 'not at all' (0 points), 'a little' (1 point), to 'quite a bit' (2 points) and 'very much' (3 points).

3. The Mental Adjustment To Cancer (MAC)- Scale
(Watson et al., 1988)

The Mental Adjustment to Cancer (MAC) Scale is a self rating scale designed to measure style of coping with cancer. It can be used as a screening device by medical and nursing staff in busy oncology clinics which handle a large number of patients. The authors (Watson et al., 1988) have found it to be acceptable to patients and easy to administer in their own extensive research with cancer patients. They also found a good test and re-test reliability.

Mental adjustment refers "to the cognitive and behavioural responses made by an individual to the diagnosis of cancer." Mental adjustment comprises:

> appraisal - i.e. how the patient perceives the implication of cancer and the ensuing reactions - i.e. what the patient thinks and does to reduce the threat posed by cancer" (Greer & Watson, 1987).

The forty items on the MAC-Scale were based on statements made by patients during structured clinical interviews in previous research by Greer et al. (1979) and Pettingale et al. (1985). In these statements patients described their thoughts and feelings to their diagnosis of cancer .

The forty items of the scale are limited to the following response categories:

Fighting Spirit (16 items)

This attitude shows the patient fully accepting the diagnosis, confronting it and being determined to fight the negative impact of the disease on the quality of life.

Helplessness/Hopelessness (6 items)

Patients show a passive response to the diagnosis of their disease.

Anxious Preoccupation (9 items)

This subscale measures anxiety and also patients' tendency to seek information. However, the latter serves to fuel their anxiety rather than reduce it.

Fatalism (8 items)

This reflects a fatalistic attitude towards the course of the illness.

Avoidance (1 item)

Patients deny or minimise the seriousness of their disease.
Patients are aware of the diagnosis and cannot "avoid" it. However, avoidance may take other forms and be reflected in the patients denial or minimising of the seriousness of the disease.

In this research results of the sub-scale Avoidance are not interpreted.

Answers are given using a Likert-type four point response categories ranging from 1-4. Categories range from "definitely does not apply to me" (1 point); "does not apply to me" (2 points) to "applies to me" (3 points) and "definitely applies to me" (4 points).

Each of the five sub-scales is individually scored. The score ranges for each sub-scale are:

Fighting Spirit	**16-64 points**
Helplessness/Hopelessness	**6 - 24 points**
Anxious Preoccupation	**9 - 36 points**
Fatalism	**8 - 32 points**
Denial/Avoidance	**1 - 4 points**

Interpretation of the scores can be done in a number of ways. In the Manual the authors suggest:

1. by comparison of raw scores to the normative scores described in the manual;

2. using standardised T-scores[2] and a profile sheet;

3. patients may be selected as "'cases', i.e.. scores above a cut-off point.

[2] T-scores for sub-scales Fighting Spirit and Helpless-Hopeless are scored for combined FSH-T.

Recommended cut-off point for cases:

These are based on a pilot study sample N=79 attending the Royal Marsden Hospital between 1986-87. They were derived by selecting the top 16% (1/6th) of the distribution of scores, that is one Standard Deviation from the distribution mean.

Cut-offs were calculated from estimates of the sample means and Standard Deviation obtained.

Thus the derived cut-offs were:

Fighting Spirit	**47 and less**
Helplessness/Hopelessness	**12 and more**
Anxious Preoccupation	**25 and more**
Fatalism	**22 and more**
Avoidance	**3 and more**

Patients who score 47 or below on Fighting Spirit and 12 and above for Helpless/Hopeless combined are considered to be a 'case' and selected for intervention.

Scale validity was tested by the patient's spouse or partner rating the patient's response, which produced a highly significant intercorrelation with the patient's own response.

Normative data are available for 500 patients.

4. The Cancer Locus Of Control (CLOC)-Scale
(Watson, Pruyn, Greer & Van Den Borne, 1990)

The Dutch Cancer Locus of Control (CLOC) Scale was specifically developed for cancer patients. (Pruyn et al., 1988). It is a measure to be used for the prediction of illness related behaviour. The original Dutch Scale measures three dimensions and is divided into three corresponding sub-scales. These sub-scales are as follows:

1. control over the c o u r s e of the disease;

2. control over the c a u s e of the disease;

3.. religious control.

To examine patients' locus of control beliefs only the sub-scale relating to control over the course and the future of the disease and disease outcome was used.

This sub-scale contains seven items. Answers on the Likert-type scale range from 1-4. Categories range from "completely disagree" (1 point), "slightly disagree" (2 points), to "slightly agree" (3 points) and "completely agree" (4 points). All questions are positively phrased. The number of points are added up. The higher the score the greater the perception of feelings of control.

In a comparative study (Watson et al., 1990) between the Cancer Locus of Control Scale and the MAC-Scale, a positive attitude in the form of a "fighting spirit" was significantly associated with a high rating of internal control over the course of the disease. However, in the same research it was stated that "there were no clear indications that perceived locus of control was related to level of depression or anxiety measured by the Hospital Anxiety and Depression Scale."

6. Taped Semi-structured Interview

(Copies of the semi-structured interview are in Appendix I).

Where patients consented, a taped interview was conducted to collect qualitative information above and beyond the information gained from the questionnaires. The interview covered the following issues:

1. Factors contributing towards the decision for transplant and the patients' perceived control in this decision making process;

This part consisted of six questions. These questions referred to:

patient's introduction to BMT
to a perceived choice between BMT and other treatments
how the choice was made and who influenced this choice.

This part was only asked once during the first interview.

The questions are based on the hypothesis that this treatment requires complex and extensive information to be explained. This information has to be imparted within a limited amount of time and this does not encourage extensive discussion between the physician and the patient-family. I expected that the decision would be strongly influenced by the physician who is "the acknowledged expert in this highly specialised field", (Patenaude et al., 1986), and less based on the weighting of two or three alternative treatment options.

2. Questions relating to patient's expectations regarding the outcome of the treatment.

Two questions referred to the patient's expectations and factors contributing to these expectations. They are asked during every interview. These questions were added to explore whether or not the patient's expectations change over time.

3. Questions relating to stressful events experienced during the preceding stage.

These questions related to stressful and frightening events and the experienced distress. They are exploratory questions to evaluate the presence of particular stressors during the different stages and the hypothesis is that some stages, e.g.

stage 4 isolation, will produce more stressors than others. These questions are asked at each interview.

4. Questions relating to the support received during the treatment procedure i.e. whether support was perceived to exist, who provided it, and how it was experienced.

Support has been shown to ameliorate the effect of stressors. This group of questions is set to explore the resources for support within the family, health and social setting of the patient.

4.3. PROCEDURE

4.3.1 Dependent Variables

The dependent variables to be investigated are:

1. Emotional distress
2. Physical distress
3. Coping and mental adjustment to cancer
4. Perception of control
5. Expectations of disease outcome
6. Social support

4.3.2 Administering of Questionnaires

In order to assess the degree of emotional and physical distress in the form of anxiety, depression, physical and psychological symptoms the HAD-Scale and the RSCL were used. The questionnaires were administered to patients at each point described in Table 4.1.1

Patients' attitude to their treatment situation, and coping strategies were assessed on the MAC-Scale at the end of the first 3 stages ; 1 (Decision/Baseline); 2 (End of Conditioning); 3 (First 7 days). It was next administered at the End of Isolation (stage 4); at Three Months (stage 6); at Twelve Months (stage 7); at Discharge (stage I) and where applicable at theFirst Rehospitalisation (stage II) and at the Relapse (stage III).

Patients' perception of control was assessed on the CLOC-Scale at stage 1 Decision/Baseline ; stage 4 (End of Isolation); stage 6 (Three Months); stage 7 (Twelve Months); stage II (First Rehospitalisation) and at stage III (Relapse).

A structured taped interview relating to distress, support and expectations was given at all stages with the exception of assessments 3a, 3b, 3c (during isolation) and stage 5 (Somnolence). At these assessments only the HAD-Scale and the RSCL were administered.

4.3.3 Patient Recruitment

Information about forthcoming transplants was gained from the BMT-co-ordinator at the Royal Marsden and from the monthly unit meeting at the Royal Free.
Patients who fulfilled the entry criteria were approached in the following ways;

1. If the patients were already attending the centre as either out-patient or in-patient they were

a) approached directly by the author in the Royal Free
b) indirectly through the BMT co-ordinator in the Royal Marsden.

2. If patients were travelling to the centre from other parts of England they were contacted by letter. The letter would contain a written explanation, a leaflet giving details of the timing and frequency of assessments and the first set of questionnaires.
(Copies of the letter and leaflet are in Appendix II).

3. If patients came from Europe or overseas and it was not possible to contact them prior to hospitalisation they were approached as soon as possible after their arrival at the centre either by the BMT-co-ordinator or by the author.

A fourth category evolved. This included patients who were emergency transplants. These patients were usually referred from hospitals who did not provide transplant as a treatment option, but had provided conventional treatment for these patients. Patients had relapsed and transplant was seen as the only feasible treatment option at this stage in their disease.

4.3.4 Informed Consent

Patients were approached for consent in the following way:

The study was explained to the patient in the presence of a member of the staff, either the BMT-co-ordinator, a doctor or a nurse. A note to this effect, signed by the researcher and the member of the staff, was added to the patient's notes, together with a information leaflet giving time and frequency of assessments (Copies in Appendix II). A red sticker identifying the patient as a participant in the study was attached to the cover of the patient's medical notes.

4.4.5 Assessment Places

Places for the assessments were the patients' home, the out-patient wards and the in-patients ward of the Royal Marsden Hospital ,Sutton, and the Royal Free Hospital, Hampstead, London.

1. Home:

When patients were not available for assessment within hospital localities, questionnaires and open-ended questions covering the topics from the structured interview were sent to these patients at their home address. These tended to be patients who were referred from outside London to the transplant centre, who later returned to their own hospitals after discharge from the ward.

2. Out-Patient Units

Patients' coming appointments to the out-patient units were recorded in available appointment books. These books were constantly checked and patients due for assessment were approached while waiting to be seen by the physician. The out-patient waiting rooms in both hospitals were in corridors adjacent to the treatment rooms. In the Royal Free Hospital (RFH) this corridor was part of a separate ward; in the Royal Marsden Hospital (RMH) it was part of a corridor system linking different wards. The out-patient treatment areas were quite different in the two hospitals. In the Royal Free single rooms were provided for treatment such as blood-transfusions, or the infusion of medication. In the Royal Marsden a large room containing four beds and a number of chairs served as an examination and treatment room.

3. In-Patient Wards

The RMH has one six-bed unit for patients who were not in isolation. The units are divided by partitions and removable doors. This unit is very small and consequently provides little privacy. The RFH has an open ward with four beds which also provides little privacy. Both hospitals ,however, provide single rooms to patients if these are available.

4. Isolation

The patient in isolation always occupied a single room with shower and washing facilities. However, the degree of isolation varied considerably between the two hospitals. This variation referred to access to the patient, the number and frequency of visitors allowed, as well as the precautions required for people entering the isolation room.

Entering isolation in the RFH required the washing of hands, putting on a new plastic apron, a new mask and sterile gloves. Any object to be taken into isolation needed to be sprayed with a special disinfectant solution. Patients were allowed two visitors at any given time. These visitors could be relatives or could be friends.

Entering isolation in the RMH required a different procedure. The person who intended to enter had to exchange his/her outfit for an unused, sterile, cotton top and cotton trousers (a pyjama-like outfit), change outdoor shoes to indoor shoes (not provided) and proceed to an area adjacent to the patient's room. The cleaning precautions had to be undertaken in the following order:

1. cover your hair with a cap
2. wash your hands
3. put on a plastic apron
4. wash your hands thoroughly up to the elbows
5. enter the room without touching the door with your hands

Questionnaires to be handed to the patient needed special treatment in both hospitals. However, the degree and procedure differed between the hospitals. (The RFH procedure has been described above). In the RMH the treatment included leaving all paper for sixty minutes in a sterilising 'oven'. After one hour the questionnaires were removed with tongs from the oven and put into a plastic box without being touched directly. The plastic box was then closed and carried to the patient's room. The room was accessible through a cupboard with two doors, one opening to the corridor, the other to the patient's room. Each room had two compartments, one for clean items, such as the questionnaires, bed-clothes and medicine and one for dirty items,such as bed-pans etc. The questionnaires were removed from the plastic box with the help of tongs and placed into the clean section, from

which the patient could retrieve them after the outside door had been securely closed.

There was some discussion prior to starting the research on how to handle the microphone for taping the interviews. In the end a microphone was allowed provided the patient did not touch it, since it could not pass through the strict sterilising procedure.

4.5 DATA COLLECTION:

4.5.1 Time

Data collection began in October 1987 with a pilot study. The main study commenced in January 1988 and was completed in spring 1991 with the last one-year follow up assessment.

Sole responsibility for the data collection was the author's. New patients were entered into the main study over the period of 27 months. Follow-up was for one year further.

4.6.2 Difficulties with Assessments

Apart from the time-consuming preparations for entering the patient's room while in isolation, the biggest problems were lack of privacy and unpredictability of the patient's physical status on the day of the assessment. Patients in isolation required almost continuous medical and nursing care e.g. blood transfusions, infusion of medication or nutrition. The room needed careful daily cleaning. It was therefore difficult to find a time when patients were on their own to be able to interview them.

A similar problem was present for patients interviewed in the hospitals ward or out-patient sections. Neither provided privacy for interviews. Interviews had to be conducted with hushed voices in the corridor amidst other patients or staff passing through. Patients were reluctant to move to a quieter or more private place for fear of missing their turn when they were due to be seen by the doctor and thus extending their 'waiting' time.

The physical condition of patients in isolation could change very quickly, often within hours. A patient who was well in the morning could be seriously ill in the afternoon, could even be in intensive care on a ventilator. Patients might have felt unable to do the assessment because of feeling too tired. Blood transfusions took a long time, at least a couple of hours, and were often performed in the late evening and at night, and patients needed to catch up on their sleep in the morning. On other occasions pain was a problem and it required strong sedating medication to provide comfort and patients could not be approached.

Interviews during isolation following the conditioning of patients with chemotherapy and TBI were not straightforward. Among the early side effects of Total Body Irradiation (TBI), mucositis is a painful condition of the mouth and throat. Patients suffering from mucositis found talking difficult and painful and could not be interviewed. Other early side-effects include vomiting and diarrhoea and interviews were interrupted by the patient's vomiting and the interviewer providing nursing care to the patient.

As nursing staff were unable to monitor what happened when questionnaires were sometimes left for patients to complete, a small number were either lost or misplaced.

4.6 STATISTICAL METHOD

4.7.1 Questionnaires

To test for differential treatment effects on psychological morbidity, quality of life and perception of control an unequal cell repeated analysis of variance was used as follows:
Factor 1 (Within groups)
Stages (Difference D.F 5) i.e. Stage 6 compared to Baseline (stage1) = 5 D.F.

Other factors controlled for in this study were:

Factor 2 Subject Sex: Females and Males

Factor 3 The two Hospitals: The Royal Marsden Hospital and The Royal Free Hospital

Factor 4 The two Transplant Types: Autologeous vs. Allogeneic

Factor 5 The two Conditioning Regimes: Chemotherapy vs. Chemotherapy and Total Body Irradiation (TBI)

If there was a significant F-ratio for Factors then a test of simple effects was made.

4.7.2 Missing Data

Missing data in sub-scales were treated in two ways according to frequency. One missing item was substituted by the calculated mean of available items. In cases of more than one missing item the sub-scale was not included into data analysis.

4.7.3 Baseline

Assessments collected at stage one formed the baseline for comparisons. Wherever stage one assessments were missing assessments from stage two were used instead. Both assessments are pre-treatment and should not show any treatment effect.

4.8.0 Taped Interview

All interviews were recorded on a tape recorder and subsequently transcribed in full. A content analysis of the interviews was conducted.

Two raters, H. Funaki and M. Wood, each with expertise in the subject matter, independently coded a selected number of ten interviews. Inter-rater reliability for this coding was established at 87% levels of concordance This was considered to be respectable for qualitative data.

CHAPTER Five: PILOT STUDY

5.1 PURPOSE OF THE PILOT STUDY

A pilot study was conducted prior to the main study
The purpose of the pilot study was:

1. **To determine the viability of the study**

2. **To assess the acceptability of the main study to patients, families and staff**

3 **To evaluate the research method**

To achieve this preliminary data were collected on seven patients.

5.2 METHOD OF THE PILOT STUDY

5.2.1 Subjects

To evaluate the three aims of the pilot-study, seven adult patients currently undergoing treatment for Leukaemia or related blood cancers on the Bud Flanagan ward of the Royal Marsden Hospital, Sutton, were approached.

Patients were at different stages of their treatment, ranging from the newly diagnosed to post-transplant relapse.

Three patients were in the acute stage of their disease and receiving chemotherapy to induce remission. Transplant had not yet been introduced as a possible later treatment option to this groups of patients. One patient was in remission and had opted for transplant as further treatment. Two patients were at the stage of seven days post-transplant. One patient had relapsed after transplant. (See Table 5.2.1).

Patients' ages ranged from twenty to forty-four years.

Table 5.2.1 Distribution Of Sample

Categories	Pre-remission	Pre-transplant	7 days post-transplant	Relapse
Numbers	3	1	2	1

5.2.2 Materials

The measures used in the pilot-study were:

(Copies of these measures are in Appendix I)

1. The Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1982)
2. The Rotterdam Symptom Check List (de Haes et al ,1990)
3. The Mental Adjustment to Cancer Scale (Watson et al., 1988)
4. A semi-structured interview

The open-ended questions were grouped around three topics:

(i) Identification of stressful events

(II) Identification of available support

(III) Evaluation of patients 'expectations' of treatment outcome.

5.3 PROCEDURE OF PILOT STUDY

5.3.1 Place Of Assessment

Patients were assessed in either the in-patient or out-patient section of the Bud-Flanagan ward of the Royal Marsden Hospital, Sutton.

5.3.2 Recruitment Of Patients

The BMT-co-ordinator approached patients she thought were suitable subjects for the pilot-study. She introduced and explained the study and asked patients whether they would be willing to participate. None refused. She then introduced the researcher and a time was arranged for the interview to be conducted.

5.3.3 Timing Of Interview

Some of the interviews took approximately twenty to thirty minutes, but many took much longer. The reason for this was that patients seemed to welcome the opportunity to talk about their experience to an 'outsider'.

5.4 RESULTS OF PILOT STUDY

5.4.1 Preliminary Data From Questionnaires

Results of the assessments are shown on Tables 5.4.1a and 5.4.1b (See below).

Table 5.4.1a
Hospital Anxiety and Depression (HAD) Scale and Rotterdam Symptom Check List (RSCL)

Subject	Age	Stage	HAD - Anxiety	HAD De-pression	RSCL
1	36	Isolation	10	14	54
2	23	Isolation	5	4	41
3	42	Decision	7	1	11
4	44	Chemo-therapy	3	2	14*
5	36	Chemo-therapy	2	0	25
6	29	Chemo-therapy	7	5	28
7	20	Relapse	10	4	27

* subject missed out second page

(i) Hospital Anxiety And Depression Scale

Anxiety and Depression as measured on the HAD-Scale were highest in patients No. 7 and No. 1. Patient No. 7 had recently relapsed and patient No. 1 was in stage four on his second transplant. Both scored above the cut off point on the subscale Anxiety and qualified as 'cases'. Patient No. 1. scored also very high on depression, score = 14 points, thus falling within the range of a major depressive disorder. (Razavi et al., 1990).

(ii) The Rotterdam Symptom Checklist

2. Scores on the Rotterdam Symptom Checklist in this small sample were taken for combined subscales. The two patients (Nos. 1 and 2) showing highest overall score on the combined subscales were 7 days post transplant in their treatment.

When comparing the two post-transplant patients with those currently receiving chemotherapy to induce remission (Nos: 4, 5 and 6) the patients at the post-transplant stage showed the highest overall level of psychological and physical symptoms.

The one patient ((No. 3)) who was an out-patient scored lowest on the combined RSCL-subscales.

Table 5.4.1b
Mental Adjustment to Cancer (MAC) Scale

Subject	Age	Stage	MAC FS	MAC AP	MAC H	MAC F
1	36	Isolation	46	28	6	12
2	23	Isolation	54	21	10	20
3	42	Decision	50	24	9	17
4	44	Chemo-therapy	63	20	6	17
5	36	Chemoth erapy	54	14	6	19
6	29	Chemo-therapy	52	24	10	14
7	20	Relapse	45	25	12	20

(iii) Mental Adjustment To Cancer Scale

Scores for the Mental Adjustment to Cancer Scale for Fighting Spirit ranged from 45 to 63 points. The scores were lowest in both patients who had experienced relapse after transplant (Nos. 1 and 7). In both these cases scores fell below the 47 threshold.

Scores for Helplessness ranged from 6 to 12 points. Scores were highest for the one patient who had recently relapsed (No. 7) and who was not receiving any further active treatment.

Fatalism scores ranged from 12 to 20 points.

Scores for Anxious Preoccupation ranged from 14 to 26 points; both patients who had relapsed scored highest.

5.5.2 RESULT OF THE PILOT STUDY OF THE INTERVIEW

Below are the data relating to answers given by patients to the following questions:

Question No. 1:

Which recent event caused you most upset?

Answers to this question are on Table 5.5.2-1

Table 5.5.2-1

Categories	Chemo-therapy	Lumbar Puncture	TBI*	Infections	Diagnosis
Numbers	1	2	2	1	1

Question No. 2:

What do you think made these treatment procedures especially upsetting to you?

Answers to this question are on Table 5.5.2-2

Table 5.5.2-2

Categories	Uncertainty	Helplessness	Pain	Fear
Numbers	3	3	1	1

Question No. 3:

Did the distress remain with you after the event?

Answers to this question are on Table 5.5.2-3

Table 5.5.2-3

Categories	Passed	Remained	Returned	Got Used To
Numbers	2	2	2	1

Question No 4:

Have you found one incident, one period of time, particularly discouraging?

Answers to this question are on Table 5.5.2-4

Table 5.5.2-4

Categories	When physically Low	Failure of Treatment	Relapse after BMT	Prospect of BMT
Numbers	2	1	1	1

Two patients had never felt discouraged. One of these was the BMT-relapse patient.

Question No. 5:

Was there a time when you actually felt scared?

Answers to this question are on Table 5.5.2-5

Table 5.5.2-5

Categories	Never	After TBI	Diagnosis	Relapse	At Night
Numbers	2	1	3	1	1

Question No 6:

What kind of support helped you most to manage these difficult times?

Answers to this question are on Table 5.5.2-6

Table 5.5.2-6

Categories	Family	Information	Colleagues	Clergy
Numbers	4	1	1	1

Question No 7:

Did your religious beliefs support you?

Answers to this question are on Table 5.5.2-7

Table 5.5.2-7

Categories	YES	NO
Numbers	3	4

Question No 8:

Was there a coping method you developed yourself. ?

Answers to this question included: reading;working; fighting the feeling of despair; tolerating pain; Gestalt Therapy; praying.

Answers to this question are on Table 5.5.2-8

Table 5.5.2-8

Categories	Keeping Busy	Fighting	Accepting	Praying	Gestalt Therapy
Numbers	2	1	2	1	1

Question No 9:

You have chosen BMT as a treatment for your Leukaemia. What are your expectations regarding the outcome of this treatment?

(This question applied to four patients only).

Answers to this question are on Table 5.5.2-7

Table 5.5.2-7

Categories	To Be Cured	To Get Better
Numbers	3	1*

***the patient undergoing his second transplant**

Question No. 10:

Have these expectations changed?

Answers to this question are on Table 5.5.2-10

Table 5.5.2-10

Categories	Yes	Many Times	No
Numbers	1	1	2

5.6 DISCUSSION

5.6.1 Aims

The pilot-study was conducted on a very small sample of seven patients who were at different stages during their treatment. The pilot-study had 3 aims:

1. To see whether a study of patients undergoing Bone Marrow Transplantation was viable.

2. To see whether a study was acceptable to patients and staff.

3 To evaluate the research methods.

5.6.2 Aim No. 1 - Viability Of Study

The pilot study has shown that it is possible to assess patients during their treatment with Bone Marrow Transplantation. It was possible for the researcher to assess patients while in isolation by following the sterile precautions established on the ward.

However, during this piloting possible difficulties emerged. These were:

(i) Changes in patients' physical states can interfere with the pre-planned timetable for assessments;

Planned assessments were interrupted or postponed due to sudden medical complications such as infections. These medical complications necessitated immediate medical attention and intervention e.g. infusions.

Planned assessments did coincide with medical treatment and the researcher had to consider the advantages and disadvantages of either conducting the interview simultaneously with on-going medical treatment or postponing the assessment to a more convenient time.

Postponement could mean that the interview would never take place, since the patient's conditions could further deteriorate.

Considering the intrinsic uncertainties of the patient's medical prognosis (any infection may lead to death) it was decided to conduct the assessment under less than ideal circumstances if the patient was able and willing to do so, even if this assessment had to be conducted simultaneously with ongoing medical treatment and often with a third party present.

(ii) The upsetting nature of the disease, treatment, and the often negative treatment outcome can be emotionally very demanding for the researcher.

The nature of the planned longitudinal study will include continuous personal contact between researcher and patients. In many cases this contact is likely to be terminated by the patient's death. The researcher will not only observe

psychological distress but great physical distress, pain and suffering. There is no psychologist on the team to support patients. Patients experiencing unbearable distress will have to be referred to the psychological medicine team in the hospital. The researcher will need support from outside sources.

(iii) It can be difficult to keep well informed about patients' changing timetable and physical status.

The unpredictable course of patients' recovery from transplant will require constant checking and good communication with the transplant team to keep the researcher informed about changes in patients' treatment. E.g. the time spent in isolation varies considerably from patient to patient and depends largely on the white blood cell count which is checked on a daily base. Whenever the white cell count reaches a satisfactory level isolation is terminated.

5.6.3 Aim No. 2 - Acceptability Of The Study To Patients And Staff:

None of the interviewed patients appeared to be distressed by the assessment. The selected questionnaires and questions asked in the taped interview were acceptable to the patients. Patients did not report back any distress to the staff about the questions in the assessment. However, there were positive comments from patients who had participated in the pilot study to the ward sister. These comments referred to being pleased to have had the opportunity to talk about the impact of their disease and its treatment on their life.

There were no complaints from the staff about the assessments' interfering with their medical treatment of patients. The assessment could be conducted without interfering with patients' treatment. On the contrary, the ward sister took the opportunity to ask advice in dealing with one particular patient. The staff accepted the researcher, and it was possible to establish a liaison with the Bone-Marrow Co-ordinator. The latter liked to be 'involved' in introducing patients to the research. The pilot-study made it possible for the researcher to get to know nurses and allowed the nurses to familiarise themselves with the researcher.

There was no contact with family members during this pilot-study and it is therefore not possible to answer the question whether this study is acceptable to the patient's family .

5.6.4 Aim 3 - Evaluation Of Research Methods

a) Questionnaires:

The three questionnaires already described and used in this pilot-study were acceptable to the patients. They are all three well established questionnaires in the research with cancer patients. They appeared to be sensitive to the varying degree of patients' reported anxiety, depression, quality of life and adjustment to cancer.

b) Taped Interview

The open ended taped questions produced on the whole informative answers, although one or two questions needed re-phrasing. Nonetheless more information is needed with regards to patients' initial decision to proceed with transplant.

Six out of seven patients named the feeling of helplessness and the uncertainty of the treatment as the most distressing quality. It was therefore decided to add a questionnaire assessing perception of control over the course of the disease experienced by this group of patients. The questionnaire will be administered at four crucial points:

1. The decision to undergo bone-marrow transplantation
2. During the period spent in isolation
3. Three months post-transplant
4. Twelve months post transplant.

5.6.5 Possible Difficulties in main study

The pilot-study indicated that a great deal of co-operation would be necessary between the researcher and the respective ward during the study as it will be difficult to get into contact with new patients and keep contact with patients at different stages of their treatment. Since this ward has never had a psychologist, it depends on the researcher how this position may be perceived in months, maybe years to come, whether nurses will feel at ease and trusting or consider the psychologist as an 'outsider'.

However, since some newly admitted transplant-patients will spend only a very brief period in stage two (Admission) before moving into the equally short stage three (transplant itself) there may be difficulties in assessing patients. One possible solution considered was to restrict the assessment at stage two to three questionnaires, to be administered by the staff. This option had to be abandoned considering the workload of the nurses. It has therefore been decided to fuse the two stages into one. This new stage will be called stage two (Conditioning).
As a rule patients undergoing BMT in the Royal Marsden Hospital do not have access to a psychologist unless they become psychiatric cases. Therefore the researcher's role in the planned study may exceed the normal function of a researcher and may include psychological support by virtue of merelybeing there, particularly during isolation.

6.6 CONCLUSION

Even within this small sample of patients there seemed to be an agreement among patients that Lumbapuncture and Total Body Irradiation (TBI) are very distressing procedures. Furthermore, there seemed to be a consensus among these patients that not being able to predict the outcome of this treatment, its uncertainty, and not being able to control the situation, created feelings of helplessness. This made the treatment for Leukaemia and the BMT procedure particularly upsetting and added to the experienced distress.

Two patients reported that this distress remained with them for a prolonged period, although one felt that he got used to it. Two patients explained that the distress was reactivated by related procedures which reminded them of the original experience, e.g. Lumbapuncture.
Two patients felt that they could fight less well at times of physical fatigue and medical complications, such as infections and fever. One had felt very discouraged at the end of a course of chemotherapy when the anticipated state of remission was not achieved. Relapse after the completed treatment was experienced as very discouraging by one of the relapsed patients, but surprisingly not by the other. Three out of seven quoted the diagnosis of the disease as being the most frightening experience. One patient found waking up after TBI very frightening; another learning about his relapse. The patient who felt scared at night feared he was going to fail in his religious beliefs.

Surprisingly , two patients had not experienced any fear during their treatment.

When considering support, the family was named as the single most important source of support by four patients. One patient quoted the information provided by the medical staff as very supportive; for another one his colleagues from work helped him most by looking after the welfare of his family. He experienced this as the single most supportive factor.

Different patients developed different methods to cope with the pressure of the treatment. For some it was keeping their minds occupied by reading and working, for others it was sleeping as much as possible and trying to fight the feeling of despair.
Three out of the four eligible patients expected to be cured by BMT. The fourth one, who had a transplant before and subsequently relapsed, expected only to

come through. One patient implied that his expectations had changed many times during the procedure. The sample is too small to yield any firm conclusions.

CHAPTER Six: RESULTS

6.0 INDEX

[1](In this and following sections the Assessments I, II, and III are referred to as 'stages', although strictly speaking they are not. This was done to ease understanding of the data and the interpretation of the data).

6.1 DEMOGRAPHIC DATA

6.1.1 Demographic and Medical Data

The final distribution of patients according to hospitals, disease, transplant type, marital status, age and gender is shown in Table 6.1.1 (below).

Table 6.1.1 Demographic and Medical Data

	ROYAL MARSDEN	ROYAL FREE	WHOLE POPULATION.
DISEASE:			
AML	35	3	38
ALL	11	6	17
Myelodis plasia	2	0	2
CGL	8	1	9
Others	5	4	9
GENDER:			
Male	36	9	45
Female	25	5	30
TRANSPLANT:			
Autologous	22	7	29
Allogenic	39	7	46
DONOR INFORMATION:			
Related Donors	36	5	41
Unrelated Donors	3	2	5

Donors for the 46 allogeneic transplants are given in Table 6.1.1 (See above)
The majority of donors were related to the patient; 40 were siblings, one was a son.

Three donors were matched unrelated donors. None of the transplants with matched unrelated donors was successful. Two patients died, and the third one failed to engraft and was autoinfused with his own previously frozen marrow.

6.1.2 Age Distribution

The majority of patients were between 31-40 years old. Patients in this age group tended to be parents of younger children, very much in need of both parents. The mean age of the study group was 34.26 years old, and the median age was 35. See Table 6.1.2 (below).

Table 6.1.2 Age Distribution

Age:	< 20	21-30	31-40	41-50	50+
Number:	2	21	31	16	5

6.1.3 Marital Status

The majority of patients were married or living with a partner (48 of 75 were married). Patients' marital status is shown on Table 6.1.3 (below).

Table 6.1.3 Marital Status

Status:	Single	Co-habiting	Married	Separated	Divorced
Number:	18	3	48	0	6

6.1.4 Disease Status Of Patient

In the majority of cases transplanted patients were not end-stage patients, but patients in first remission who still had a good prognosis. Twenty-two patients were in their second remission, and further 22 were transplanted while in relapse.
See Table 6.1.4 (below).

Table 6.1.4 Disease Status Of Patient

Status:	1st Remission	2nd Remission	Relapse /Original Disease
Number:	31	22	22

6.1.5 Patients' Place Of Origin

Forty-three of the patients were resident in Greater London, and these had the easiest access to their families.
Twenty-seven patients came from other parts of England and Ireland and had only limited access to family and friends. With increasing distance, support provided by friends, and to some extent by families, decreased.
Patients arriving from Europe and overseas were either accompanied by one family member (usually the partner), or came on their own. Although all the patients participating in this study were fluent in English, often their partners were not.
Distribution of patients' place of origin is shown on Table 6.1.5 (below).

Table 6.1.5 Patients' Place Of Origin

Greater London	England	Ireland	Europe	Overseas
43	23	4	3	2

6.1.6 Attrition Of Patients Throughout The Stages

It is evident from Table 6.1.6 that there was substantial subject attrition during the study, much of which is accounted for by patients' deaths.
Complete details on attrition are shown in Table 6.1.6 below.

Table 6.1.6 Reasons for Patient Attrition

STAGES:	Patient refused	Patient too ill	Patient died*	Unable to contact	Other reasons
(1) Baseline	1	-	-	10	1
(2) Conditioning	3	11	2	-	1
(3) First 7 days	4	11	5	-	1
(4) Isolation ends	6	-	18	-	1
(I) Discharge	-	-	18	5	3
(5)** Somnolence	7	-	23	-	-
(II) Rehospitalization	8	1	23	-	1
(6) 3 months	8	1	32	-	4
(7) 12 months	7	-	45	-	3

* concurrent number of deaths
** 48 patients received TBI

6.1.7 Protocol Violations

1. Refusals

Three subjects refused to continue after they had initially agreed to participate. One refused immediately after the first assessment: the patient did not like the questions on the Mental Adjustment to Cancer (MAC) Scale. The patient felt that the questions forced him to confront the disease, something he did not want to do.

The second patient opted out after the first assessment. She did not like to be reminded of the disease and felt very upset. This patient needed continuous psychological support both during and after transplant.

The third patient had initially agreed to participate but changed his mind when hospitalised for transplant. He did not give an explanation.

The greatest number of refusals occurred at the end of isolation and discharge. These patients had some features in common; they expressed anger about the treatment, they found it harsher than expected, and encountered unexpected side-effects. One patient, "typical" for this group, had developed GvHD a few days after he had been assured that he was fine and would be discharged shortly. Another "typical" patient relapsed. He challenged me, arguing that he had done his part throughout transplant, had always taken the medicine, done the mouthwash and so on, but that 'we' (the hospital) had not kept our side of the bargain.

2. Patients Were Too Ill

Stages 2 (Conditioning) and 3 (First 7 Days) show the highest number of patients who were too ill to be assessed. During these stages the first wave of side effects such as 'sore mouth', vomiting, diarrhoea and infections, occurred. During this period 16 patients died.

3. Patients Died

Death played a significant role in reducing the number of patients available for assessment. By stage 7 (12 Months) 45 patients participating in this study had died, 63% of the original group.

4. Other Reasons

Other reasons accounting for attrition were lost questionnaires. This happened when patients filled out questionnaires and handed them over to staff or left them in their room before discharge.

Other patients left isolation but never left the hospital. One patient was discharged but developed temporary blindness, and therefore could not fill out the questionnaires.

6.2 QUESTIONNAIRE DATA

6.2.1 Order Of Questionnaires

The data from the questionnaires are presented in the following order:

6.3 1. The Hospital Anxiety and Depression (HAD) Scale
6.4 2. The Rotterdam Symptom Check List (RSCL)
6.5 3. The Mental Adjustment to Cancer (MAC) Scale
6.6 4. The Cancer Locus of Control (CLOC) Scale
6.7 5. Data from Interviews

6.2.2 Order of Data

Results for all stages on the subscale Anxiety (HAD) are presented in the following order:

(i) Results for the whole sample
(ii) Comparison between Males and Females
(iii) Comparison between the two hospitals
(iv) Comparison between the two types of transplants
(v) Comparison between the two types of conditioning

6.2.3 Order of Stages

Stages on tables and figures are given in the following order:

Stage 1	Baseline (Decision for transplant)
Stage 2	End of conditioning and transplant
Stage 3	7 days post-transplant
Stage 3a	2nd week post-transplant in isolation
Stage 3b	3rd week post-transplant in isolation
Stage 3c	4th week post-transplant in isolation
Stage 4	End of isolation
Assessment I	Discharge
Stage 5	Somnolence
Assessment II	First Rehospitalization
Stage 6	3 months post-transplant
Stage 7	12 months post-transplant

Stages 1-4 (from Baseline to End of Isolation) are followed by Stage I (Discharge). This was the most likely sequence experienced by patients. Patients left isolation and were discharged after a varying period of time. Some patients only stayed a few days out of isolation before being discharged, others stayed up to a week. However, a number of patients did not leave hospital after they had left isolation, but remained in hospital due to complications, later leading to death.

Stage 5 (Somnolence) usually fell between stages I (Discharge) and II (1st Rehospitalization). By three months post-transplant most patients had been hospitalised once since discharge. For 15 patients stage II occurred during somnolence. This may indicate greater physical vulnerability during somnolence. Stages 6 (3 Months) and 7 (12 Months) were kept in their numerical sequences.

Stage III was kept separate: It was a less likely event than stages I or II, and difficult to integrate into the transplant timetable. The number of patients who relapsed remained small, but the psychological impact was great and out of line with the other assessments. Figuratively including stage III would confuse the picture, which showed a gradual resolution of emotional problems with time. In two cases[2] relapse occurred as early as during isolation when patients were reinfused with their own marrow after rejecting the transplanted marrow. In one case relapse occurred as late as 18 months post-transplant.

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[2] Neither patient was assessed since both refused to be interviewed.

6.3 HOSPITAL ANXIETY AND DEPRESSION SCALE (HAD)

6.3.0 Results of the HAD Scale

The results of the HAD-Scale are presented in the following order:

A:6.3 Anxiety Subscale
D:6.3 Depression Subscale

For each subscale, results are given in the following order:

6.3.1 (i) Results for the whole sample
6.3.2 (ii) Comparison between Males and Females
6.3.3 (iii) Comparison between the two Hospitals
6.3.4 (iv) Comparison between the two types of Transplants
6.3.5 (v) Comparison between the two types of Conditioning

A:6.3 ANXIETY SUBSCALE

A:6.3.0 Results of the Anxiety Subscale

Results are given in the following order:

A:6.3.1	**(i)**	**Results for the whole sample**
A:6.3.2	**(ii)**	**Comparison between Males and Females**
A:6.3.3	**(iii)**	**Comparison between the two Hospitals**
A:6.3.4	**(iv)**	**Comparison between the two types of transplants**
A:6.3.5	**(v)**	**Comparison between the two types of conditioning**

Results of the HAD subscale Anxiety are shown on Table A:6.3.1 and Figure A:6.3.1. (See below)

Table A:6.3.1 shows Anxiety mean scores at Baseline and differences from Baseline for the entire sample at all stages. It shows the number of patients for whom data are available and statistical significance of the comparison of the difference from Baseline of increases (+) and decreases (-) to baseline mean.

Table A:6.3.1 also shows the percentages of patients scoring above the cut-off point (8 and above) and qualifying as 'cases' at each stage.

Table A:6.3.1

HAD-Anxiety: The difference from the baseline of the mean scores (for the entire sample) at each stage.

Stages:	Difference from baseline mean	SD	n	2-talled p*	Cases in %
Stage 1 Baseline	mean 6.81	3.54	72	n.a.	24%
Stage 2 Conditioning	+0.57	3.97	58	0.08	26%
Stage 3 First 7 Days	-1.10	3.16	52	0.003	12 %
Stage 3a Week 2	-1.43	3.36	18	0.01	13%
Stage 3b Week 3	-1.22	2.94	18	0.10	7%
Stage 3c Week 4	-1.00	2.83	6	0.13	0%
Stage 4 End of Isolation	-0.84	4.62	49	0.03	19%
Assessment I Discharge	-2.36	3.58	28	0.04	8%
Stage 5 Somnolence	-2.04	3.88	28	0.02	19%
Assessment II Rehospitalization	-1.40	3.95	30	0.11	18%
Stage 6 3 Months	-2.52	3.41	29	0.02	10%
Stage 7 12 Months	-3.84	2.48	19	0.03	4%
Stage III	+4.5		8	**	38%

* p=values are based on the statistical analysis of the differences to baseline on the Non-Parametric Wilcoxon Matched Pairs Test.

** not enough cases

A:6.3.1 Comparison of changes from baseline at all Stages

At 'Baseline' the mean scores of this sample is 6.81 and higher than the mean obtained from a comparative sample of 568 cancer patients reported by Moorey et al. (1991). From baseline the level of anxiety increases only once at the end of stage 'Conditioning'(stage 2). This increase is not significant.

At 'First 7 Days' (stage 3); 'Week 2' (stage 3a), 'End of Isolation' (stage 4), 'Somnolence' (stage 5); 'Three Months' (stage 6) and 'Twelve Months' (stage 7). compared to baseline there are significant decreases in the level of anxiety. At 'Discharge' (stage I) anxiety also significantly decreases compared to 'Baseline' (stage 1). 'Rehospitalization' (stage II) does also show a decrease from 'Baseline' (stage 1), although this decrease is not significant.

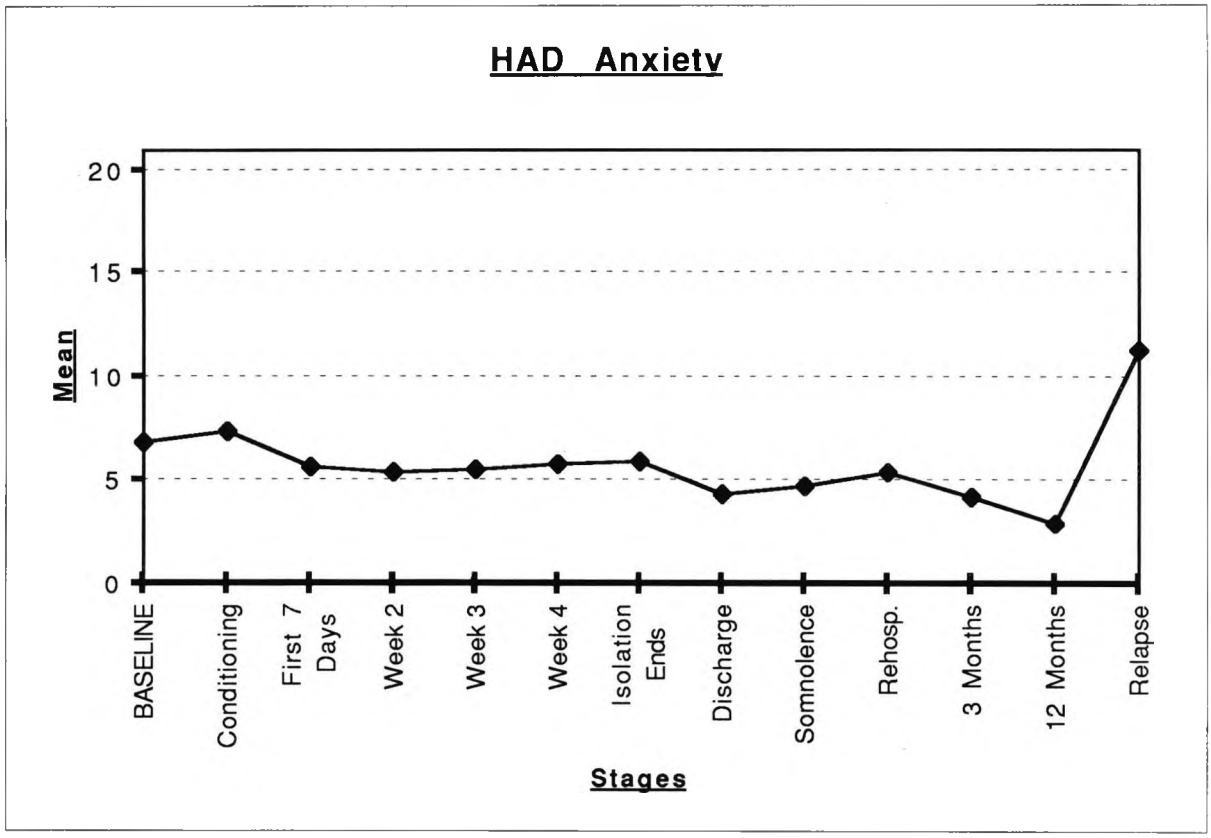
From these data it appears that anxiety is highest at the end of the 'Conditioning' (stage 2). All later assessments show a decrease when compared to 'Baseline' (stage 1). The number of patients scoring above the cut-off point for Anxiety on the HADS qualifying for 'cases' is also highest at 'Conditioning' (stage 2).

The present data confirm Hypothesis One which says:

"The degree of Anxiety and Depression does not remain constant during the treatment. It is influenced by the changes in the medical treatment during the different stages."

Figure A:6.3.1

HAD-Anxiety: The difference from the Baseline of the mean scores (for the entire sample) at each stage.



A:6.3.2 Comparison Between Males And Females

The sample was divided into males and females and compared. Results are shown on Table A:6.3.2 and Figure A:6.3.2. The percentages of males and females scoring above the cut-off point and qualifying as 'cases' are compared and shown on Table A:6.3.2b and Figure 6.3.2b.

At 'Baseline' (stage 1) Females (mean=7.71) are significantly more anxious than Males (mean=6.23). Two-tailed p=0.03.

At 'Somnolence' (stage 5), mean Anxiety scores for Males decreased by 1.95 and for Females by 2.22. The difference is significant; p=0.03.

Table A:6.3.2

HAD-Anxiety: The difference from the baseline of the mean scores (at each stage) for Male and Female patients.

ANXIETY	MALE			FEMALE			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**6.23**	3.3	44	**7.71**	3.8	28	0.03
Conditioning	+0.53	4.1	36	+0.64	3.8	22	0.81
First 7 Days	-1.09	3.3	34	-1.11	2.9	18	0.88
Week 2	-1.56	4.1	18	-1.25	1.9	12	0.81
Week 3	-1.00	2	11	-1.57	4.2	7	0.7
Week 4	-1.00	2.8	6	-	-	-	-
Isolation ends	-1.09	5.2	32	-0.35	3.4	17	0.67
Discharge	-1.87	3.7	19	-3.33	3.3	9	0.33
Somnolence	-1.95	3.8	28	-2.22	4.3	9	0.03
Rehospitalisation	-1.70	3.6	20	-0.80	4.7	10	0.44
3 Months	-2.68	3.8	19	-2.20	2.7	10	0.72
12 Months	-4.00	2.7	13	-3.50	2.1	6	0.8
Relapse	+3.00	6.8	6	+9.00	2.8	2	0.29

Figure A:6.3.2

HAD-Anxiety: The mean scores (at each stage) for Male and Female patients.

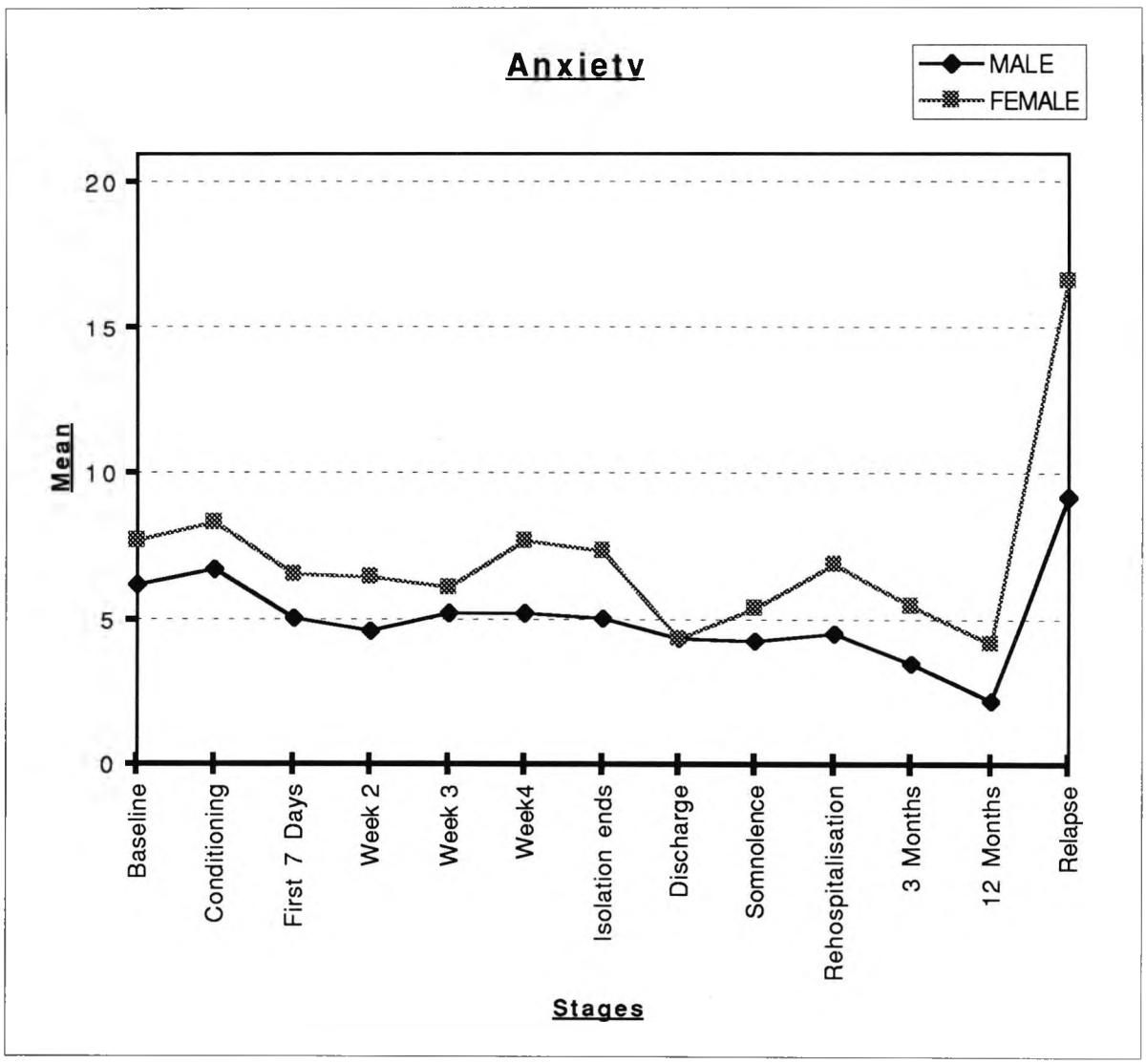


Table A:6.3.2.b

Comparison (at all stages) between the percentages of Male and Female patients scoring above the cut-off level (8) on HAD-Anxiety, and thus qualifying for 'caseness'.

ANXIETY	MALE				FEMALE			
STAGES	Normal		Cases		Normal		Cases	
	n	%age	n	%age	n	%age	n	%age
Baseline	29	81%	7	19%	19	70%	8	30%
Conditioning	29	81%	7	19%	14	64%	8	36%
First 7 Days	31	91%	3	9%	17	85%	3	15%
Week 2	16	89%	2	11%	11	85%	2	15%
Week 3	11	100%	0	0%	6	86%	1	14%
Week 4	6	100%	0	0%	0	0%	0	0%
Isolation ends	27	84%	5	16%	14	78%	4	22%
Discharge	18	95%	1	5%	9	90%	1	10%
Somnolence	18	95%	1	5%	6	67%	3	32%
Rehospitalisation	19	95%	1	5%	7	70%	3	30%
3 Months	18	95%	1	5%	9	82%	2	18%
12 Months	12	92%	1	8%	6	100%	0	0%
Relapse	5	83%	1	17%	1	33%	2	67%

A:6.3.2b Comparison 'cases', at all stages./Males -Females

Comparison between Groups

Percentages of females whose scores fall within the level of "caseness" on the sub-scale Anxiety are consistently higher than those of the male sample.

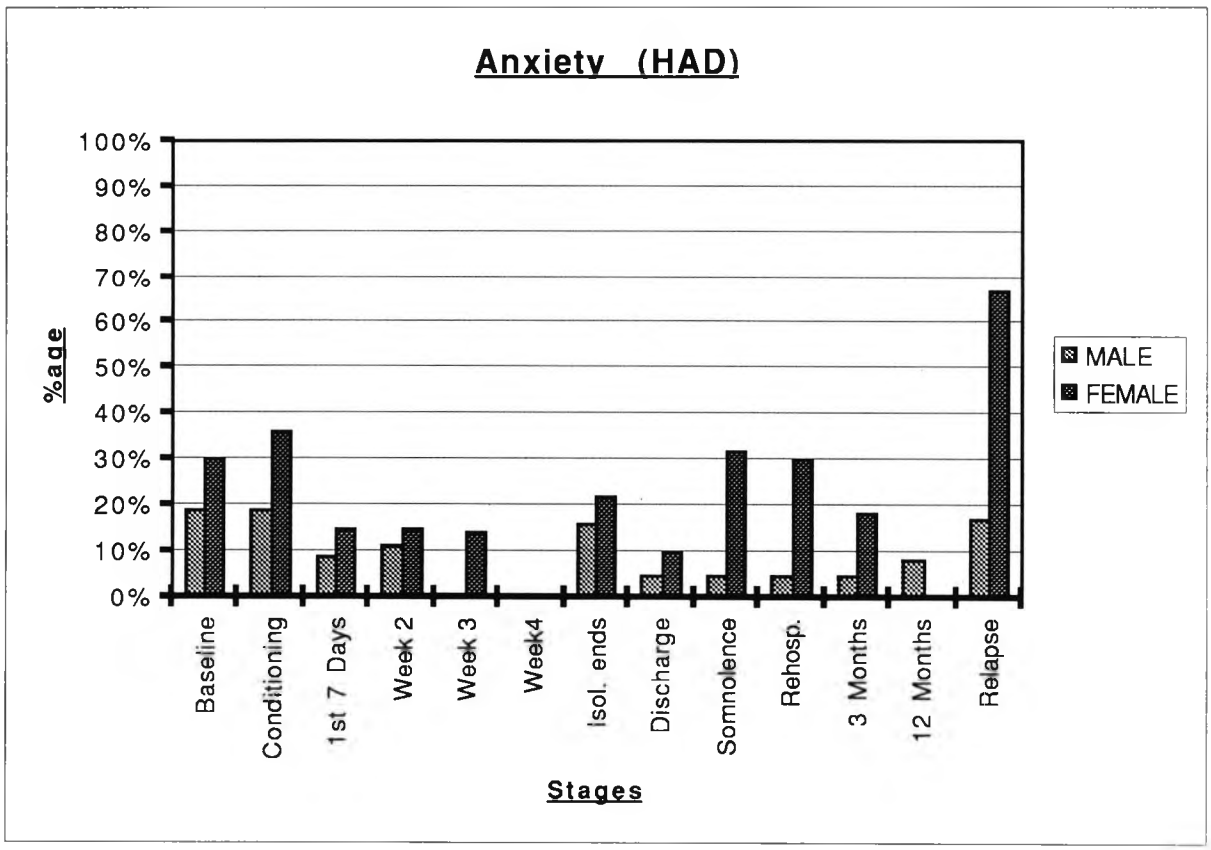
Chi-Square Test at stages:

Stage 5 (somnolence) :	**2-tailed p=0.084**
Stage II (Rehospitalization):	**2-tailed p=0.095**
Stage III (Relapse):	**2-tailed p=0.23**

The differences between the two genders are not significant, although they show a trend.

Figure A:6.3.2.b

Comparison (at all stages) between the percentages of Male and Female patients scoring above the cut-off level (8) on HAD-Anxiety, and thus qualifying as 'cases'.



A:6.3.3 Comparison Between Patients At The Two Hospitals

The sample was divided into patients treated at the Royal Marsden Hospital and the Royal Free Hospital and compared. Results are shown on Table A:6.3.3 and Figure A:6.3.3. The percentages of patients in the Royal Marsden Hospital and in the Royal Free Hospital scoring above the cut-off point (8 and above) and qualifying as cases are compared and shown on Table A:6.3.3.b and Figure 6.3.3b.

During isolation, at stages 'Week 2' (stage 3a) and 'Week 4' (stage 3c), there is a significant difference between the two hospitals. Patients in the Royal Marsden Hospital show significantly higher anxiety scores than those in the Royal Free Hospital. At 'Week 4' (stage 3c) patients in the Royal Free show a decrease, while patients in the Royal Marsden show an increase in the level of anxiety.

At 'Week 2' (stage 3a) scores for the patients in the Royal Free Hospital show a significant decrease from baseline (2-tailed p=0.02)* while the decrease for patients in the Royal Marsden is not significant (2-tailed p=0.07)*, although there is a trend for the latter group.

At 'Week 4' (stage 3c) patients in the Royal Free show a decrease from 'Baseline' (stage 1), while patients in the Royal Marsden show an increase from 'Baseline' (stage 1). For patients in the Royal Free the decrease from 'Baseline' (stage 1) is not significant (2-tailed p=0.18)*; and for those in the Royal Marsden the increase from 'Baseline' (stage 1) is also not significant (2-tailed p=0.32).*

However, when comparing the two hospitals the unequal sample size between the two hospitals should be kept in mind.

*Non Parametric Wilcoxon Matched-Pairs Test Signed Rank Test.

Table A:6.3.3

HAD-Anxiety: The difference from the baseline of the mean scores (at each stage) for the two Hospitals.

ANXIETY	ROYAL FREE			ROYAL MARSDEN			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**6.86**	3.9	14	**6.79**	3.5	58	0.96
Conditioning	-0.54	5.5	13	+0.89	3.4	45	0.22
First 7 Days	-2.45	4	11	-0.73	2.8	41	0.09
Week 2	-3.88	4	8	-0.55	2.7	22	0.01
Week 3	-1.25	2.2	8	-1.20	3.5	10	0.97
Week 4	-2.50	1.3	4	+2.00	2.8	2	0.04
Isolation ends	-1.80	6.2	10	-0.59	4.2	39	0.43
Discharge	-4.25	4.7	4	-2.04	3.4	24	0.26
Somnolence	-3.67	5.5	6	-1.59	3.4	22	0.93
Rehospitalisation	-3.20	6.1	5	-1.04	3.4	25	0.32
3 Months	-3.50	2	6	-2.26	3.7	23	0.44
12 Months	-3.00	2.6	3	-4.00	2.5	16	0.6
Relapse	-	-	1	+5.14	6.7	7	0.5

Figure A:6.3.3

HAD-Anxiety: The mean scores (at each stage) for the two Hospitals.

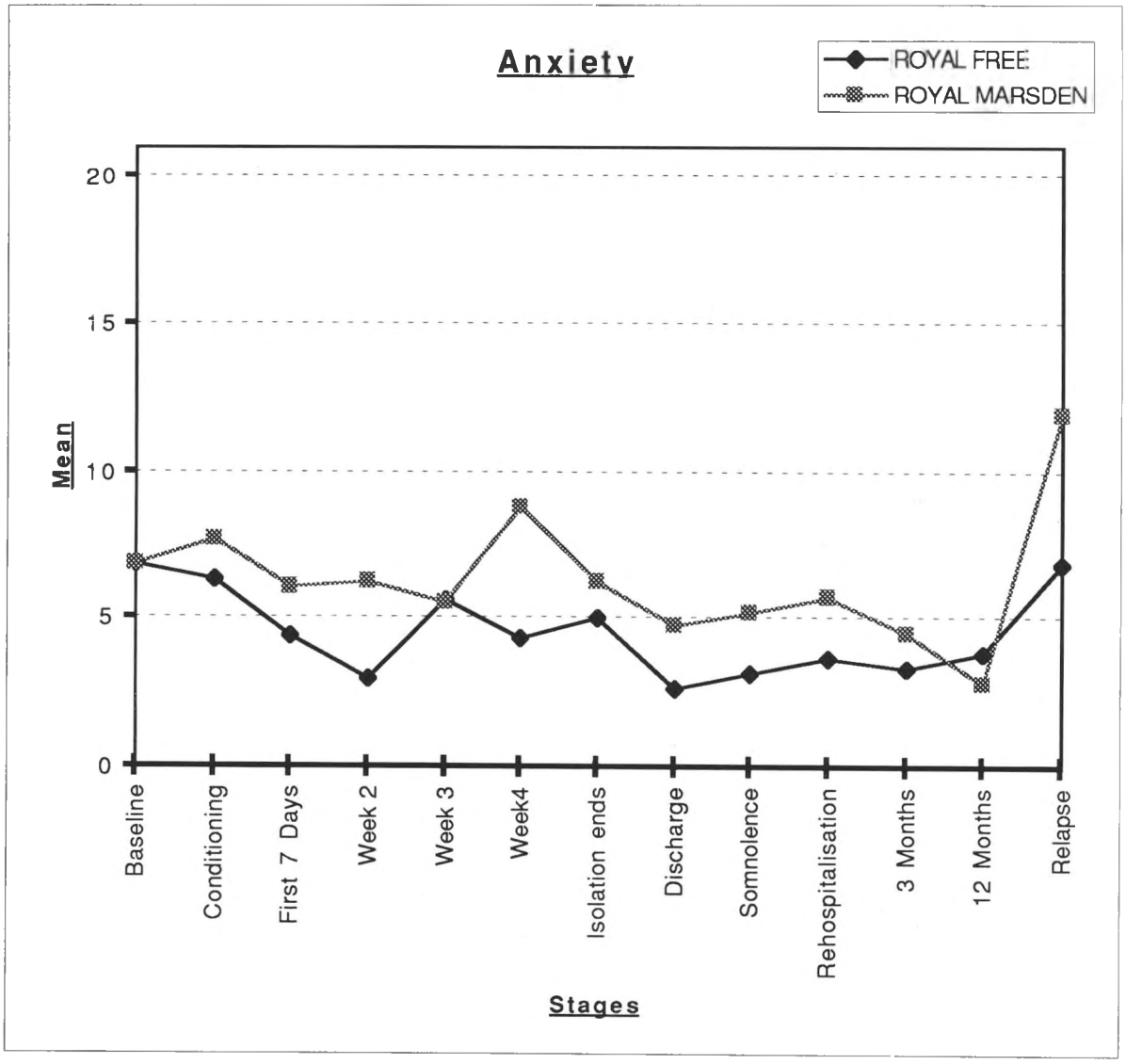


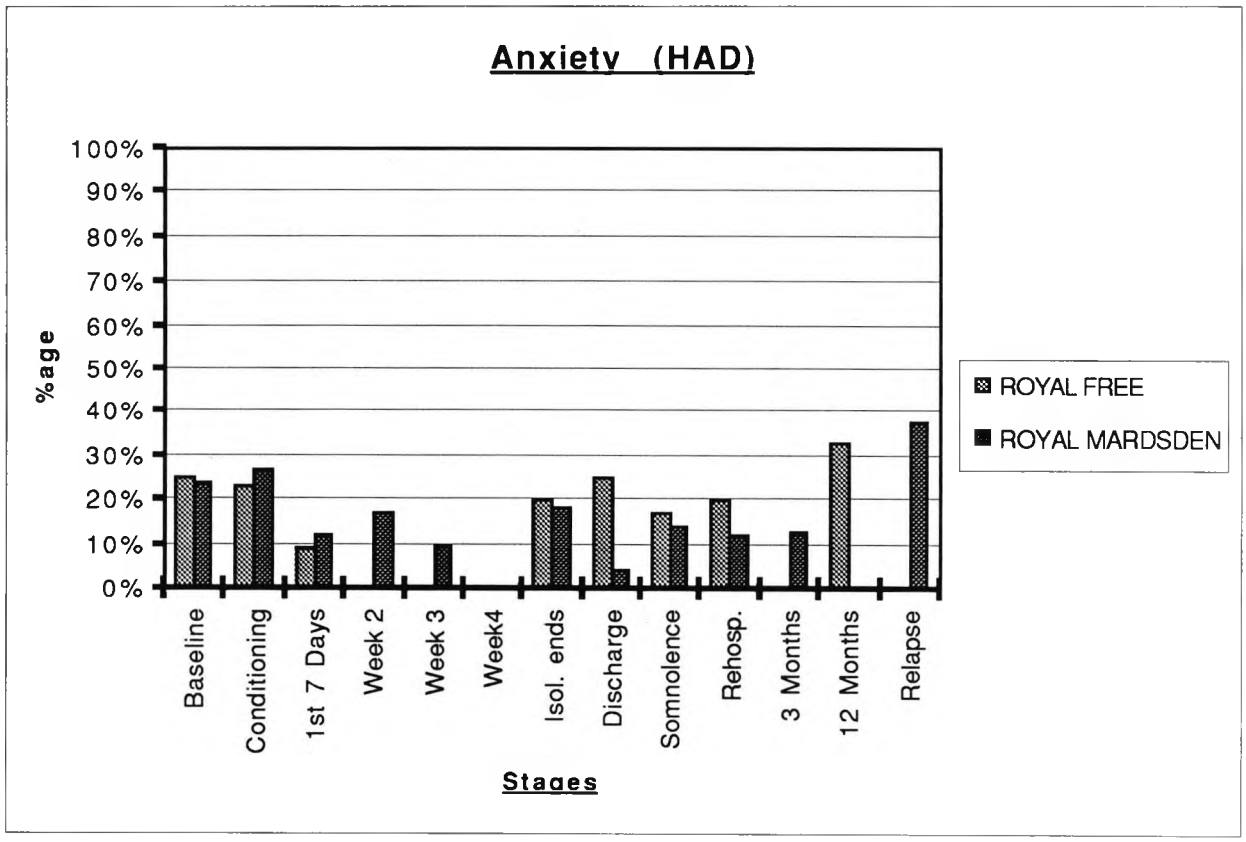
Table A:6.3.3.b

Comparison (at all stages) between the two Hospitals of the percentages of patients scoring above the cut-off point (8 and above) on HAD-Anxiety, and thus qualifying for 'cases'.

ANXIETY	ROYAL FREE				ROYAL MARDSDEN			
STAGES	Normal		Cases		Normal		Cases	
	n	%age	n	%age	n	%age	n	%age
Baseline	9	75%	3	25%	39	77%	12	24%
Conditioning	10	77%	3	23%	33	73%	12	27%
First 7 Days	10	91%	1	9%	38	88%	5	12%
Week 2	8	100%	0	0%	19	83%	4	17%
Week 3	8	100%	0	0%	9	90%	1	10%
Week 4	4	100%	0	0%	2	100%	0	0%
Isolation ends	8	80%	2	20%	33	83%	7	18%
Discharge	3	75%	1	25%	24	96%	1	4%
Somnolence	5	83%	1	17%	19	86%	3	14%
Rehospitalisation	4	80%	1	20%	22	88%	3	12%
3 Months	6	100%	0	0%	21	88%	3	13%
12 Months	2	67%	1	33%	16	100%	0	0%
Relapse	1	100%	0	0%	5	63%	3	38%

Figure A:6.3.3.b

Comparison (at all stages) between the two Hospitals of the percentages of patients scoring above the cut-off point (8) on HAD-Anxiety, and thus qualifying as 'cases'.



A:6.3.4 Comparison Between The Two Types Of Transplants

The sample was divided into patients who received allogeneic and those who received an autologous transplants. The two groups were compared. Results are shown on Table A:6.3.4 and Figure A:6.3.4. The percentages of patients with allogeneic and autologeous transplants scoring above the cut-off point and qualifying as cases are compared and shown on Table A:6.3.4.b and Figure 6.3.4b.

There are no significant differences between the two groups at any stage. (The one patient at stage 3c - week 4- who scored extremely high on anxiety does not allow real comparison between the two groups, although the difference appears significant at this stage).

Table A:6.3.4

HAD-Anxiety: The difference from the baseline of the mean scores (at each stage) for the two types of Transplant.

ANXIETY	AUTOGRAFT			ALLOGRAFT			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**6.57**	3.3	28	**6.95**	3.7	44	0.64
Conditioning	+1.19	3.8	21	+0.22	4.1	37	0.29
First 7 Days	-0.95	2.7	20	-1.19	3.5	32	0.9
Week 2	-1.57	1.7	14	-1.31	4.4	16	0.84
Week 3	-1.80	2.2	10	-0.50	3.7	8	0.37
Week 4	-2.00	1.6	5	+4.00	-	1	0.03
Isolation ends	-0.83	2.6	18	-0.70	5.5	30	0.94
Discharge	-3.25	3.4	8	-2.00	3.7	20	0.41
Somnolence	-1.38	4.2	8	-2.30	3.8	20	0.52
Rehospitalisation	+/- 0.00	4.2	9	-2.0	3.8	21	0.14
3 Months	-2.08	2.1	12	-2.82	4.1	17	0.57
12 Months	-3.33	1.6	9	-4.30	3.1	10	0.29
Relapse	+3.50	5	6	+7.50	12	2	0.49

Figure A:6.3.4

HAD-Anxiety: The mean scores (at each stage) for the two types of Transplant.

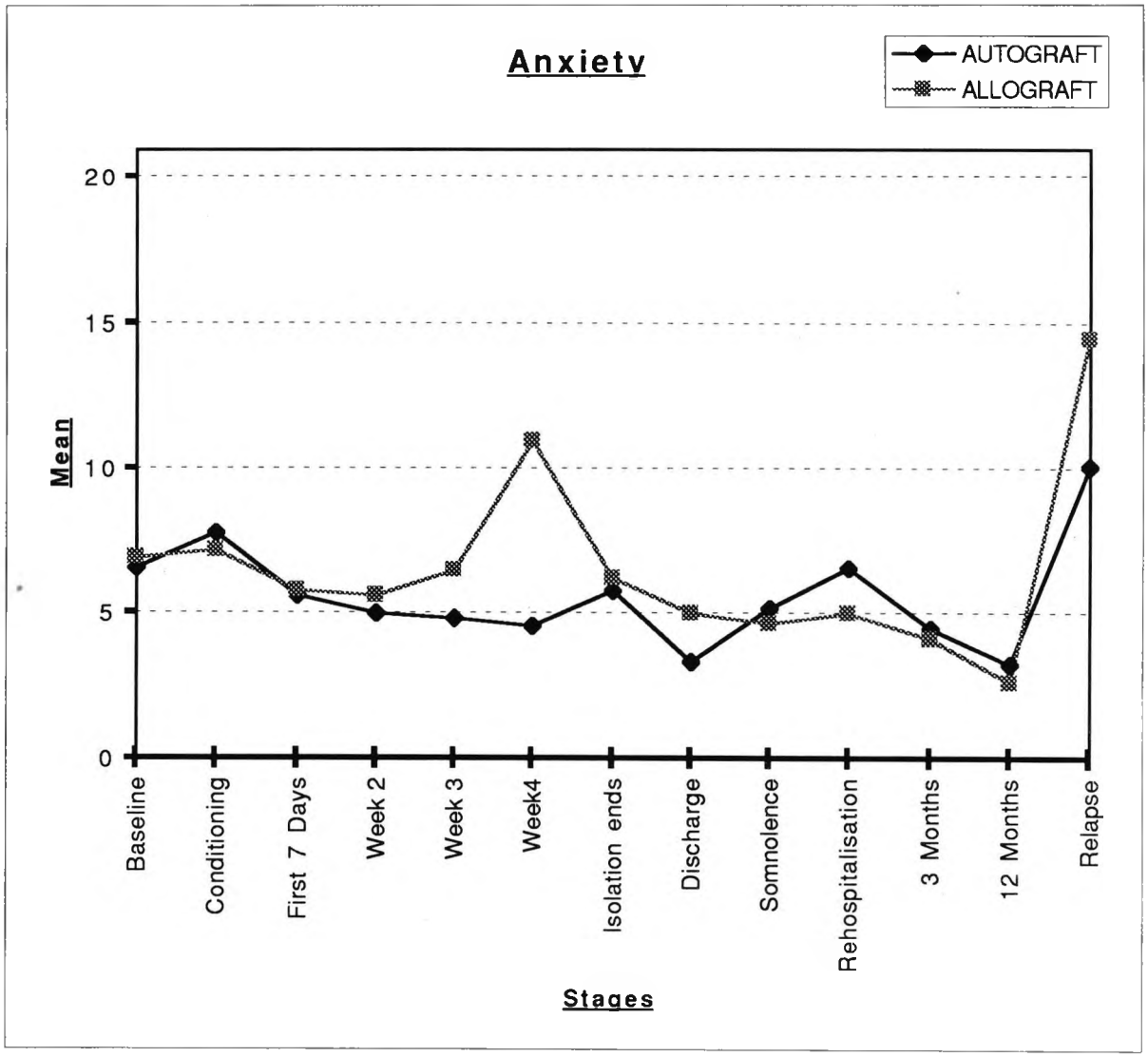


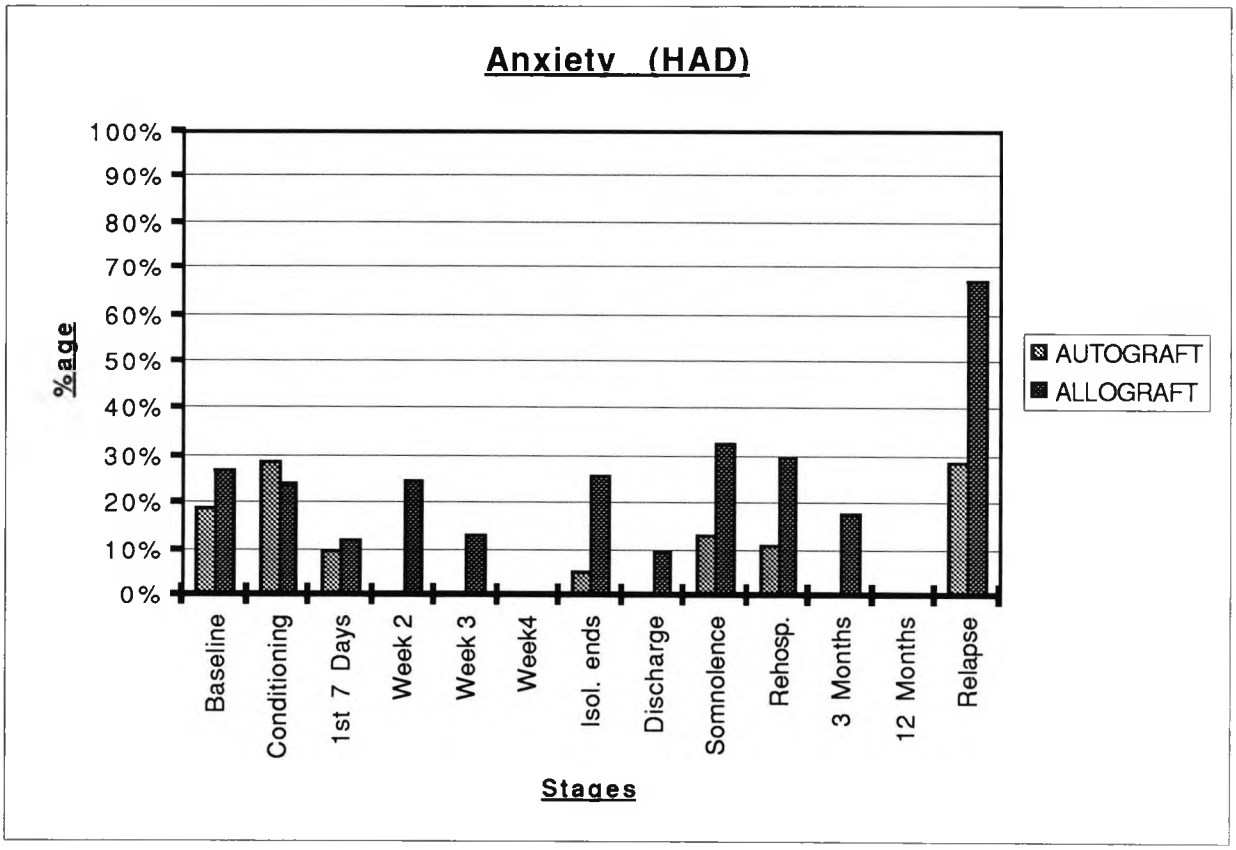
Table A:6.3.4.b

Comparison (at all stages) between the two types of transplant of the percentages of patients scoring above the cut-off point (8) on HAD-Anxiety, and thus qualifying as 'cases'.

ANXIETY	AUTOGRAFT				ALLOGRAFT			
STAGES	Normal		Cases		Normal		Cases	
	n	%age	n	%age	n	%age	n	%age
Baseline	21	81%	5	19%	27	73%	10	27%
Conditioning	15	71%	6	29%	28	76%	9	24%
First 7 Days	19	91%	2	10%	29	88%	4	12%
Week 2	15	100%	0	0%	12	75%	4	25%
Week 3	10	100%	0	0%	7	88%	1	13%
Week4	5	100%	0	0%	1	100%	0	0%
Isolation ends	18	95%	1	5%	23	74%	8	26%
Discharge	9	100%	0	0%	18	90%	2	10%
Somnolence	7	88%	1	13%	17	67%	3	33%
Rehospitalisation	8	89%	1	11%	18	70%	3	30%
3 Months	13	100%	0	0%	14	82%	3	18%
12 Months	9	100%	0	0%	9	100%	1	0%
Relapse	5	71%	2	29%	1	33%	1	67%

Figure A:6.3.4.b

Comparison (at all stages) between the two types of transplant of the percentages of patients scoring above the cut-off point (8) on HAD-Anxiety, and thus qualifying as 'cases'.



Comparison between Groups

The differences in percentages of 'cases' between the groups do not reach the level of significance at any stage, tested on Chi-Square Test.

A:6.3.5 Comparison Between The Two Types Of Conditioning

The sample was divided into patients treated with chemotherapy alone and those treated with a combination of chemotherapy and Total Body Irradiation (TBI). The groups were then compared. Results are shown on Table A:6.3.5 and Figure A:6.3.5. The percentages patients in each group scoring above the cut-off point and qualifying as cases are compared and shown on Table A:6.3.5.b and Figure 6.3.5b.

There are no significant differences between the two groups at any stage.

Table A:6.3.5

HAD-Anxiety: The difference from the baseline of the mean scores (at each stage) for the two types of Pre-Treatment Conditioning.

ANXIETY	CHEMO.			CHEMO. + TBI			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**6.67**	3	18	**6.86**	3.7	50	0.64
Conditioning	+0.65	3.2	17	+0.54	4.3	41	0.77
First 7 Days	-0.43	2.7	14	-1.34	3.3	38	0.41
Week 2	-2.00	0.8	7	-1.26	3.8	23	0.62
Week 3	-0.50	1.9	4	-1.43	3.2	14	0.59
Week 4	-2.00	1.4	2	-0.50	3.4	4	0.6
Isolation ends	-0.50	2.8	12	-0.95	5.1	37	0.83
Discharge	-4.20	2.2	5	-1.96	3.7	23	0.21
Somnolence	-	-	-	-2.00	4	27	-
Rehospitalisation	-2.60	1.8	5	-1.16	4.2	25	0.53
3 Months	-2.40	3.7	5	-2.54	3.4	24	0.93
12 Months	-4.25	2.1	4	-3.73	2.6	15	0.65
Relapse	+3.00	5.7	2	+5.00	7.1	6	0.74

Figure A:6.3.5

HAD-Anxiety: The mean scores (at each stage) for the two types of Pre-Treatment Conditioning.

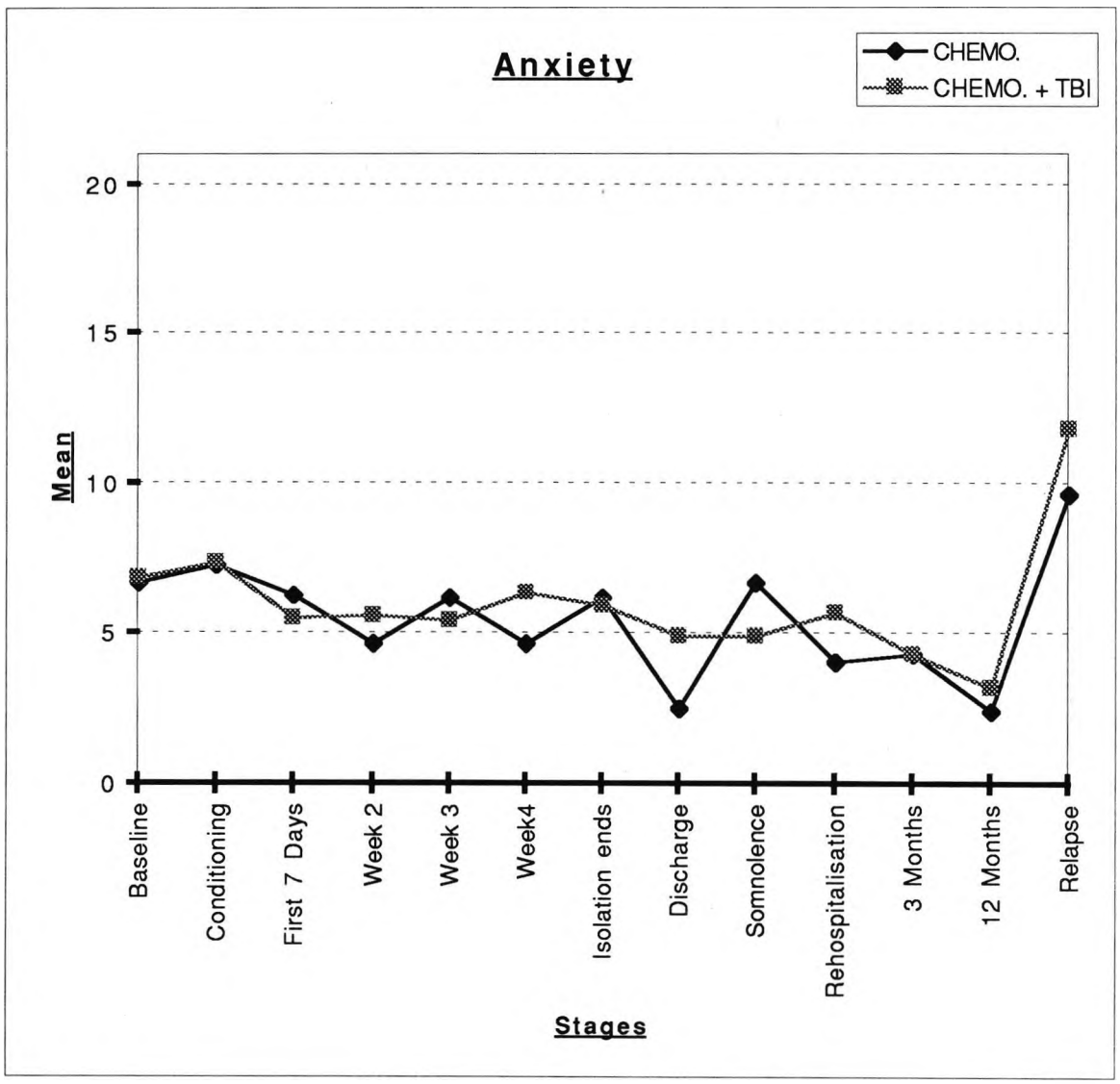


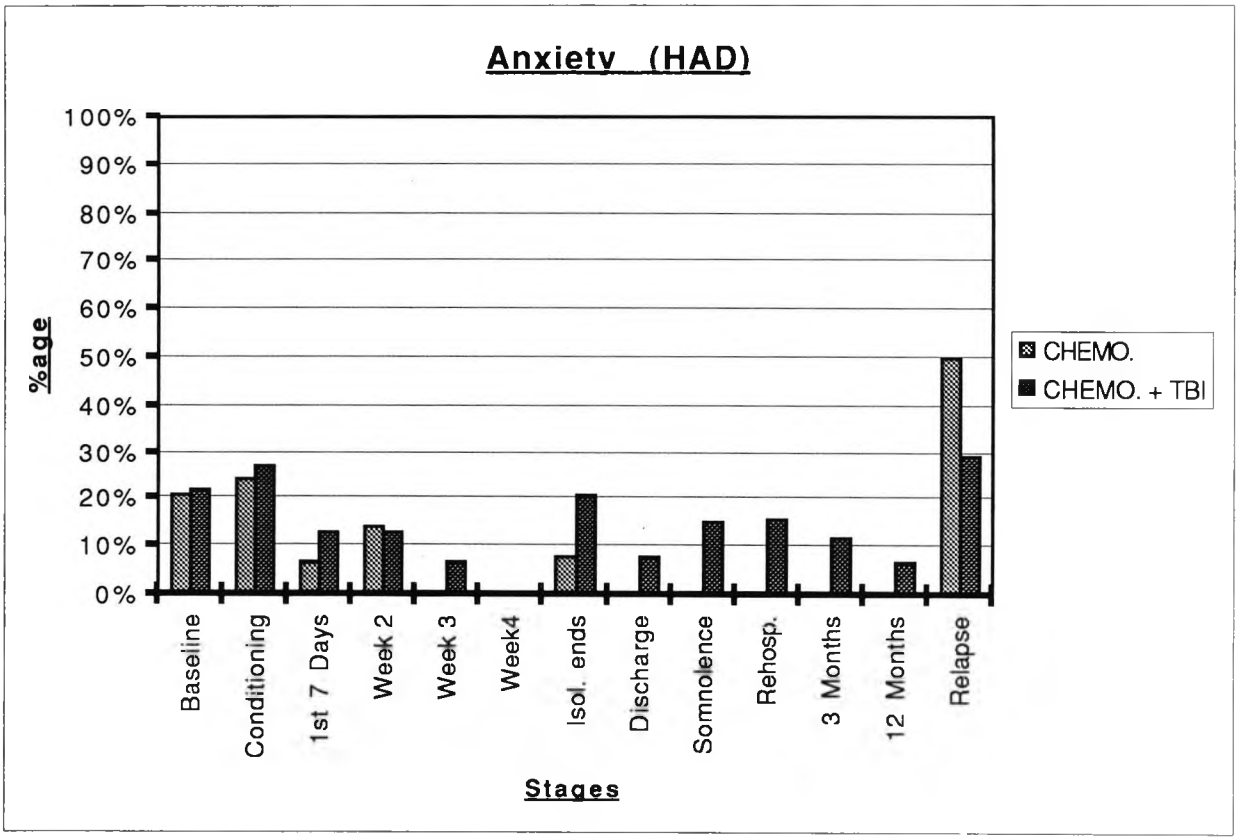
Table A:6.3.4.b

Comparison (at all stages) between the two pre-treatment conditionings of the percentages of patients scoring above the cut-off point (8) on HAD-Anxiety, and thus qualifying as 'cases'.

ANXIETY	CHEMO.				CHEMO. + TBI			
STAGES	Normal		Cases		Normal		Cases	
	n	%age	n	%age	n	%age	n	%age
Baseline	11	79%	3	21%	35	78%	10	22%
Conditioning	13	77%	4	24%	30	73%	11	27%
First 7 Days	13	93%	1	7%	35	88%	5	13%
Week 2	6	86%	1	14%	21	88%	3	13%
Week 3	4	100%	0	0%	13	93%	1	7%
Week 4	2	100%	0	0%	4	100%	0	0%
Isolation ends	11	92%	1	8%	30	79%	8	21%
Discharge	5	100%	0	0%	22	92%	2	8%
Somnolence	1	100%	0	0%	23	85%	4	15%
Rehospitalisation	5	100%	0	0%	21	84%	4	16%
3 Months	5	100%	0	0%	22	88%	3	12%
12 Months	4	100%	0	0%	14	93%	1	7%
Relapse	1	?	1	50%	5	71%	2	29%

Figure A:6.3.4.b

Comparison (at all stages) between the two pre-treatment conditionings of the percentages of patients scoring above the cut-off point (8) on HAD-Anxiety, and thus qualifying as 'cases'.



D:6.3 DEPRESSION SUBSCALE

D:6.3.0 Results Of The Depression Subscale

Results are given in the following order:

D:6.3.1	**(i)**	**Results for the whole sample**
D:6.3.2	**(ii)**	**Comparison between Males and Females**
D:6.3.3	**(iii)**	**Comparison between the two Hospitals**
D:6.3.4	**(iv)**	**Comparison between the two types of Transplants**
D:6.3.5	**(v)**	**Comparison between the two types of Conditioning**

Results of the HAD sub-scale Depression are shown on Table D:6.3.1 and Figure D:6.3.1.

The Table D:6.3.1 shows depression mean scores at baseline and differences from baseline for entire sample at all stages. It shows the number of patients for whom data are available and statistical significance of the comparison of the difference from baseline of increases (+) and decreases (-) to baseline mean.

Table D:6.3.1 also shows the percentages of patients scoring above the cut-off point and qualifying as 'cases' at each stage.

Table D:6.3.1

HAD-Depression: The difference from the baseline of the mean scores (for the entire sample) at each stage.

Stages	Differences from baseline mean	S.D.	n	2-tailed p *	cases in %
Stage 1 Baseline	mean 3.53	3.39	72	n.a.	12%
Stage 2 Conditioning	+2.62	4.44	58	≤0.001	34%
Stage 3 First 7 Days	+3.06	4.01	52	<0.001	29%
Stage 3a Week 2	+3.10	3.94	30	0.01	31%
Stage 3b Week 3	+3.61	4.16	18	0.005	40%
Stage 3c Week 4	+1.83	3.54	6	0.02	25%
Stage 4 End of Isolation	+3.27	3.98	49	0.02	27%
Assessment I Discharge	+1.96	3.54	28	0.01	25%
Stage 5 Somnolence	+2.96	4.19	28	0.12	32%
Assessment II Rehospitalization	+3.37	3.33	30	0.11	34%
Stage 6 3 Months	+1.59	3.26	29	0.24	21%
Stage 7 12 Months	-0.84	2.97	19	0.13	20%

*p=values are based on the statistical analysis of the differences to baseline on the Non-Parametric Wilcoxon Matched Pairs Test.

From 'Baseline' (stage 1) the level of depression decreases only once at 'Twelve Months' (stage 7). This decrease is statistically not significant. (2-tailed p=0.13).

At stages 'End of Conditioning' (stage 2), 'First Seven Days' (stage 3), 'Week 2' (stage 3a); 'End of isolation' (stage 4) and 'Discharge' (stage I) there is a significant increase in the level of depression compared to 'Baseline' (stage 1). Increases at stages 'Somnolence' (stage 5) and 'First rehospitalization' (stage II) are not significant.

From these data it appears that depression is highest throughout isolation and at the first rehospitalisation after discharge. Only after a twelve months period does depression show a decrease when compared to baseline. The number of patients scoring above the cut-off point for depression on the HADS qualifying for 'cases' is also highest during the third week post-transplant while in isolation.

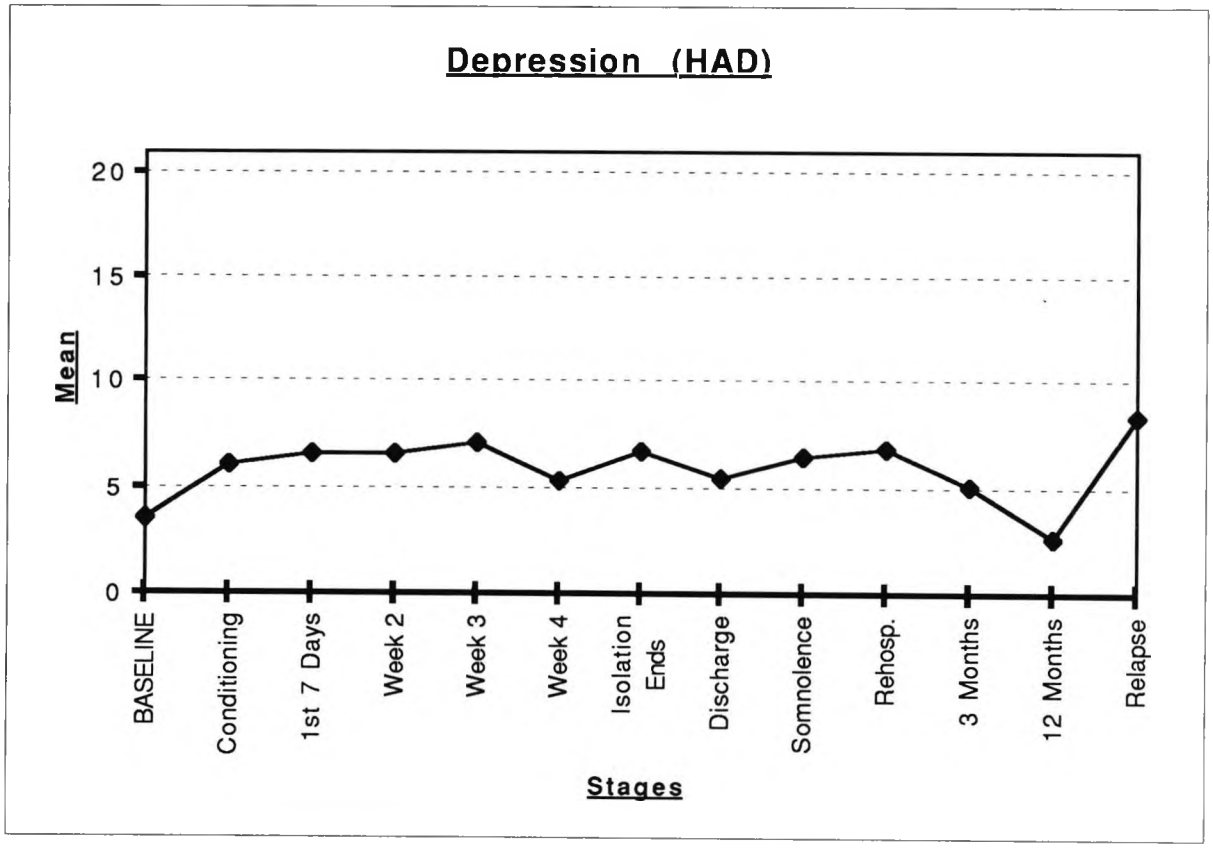
The percentages of subjects scoring above the cut-off point on the subscale Depression is lowest at 'Baseline' (stage 1) and does not regain pre-transplant level throughout the whole of the transplant procedure. At 'Twelve Months.' (stage 7) the number of 'cases' is still higher than at 'Baseline' (stage 1).

Data confirm Hypothesis number one which says:

"The degree of (Anxiety and) Depression does not remain constant during the treatment. It is influenced by the changes in the medical treatment during the different stages."

Figure D:6.3.1

HAD-Depression: The difference from the baseline of the mean scores (for the entire sample) at each stage.



D:6.3.2 Comparison Between Males And Females

The sample was divided into two groups, one for males and one for females and compared. Results are shown on Table D:6.3.2 and Figure D:6.3.2. The percentages of Males and Females scoring above the cut-off point and qualifying as cases are compared and shown on Table D:6.3.2.b and Figure D:6.3.2b.

Comparison between Groups:

The is no significant difference between the two groups at 'Baseline' (stage 1). (Table D:6.3.2) However, at 'First 7 Days' (stage 3) females show a greater increase than males. Although a trend, the difference is not significant. ($p=0.09$).

Compared to 'Baseline' (stage 1) the increase at 'First 7 Days' (stage 3) is significant for both males and females. (For males: 2-tailed $p<0.001$ and for females: 2-tailed $p=0.04$).
Tested on the Non Parametric Wilcoxon Matched-Pairs Test Signed Rank Test.

Table D:6.3.2

HAD-Depression: The difference from the baseline of the mean scores (at each stage) for Male and Female patients.

DEPRESSION	MALE			FEMALE			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**3.27**	3.1	44	**3.93**	3.8	28	0.44
Conditioning	+2.97	4.8	36	+2.05	3.8	22	0.32
First 7 Days	+3.73	4.4	34	+1.78	3	18	0.1
Week 2	+2.72	4.1	18	+3.67	3.9	12	0.53
Week 3	+3.64	3.9	11	+3.57	4.9	7	0.97
Week 4	+1.83	3.5	6	-	-	-	-
Isolation ends	+3.16	4.1	32	+3.47	3.9	17	0.79
Discharge	+2.26	4	19	+1.33	2.2	9	0.53
Somnolence	+3.11	4.4	19	+2.67	4	9	0.17
Rehospitalisation	+2.95	3	20	+4.20	3.8	10	0.34
3 Months	+1.50	3.3	18	+1.50	3.3	10	1
12 Months	-0.62	3.2	13	-1.33	2.7	6	0.82
Relapse	+3.83	4.8	6	+8.00	4.2	2	0.32

Figure D:6.3.2

HAD-Depression: The mean scores (at each stage) for Male and Female patients.

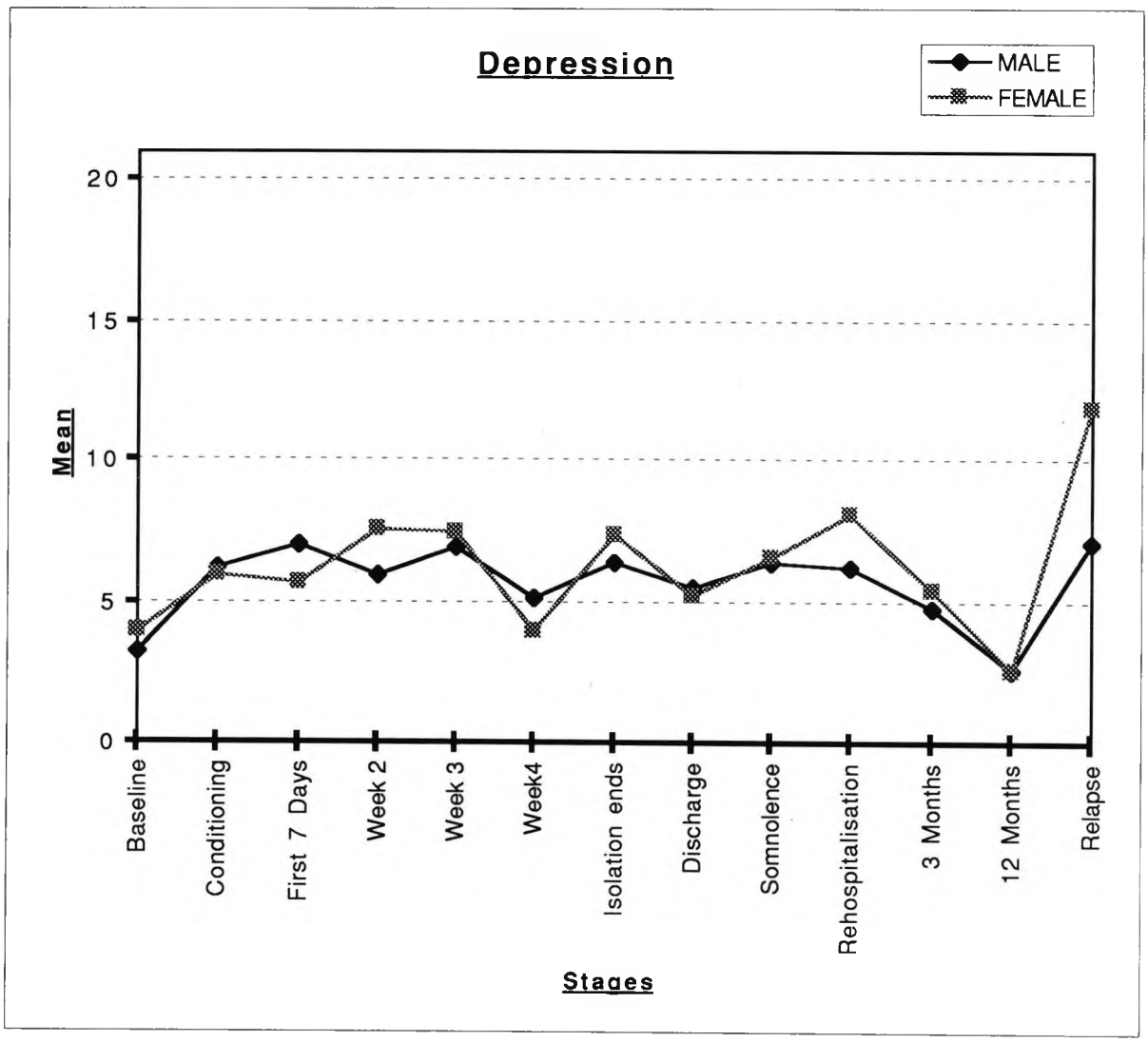


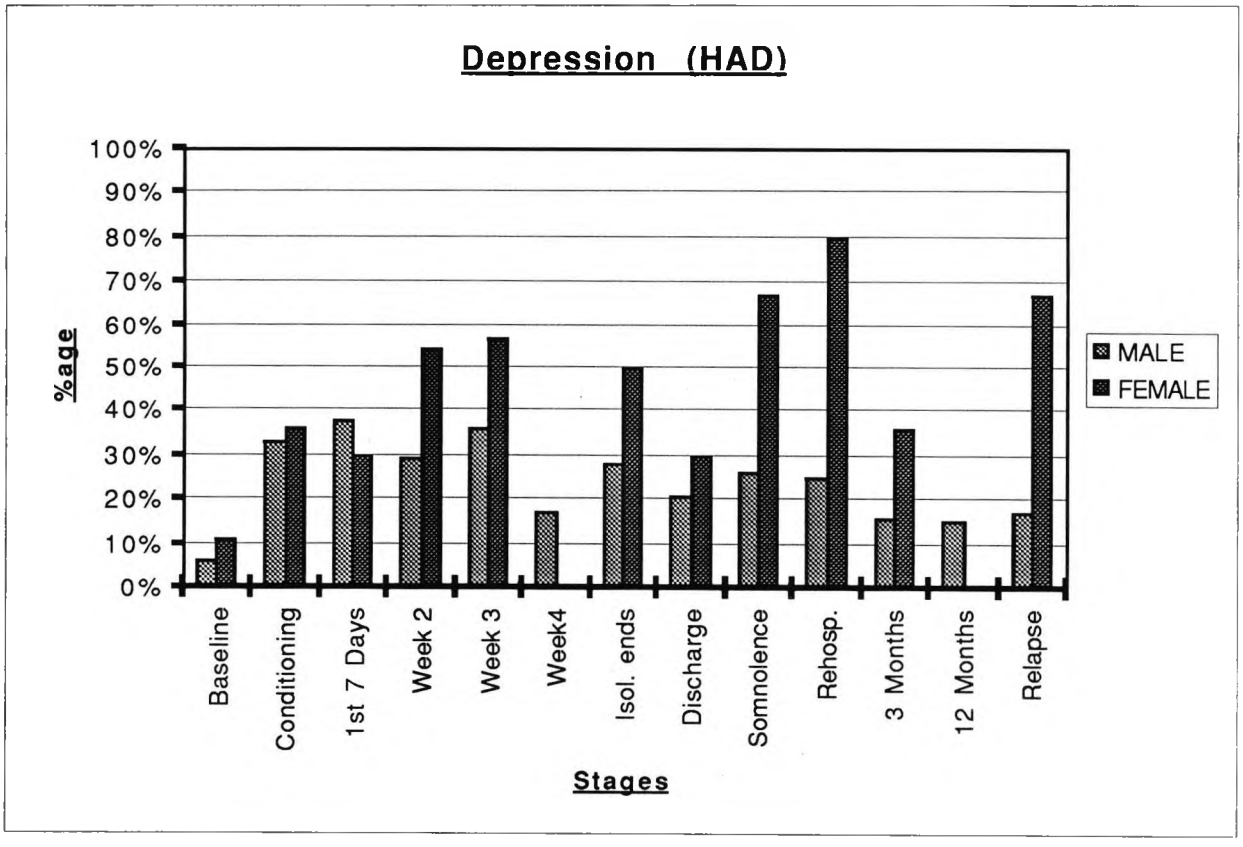
Table D:6.3.2.b

Comparison (at all stages) between the percentages of Male and Female patients scoring above the cut-off point (8) on HAD-Depression, and thus qualifying as 'cases'.

DEPRESSION	MALE				FEMALE			
STAGES	Normal		Cases		Normal		Cases	
	n	%age	n	%age	n	%age	n	%age
Baseline	34	94%	2	6%	24	89%	3	11%
Conditioning	24	67%	12	33%	14	64%	8	36%
First 7 Days	21	62%	13	38%	14	70%	6	30%
Week 2	13	72%	5	29%	6	47%	7	54%
Week 3	7	64%	4	36%	3	43%	4	57%
Week 4	5	83%	1	17%	0	0%	0	0%
Isolation ends	23	72%	9	28%	9	50%	9	50%
Discharge	15	79%	4	21%	7	70%	3	30%
Somnolence	14	74%	5	26%	3	33%	6	67%
Rehospitalisation	15	75%	5	25%	2	20%	8	80%
3 Months	16	84%	3	16%	7	64%	4	36%
12 Months	11	85%	2	15%	6	100%	0	0%
Relapse	5	83%	1	17%	1	33%	2	67%

Figure D:6.3.2.b

Comparison (at all stages) between the percentages of Male and Female patients scoring above the cut-off level (8) on HAD-Depression, and thus qualifying as 'cases'.



D:6.3.2.b Comparison Of Percentages Of 'Cases' - Males -Females

At 'Rehospitalization (stage II) 80% of the female group score above the cut-off point and classify as "cases" while 25 % of the males score above the cut-off point. The difference between the groups is significant (Chi-Square, 2-tailed p=0.007).
At 'Somnolence' (stage 5) females show a higher percentage of 'cases', the difference between the two groups is not significant, but there is a trend. (2-tailed p=0.09, tested on Chi-Square Test). At 'Relapse' (stage III) the difference between the two groups is not significant (2-tailed p=0.23 on the Chi-Square).

D:6.3.3 Comparison Between The Hospitals

The sample was divided into patients treated at the Royal Marsden Hospital and the Royal Free Hospital and compared. Results are shown on Table D:6.3.3 and Figure D:6.3.3. The percentages of patients at the Royal Marsden Hospital and at the Royal Free Hospital scoring above the cut-off point and qualifying as cases are compared and shown on Table D:6.3.3.b and Figure D:6.3.3.b.

Comparison between Groups:

The is no significant difference between the two groups at 'Baseline' (stage 1). (Table D:6.3.3) However, throughout isolation there are significant differences between the two groups. Patients at the Royal Marsden Hospital are significantly more depressed. At stages 'First 7 Days' (stage 3), 'Week 2' (stage 3a), and 'End of Isolation' (stage 4) the differences between the two groups are significant. At stages 'Week 3' (stage 3b) and 'Week 4' (stage 3c) there is a trend for patients at the Royal Marsden to be more depressed than those at the Royal Free.

Compared to 'Baseline' (stage 1) the increase in depression for patients at the Royal Free Hospital at stages 'First 7 Days' (stage 3), 'Week 2' (stage 3a) and 'End of Isolation' (stage 4) are not significant, while they are for patients at the Royal Marsden Hospital at these stages.

Comparison during Isolation

The Royal Free	2-tailed p*	% of cases at stage	The Royal Marsden	2-tailed p*	5 of cases
stage 1-3	p=0.83	18%	stage 1-3	p<0.0001	40%
stage 1-3a	p=0.79	13%	stage 1-3a	p=0.0002	48%
stage 1-4	p=0.89	10%	stage 1-4	p<0.0001	43%

*Tested on the Non Parametric Wilcoxon Matched-Pairs Test Signed Rank Test.

Table D:6.3.3

HAD-Depression: The difference from the baseline of the mean scores (at each stage) for the two Hospitals.

DEPRESSION	ROYAL FREE			ROYAL MARSDEN			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**3.64**	2.8	14	**3.5**	3.5	58	0.52
Conditioning	+1.62	2.9	13	+2.91	4.8	45	0.28
First 7 Days	+0.82	3.4	11	+3.66	4	41	0.04
Week 2	+/- 0.00	3.4	8	+4.23	3.6	22	0.01
Week 3	1.75	2.6	8	+5.10	4.7	10	0.09
Week 4	+/- 0.00	2.7	4	+5.50	0.7	2	0.05
Isolation ends	+0.20	2.9	10	+4.05	3.9	39	0.01
Discharge	-0.25	3.9	4	+2.33	3.4	24	0.18
Somnolence	+/- 0.00	2.8	6	+3.77	4.2	22	0.12
Rehospitalisation	+1.40	3.6	5	+3.76	3.2	25	0.15
3 Months	+1.33	2.6	6	+1.65	3.5	23	0.89
12 Months	+1.67	3.8	3	-1.31	2.7	16	0.06
Relapse	-	-	1	+5.57	4.7	7	0.31

Figure D:6.3.3

HAD-Depression: The mean scores (at each stage) for the two Hospitals.

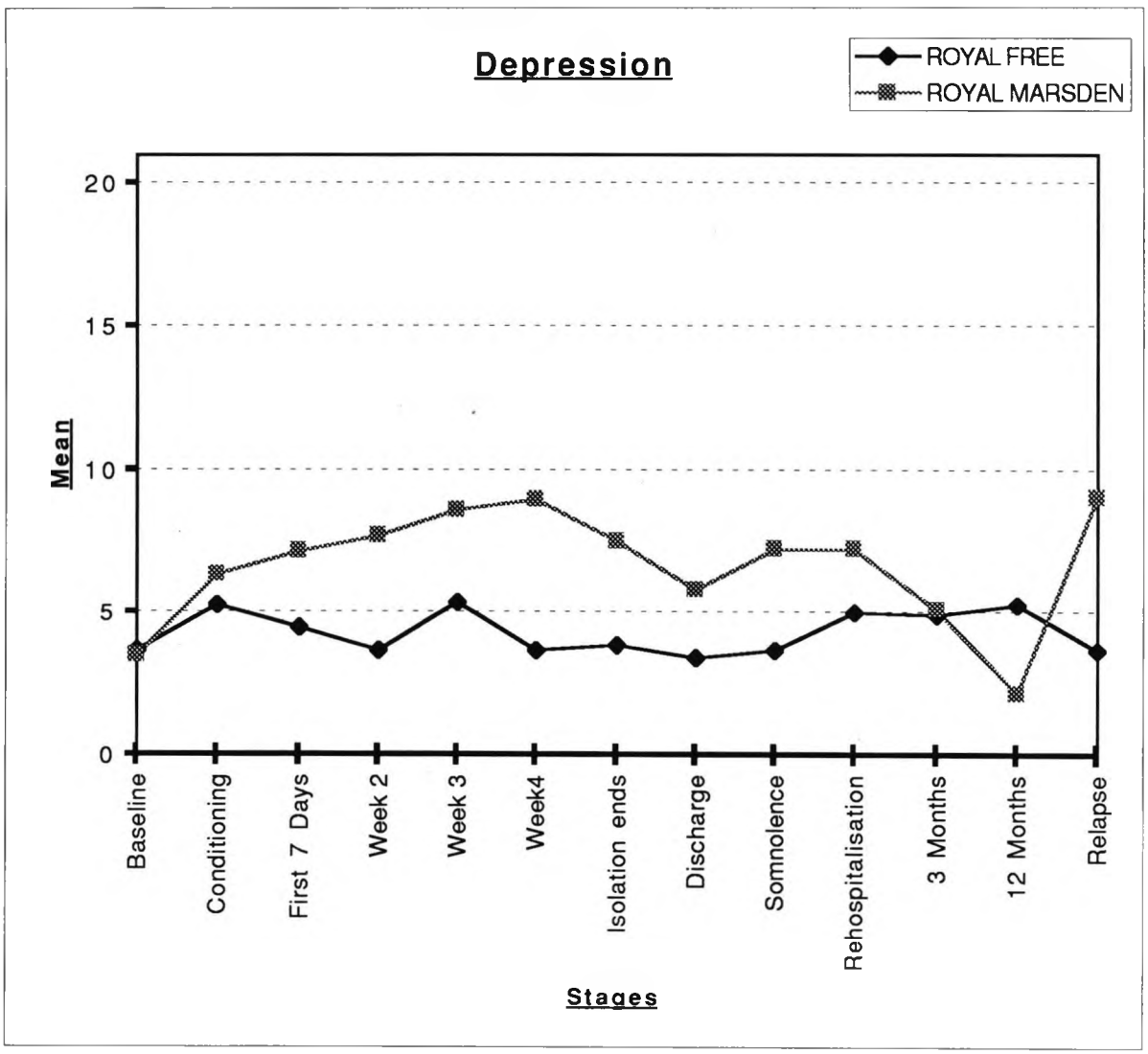


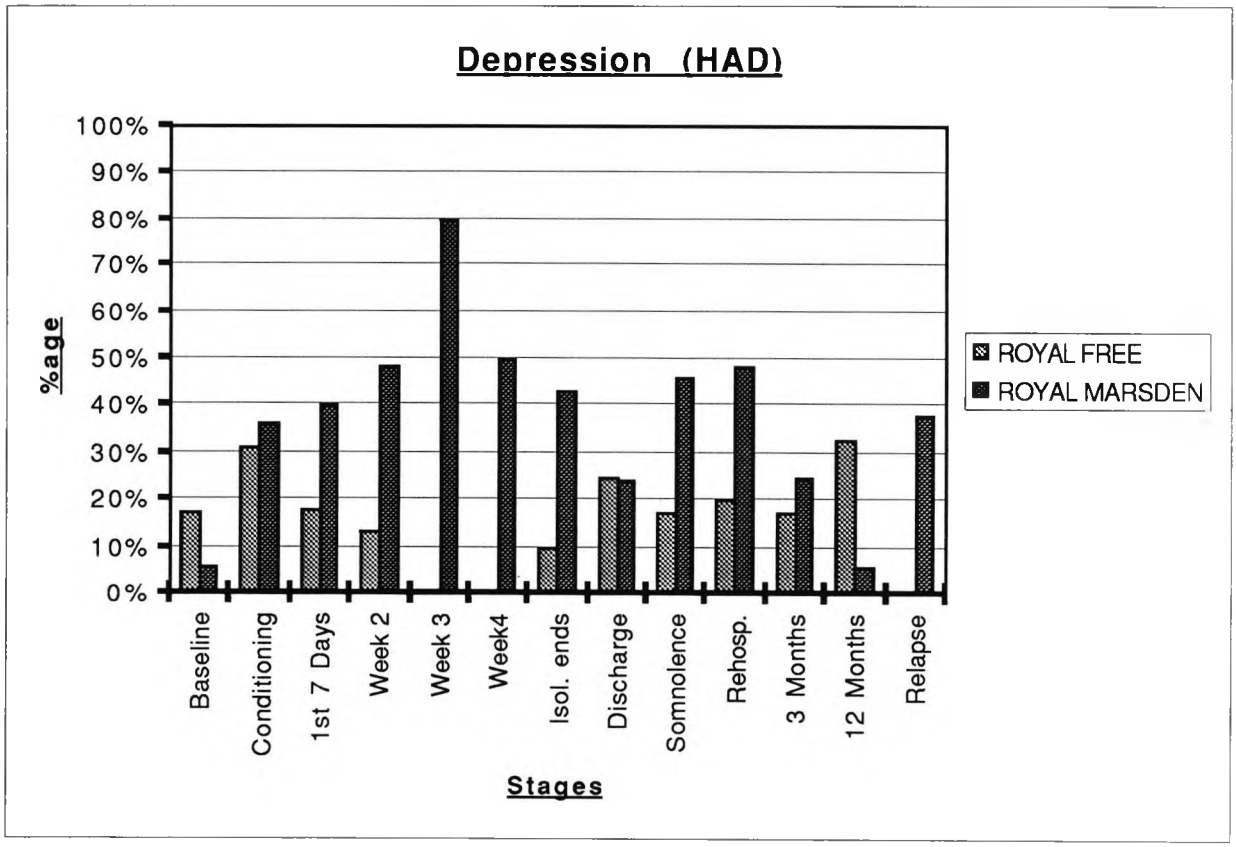
Table D:6.3.3.b

Comparison (at all stages) between the two Hospitals, of the percentages of patients scoring above the cut-off point (8) on HAD-Depression, and thus qualifying as 'cases'.

DEPRESSION	ROYAL FREE				ROYAL MARSDEN			
STAGES	Normal		Cases		Normal		Cases	
	n	%age	n	%age	n	%age	n	%age
Baseline	10	83%	2	17%	48	94%	3	6%
Conditioning	9	69%	4	31%	29	64%	16	36%
First 7 Days	9	82%	2	18%	26	61%	17	40%
Week 2	7	80%	1	13%	12	52%	11	48%
Week 3	8	100%	0	0%	2	20%	8	80%
Week 4	4	100%	0	0%	1	50%	1	50%
Isolation ends	9	90%	1	10%	23	58%	17	43%
Discharge	3	75%	1	25%	19	76%	6	24%
Somnolence	5	83%	1	17%	12	55%	10	46%
Rehospitalisation	4	80%	1	20%	13	52%	12	48%
3 Months	5	83%	1	17%	18	75%	6	25%
12 Months	2	67%	1	33%	15	94%	1	6%
Relapse	1	100%	0	0%	5	63%	3	38%

Figure D:6.3.2.b

Comparison (at all stages) between the two Hospitals, of the percentages of patients scoring above the cut-off point (8) on HAD-Depression, and thus qualifying as 'cases'.



D:6.3.3.b Comparison Of Percentages Of 'Cases' - Hospitals

Throughout isolation the number of patients qualifying as 'cases' are higher among patients treated in the Royal Marsden Hospital than those in the Royal Free Hospital. At stages 'Week 3' (stage 3b) and 'End of Isolation' (stage 4)the difference between the two hospital is significant. (Stage 3b:2-tailed p=0.001 on the Chi-Square and at stage 4: 2-tailed p=0.073 on the 90% level, Chi-Square).

D:6.3.4 Comparison Between The Two Types Of Transplant

The sample was divided into patients who received Allografts and those who received Autografts. Results are shown on Table D:6.3.4 and Figure D:6.3.4. The percentages of patients of both groups scoring above the cut-off point and qualifying as 'cases' are compared and shown on Table D:6.3.4 b and Figure D:6.3.4 b.

At 'Baseline' (stage 1) patients allocated to allogeneic transplant tend to be more depressed than those allocated to autologous transplant. The difference in levels of depression is not significant, although there is a trend. (Significance of F-value =0.08).

Throughout transplant the increase of depression is consistently higher for the group Allograft than Autograft, the difference reaches statistical significance at 'Week 3' (stage 3b) during isolation. (Significance of F-value=0.007). The number of 'cases' at this stage differ for the two types of transplant. For Autograft 30% of all assessed patients score above the cut-off and for Allograft 63%.

Increases from 'Baseline' (stage 1) at stages 'End of Isolation' (stage 4) and 'Three Months' (stage 6) are also higher for Allografts than Autografts. These differences are not significant, although there is a trend: stage 4 significance of F-value =0.08; at stage 6 significance of F-value =0.087.

At 'End of Isolation' (stage 4) the number of 'cases' between the two groups varies, too: 21 % for Autograft; 45% for Allograft. At 'Three Months' (stage 6) the number of 'cases' for Autograft is 8 % and for Allograft 35%.

Comparison from baseline:

Stages	Autograft	Allograft
1-3b	2-tailed p=0.13	2-tailed p=0.17
1-4	2-tailed p=0.26	2-tailed p=0.032
1-6	2-tailed p=0.35	2-tailed p=0.53

From 'Baseline' at the 'End of Isolation' (stage 4) patients in the group Allograft show significant increase in depression while those in Autograft do not.

Table D:6.3.4

HAD-Depression: The difference from the 'Baseline' (stage 1) of the mean scores (at each stage) for the two types of Transplant.

DEPRESSION	AUTOGRAFT			ALLOGRAFT			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**3.04**	3.8	28	**3.84**	3.1	44	0.08
Conditioning	+2.81	3.7	21	+2.51	4.9	37	0.96
First 7 Days	+3.75	4.4	20	+2.63	3.9	32	0.34
Week 2	+2.50	3	14	+3.63	4.7	16	0.45
Week 3	+1.40	2.7	10	+6.38	3.1	8	0.01
Week4	+1.20	3.6	5	+5.00	-	1	0.39
Isolation ends	+1.94	2.4	18	+4.03	4.5	31	0.08
Discharge	+1.50	2.6	8	+2.15	3.9	20	0.67
Somnolence	+2.88	4.8	8	+3.00	4.1	20	0.17
Rehospitalisation	+2.89	3.5	9	+3.57	3.3	21	0.62
3 Months	+0.50	2.4	12	+2.35	3.6	17	0.09
12 Months	-1.33	2.3	9	-0.40	3.5	10	0.75
Relapse	+3.67	4.1	6	+8.50	6.4	2	0.24

Figure D:6.3.4

HAD-Depression: The mean scores (at each stage) for the two types of Transplant.

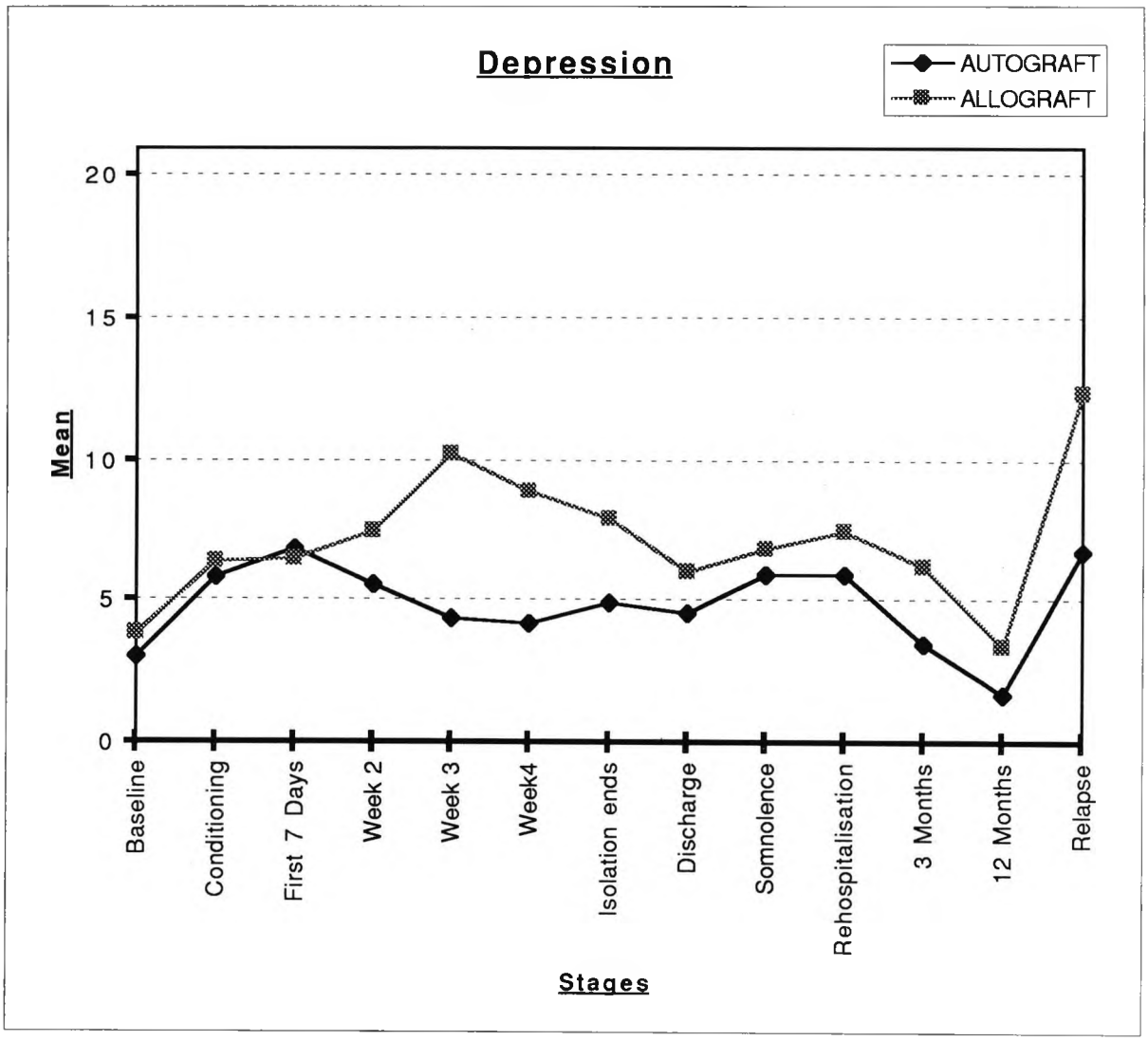


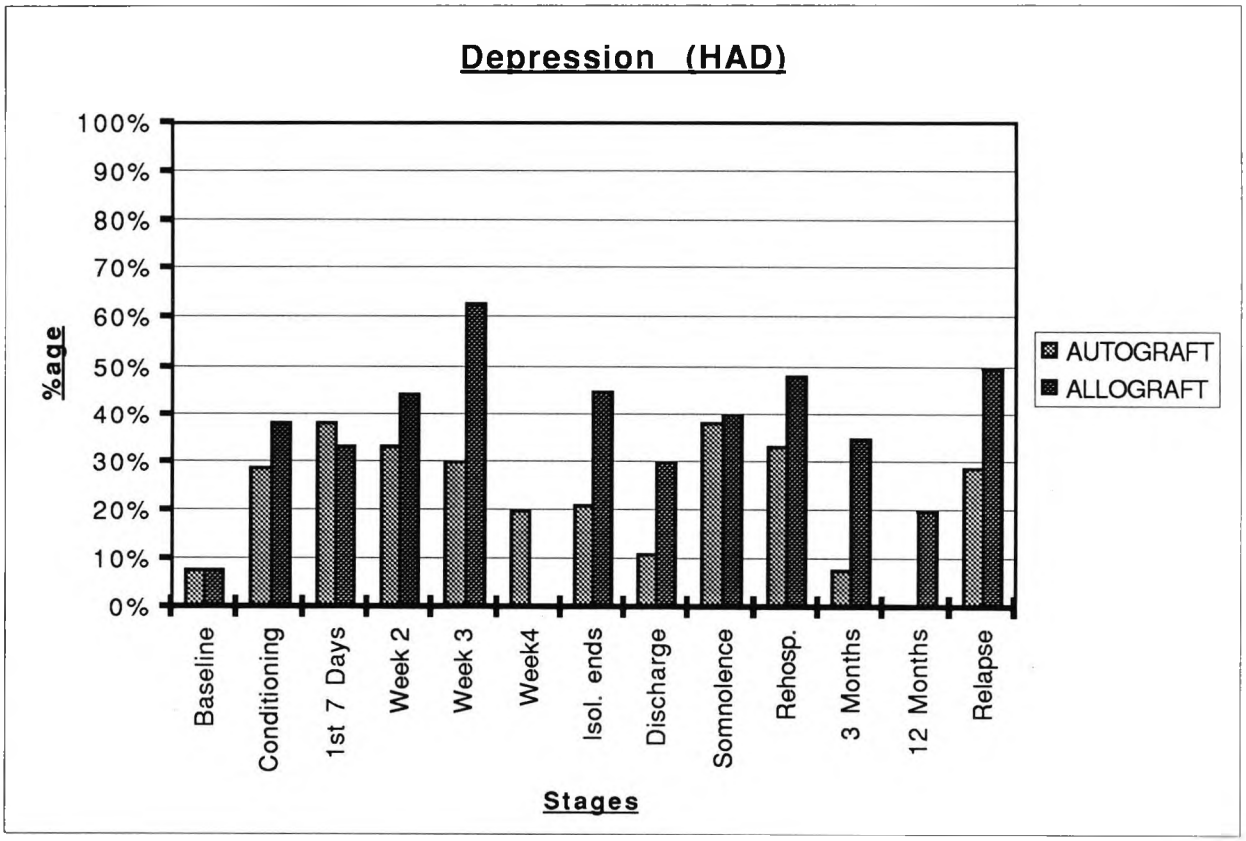
Table D:6.3.4.b

Comparison (at all stages) between the two types of Transplants, of the percentages of patients scoring above the cut-off point (8) on HAD-Depression, and thus qualifying as 'cases'.

DEPRESSION	AUTOGRAFT				ALLOGRAFT			
STAGES	Normal		Cases		Normal		Cases	
	n	%age	n	%age	n	%age	n	%age
Baseline	24	92%	2	8%	34	92%	3	8%
Conditioning	15	71%	6	29%	23	62%	14	38%
First 7 Days	13	62%	8	38%	22	67%	11	33%
Week 2	10	67%	5	33%	9	56%	7	44%
Week 3	7	70%	3	30%	3	38%	5	63%
Week 4	4	80%	1	20%	1	100%	0	0%
Isolation ends	15	79%	4	21%	17	55%	14	45%
Discharge	8	89%	1	11%	14	70%	6	30%
Somnolence	5	63%	3	38%	12	60%	8	40%
Rehospitalisation	6	67%	3	33%	11	52%	10	48%
3 Months	12	92%	1	8%	11	65%	6	35%
12 Months	9	100%	0	0%	8	80%	2	20%
Relapse	5	71%	2	29%	1	50%	1	50%

Figure D:6.3.4.b

Comparison (at all stages) between the two types of Transplants, of the percentages of patients scoring above the cut-off point (8) on HAD-Depression, and thus qualifying as 'cases'.



D:6.3.5 Comparison Between The Two Pre-Transplant Conditionings

The sample was divided into two groups, one for patients treated with Chemotherapy alone and one for patients treated with the combination of Chemotherapy + Total Body Irradiation (TBI). Scores of the two groups were compared and the results are shown on Table D:6.3.5 and Figure D:6.3.5. The percentages of patients scoring above the cut-off point (8) and qualifying as 'cases' are compared and shown on Table D:6.3.5.b and Figure D:7.3.5.b.

Comparison between Groups:

The group treated with Chemotherapy + TBI scores higher on depression at 'Baseline' (stage 1). The difference is not significant (significance of F value= 0.29). (Table D:6.3.5). The number of 'cases' at this stage differs between the two groups. In the Chemotherapy group there are no 'cases', while 11% of the Chemotherapy + TBI group qualify as 'cases'.

At 'Week 4' (stage 3c) patients in the Chemotherapy group show a decrease in the level of depression, while those in Chemotherapy + TBI show an increase. The difference is not significant. (Significance of F-level =0.19).

However, there is a difference in the number of 'cases' at this stage between the two groups. While there are no 'cases' for the Chemotherapy group, 25% of the Chemotherapy + TBI group qualify as 'cases'.

During isolation the whole sample shows a significant increase from baseline in depression . However, the increase is not significant for the Chemotherapy group but is significant for the Chemotherapy + TBI group. (See Table D:6.3.5-Isolation below).

During isolation the number of 'cases' in the Chemotherapy + TBI group remains consistently higher than in the Chemotherapy group. At 'Week 3' (stage 3b) the difference in the percentage of 'cases' is not significant although there is a trend. (Chi-Square; p=0.09).

Table D:6.3.5 Isolation

	Chemotherapy	Chemotherapy + TBI
Stages 1-3 (Conditioning)	2-tailed p=0.68	2-tailed p<0.001
Stages 1-3b(Week 3)	2-tailed p=0.28	2-tailed p=0.01
Stages 1-3c(Week 4)	2-tailed p=0.29	2-tailed p=0.04
stages 1-4(Isolation ends)	2-tailed p=0.20	2-tailed p=0.04

Table D:6.3.5

HAD-Depression: The difference from the baseline of the mean scores (at each stage) for the two types of Pre-Treatment Conditioning.

DEPRESSION	CHEMO.			CHEMO. + TBI			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**2.5**	1.6	18	**3.98**	3.8	50	0.29
Conditioning	+3.59	5	17	+2.22	4.2	41	0.36
First 7 Days	+2.86	2.9	14	+3.13	4.5	38	0.83
Week 2	+2.57	3.2	7	+3.26	4.2	23	0.69
Week 3	+0.75	2.2	4	+4.43	4.3	14	0.12
Week 4	-1.00	0	2	+3.25	3.6	4	0.19
Isolation ends	+2.01	2.8	12	+3.65	4.3	37	0.24
Discharge	+1.00	1.9	5	+2.17	3.8	23	0.51
Somnolence	-	-	-	+3.07	4.2	27	-
Rehospitalisation	+2.40	2.9	5	+3.56	3.4	25	0.49
3 Months	+2.20	2.1	5	+1.46	3.5	24	0.87
12 Months	+1.00	2.5	4	-1.33	3	15	0.47
Relapse	+4.50	0.7	2	+5.00	5.7	6	0.91

Figure D:6.3.5

HAD-Depression: The mean scores (at each stage) for the two types of Pre-Treatment Conditioning.

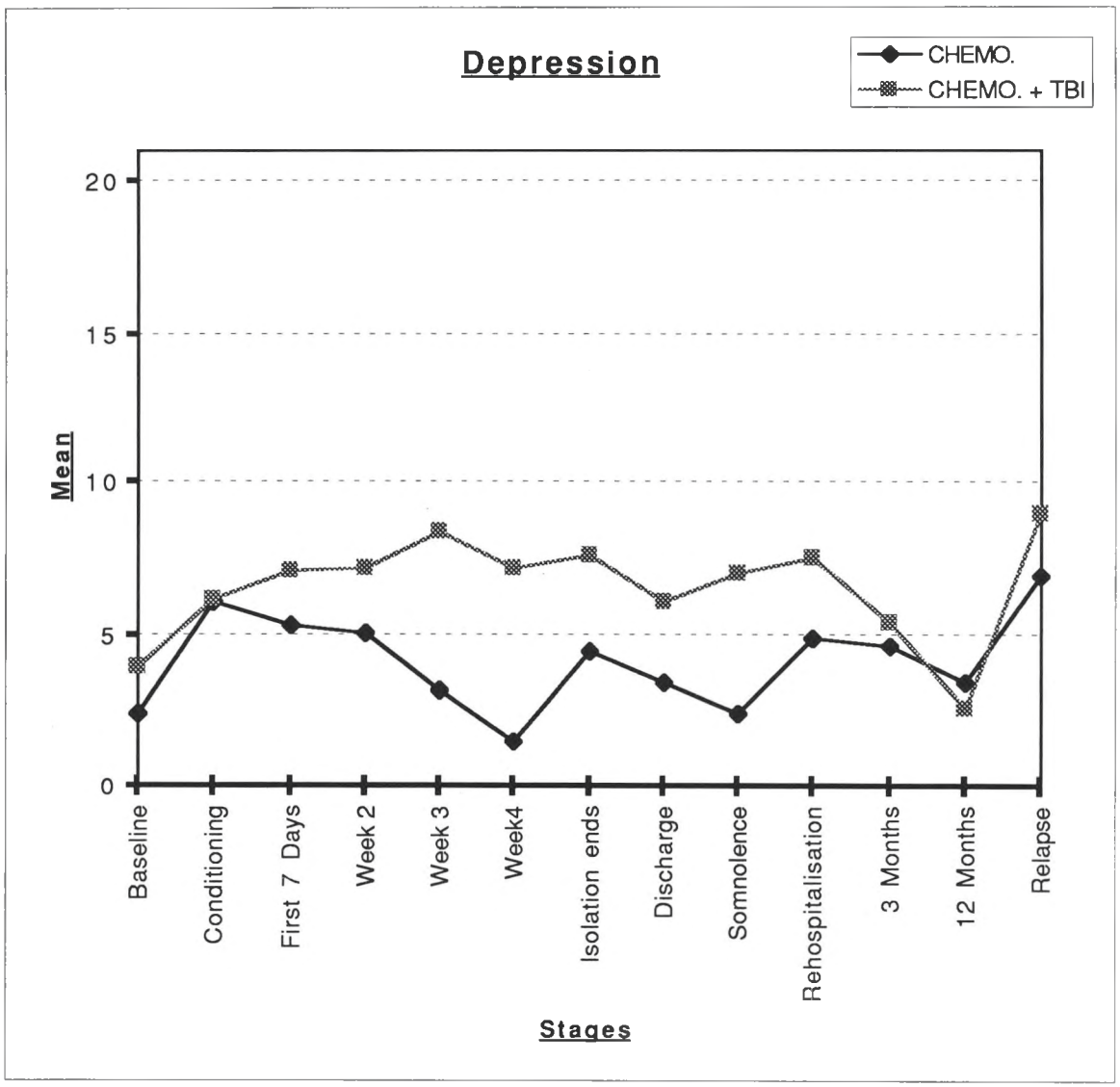


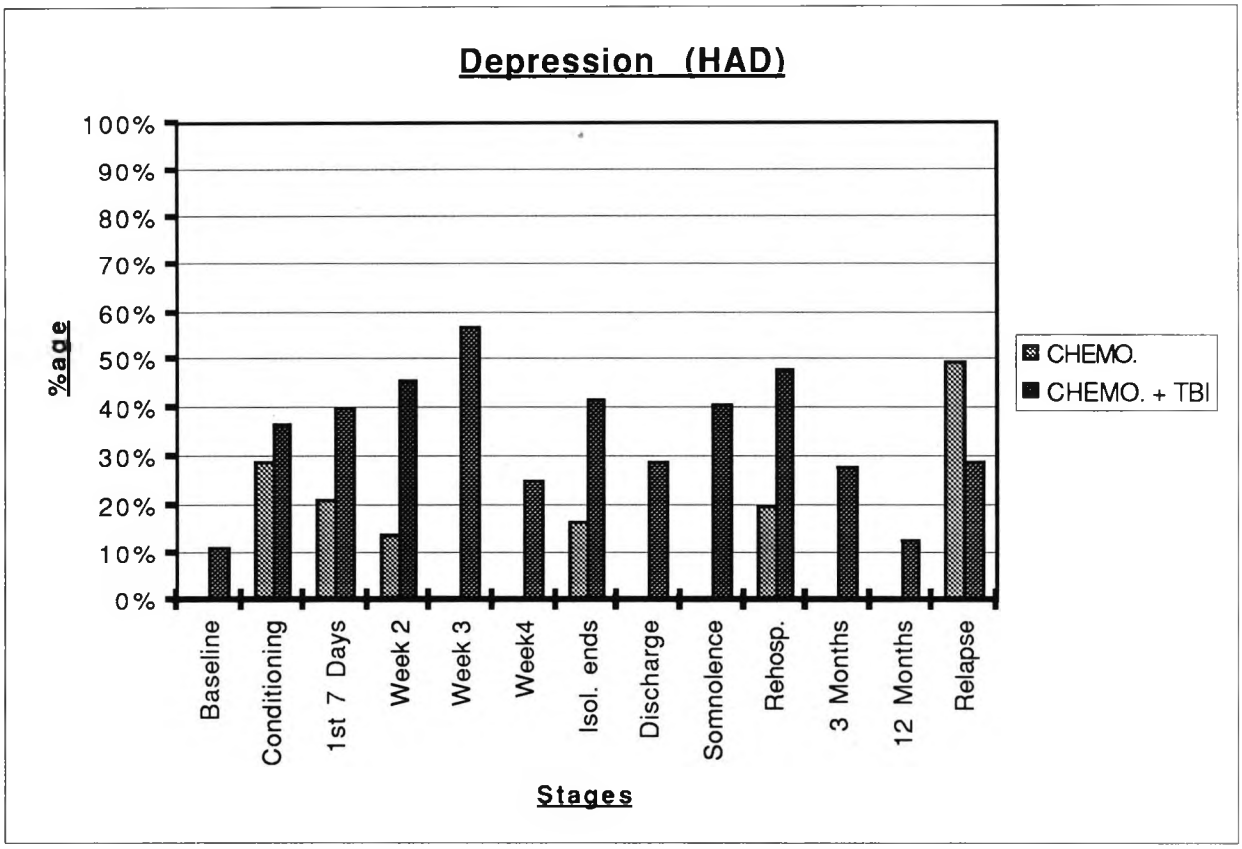
Table D:6.3.5.b

Comparison (at all stages) between the two types of Pre-Treatment Conditioning, of the percentages of patients scoring above the cut-off point (8) on HAD-Depression, and thus qualifying as 'cases'.

DEPRESSION	CHEMO.				CHEMO. + TBI			
STAGES	Normal		Cases		Normal		Cases	
	n	%age	n	%age	n	%age	n	%age
Baseline	14	100%	0	0%	40	89%	5	11%
Conditioning	12	71%	5	29%	26	63%	15	37%
First 7 Days	11	79%	3	21%	24	60%	16	40%
Week 2	6	86%	1	14%	13	54%	11	46%
Week 3	4	100%	0	0%	6	43%	8	57%
Week 4	2	100%	0	0%	3	75%	1	25%
Isolation ends	10	83%	2	17%	22	58%	16	42%
Discharge	5	100%	0	0%	17	71%	7	29%
Somnolence	1	100%	0	0%	16	59%	11	41%
Rehospitalisation	4	80%	1	20%	13	52%	12	48%
3 Months	5	100%	0	0%	18	72%	7	28%
12 Months	4	100%	0	0%	13	87%	2	13%
Relapse	1	50%	1	50%	5	71%	2	29%

Figure D:6.3.5.b

Comparison (at all stages) between the two types of Pre-Treatment Conditioning, of the percentages of patients scoring above the cut-off point (8) on HAD-Depression, and thus qualifying as 'cases'.



6.4 THE ROTTERDAM SYMPTOM CHECKLIST (RSCL)

6.4.0 Results Of The RSCL

The results of the RSCL Scale are presented in the following order:

PS:6.4 Psychology Subscale
PH:6.4 Physiology Subscale

For each subscale, results are given in the following order:

6.4.1 (i) Results for the whole sample
6.4.2 (ii) Comparison between Males and Females
6.4.3 (iii) Comparison between the two Hospitals
6.4.4 (iv) Comparison between the two types of Transplants
6.4.5 (v) Comparison between the two types of Conditioning

PS:6.4 PSYCHOLOGICAL SYMPTOMS SUBSCALE

PS:6.4 Results Of The Psychological Symptoms Subscale

Results are given in the following order:

PS:6.3.1	**(i)**	**Results for the whole sample**
PS:6.3.2	**(ii)**	**Comparison between Males and Females**
PS:6.3.3	**(iii)**	**Comparison between the two Hospitals**
PS:6.3.4	**(iv)**	**Comparison between the two types of transplants**
PS:6.3.5	**(v)**	**Comparison between the two types of conditioning**

Results of the RSCL sub-scale Psychological Symptoms are shown on Table PS:6.4.1 and Figure PS:6.4.1.

The Table PS:6.1.1 shows mean of Psychological Symptoms scores at baseline and differences from baseline for entire sample at all stages. It shows the number of patients for whom data are available and statistical significance of the comparison of the difference from baseline of increases (+) and decreases (-) to baseline mean.

Table PS:6.4.1

RSCL Psychological Symptoms: The difference from the baseline of the mean scores (for the entire sample) at each stage.

Stages	Differences from baseline/ mean	S.D.	n	Comparison-Baseline 2-tailed p*
Stage 1 Baseline	mean 6.92	4.3	72	n.a.
Stage 2 Conditioning	+1.88	5.3	57	0.68
Stage 3 First 7 Days	+0.16	3.8	51	0.18
Stage 3a Week 2	-0.60	4.8	30	0.61
Stage 3b Week 3	-0.33	3.6	18	0.73
Stage 3c Week 4	+1.33	4.8	6	0.35
Stage 4 End of Isolation	-0.22	5.6	49	0.04
Assessment I Discharge	-2.36	4.6	28	0.54
Stage 5 Somnolence	-2.59	4.5	27	0.05
Assessment II Rehospitalization	-1.17	5.2	30	0.11
Stage 6 3 Months	-2.68	3.3	28	0.01
Stage 7 12 Months	-3.58	3.3	19	0.15

*p=values are based on the statistical analysis of the differences to baseline on the Non-Parametric Wilcoxon Matched Pairs Test.

PS:6.4.1 Comparison from Baseline

The level of psychological symptoms increases compared to baseline at stages 'Conditioning' (stage 2), First 7 Days' (stage 3) and 'Week 4' (stage 3c)i. The level of psychological symptoms is highest at 'Conditioning' (stage 2). However compared to 'Baseline' (stage 2) the difference is not statistically significant (2-tailed p=0.68).

At all other stages the level of psychological symptoms decreases compared to 'Baseline' (stage 1).

The decreases are significant at Stages 'End of isolation' (stage 4); 'Somnolence' (stage 5) and 'Three Months' (stage 6).

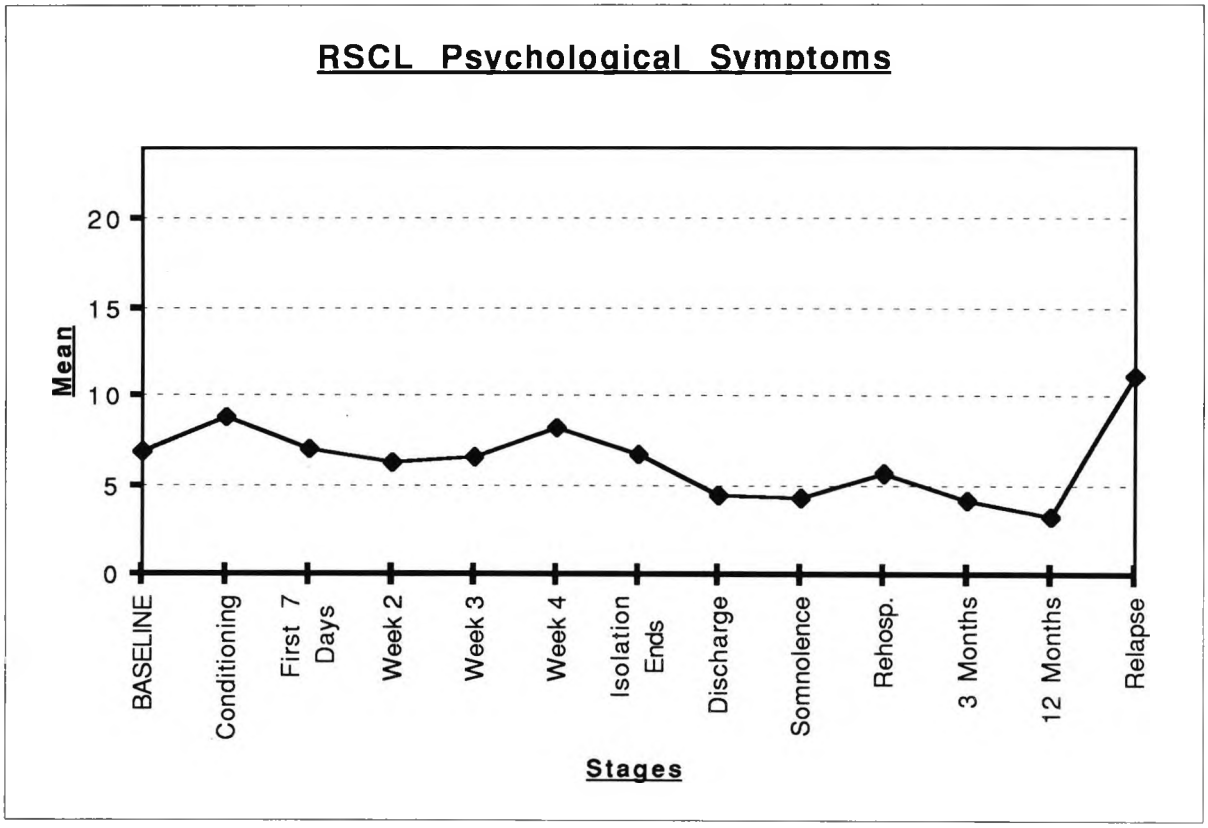
From these data it appears that psychological symptoms as measured on the RSCL are highest at 'Conditioning' (stage 2). However, the difference compared to 'Baseline' (stage 1) is not statistically significant (2-tailed p=0.68).

These data confirm Hypothesis number two which says:

"The quality of life does not remain constant during the treatment. It is influenced by the changes in the treatment during the different stages."

Figure PS:6.4.1

RSCL-Psychological Symptoms: The difference from the baseline of the mean scores (for the entire sample) at each stage.



PS:6.4.2 Comparison Between Males And Females

The sample was divided into Males and Females and compared. Results are shown on Table PS:6.4.2.

At 'Baseline' (stage 1) there is no significant difference between the two genders. (Significance of F-value = 0.15).

However at stages 'Discharge' (stage I) and 'Somnolence' (stage 5) the level of psychological symptoms shows a greater decrease for Females than for Males. At 'Discharge' (stage I) the difference is not significant, although there is a trend. (Significance of F-value = 0.08). At 'Somnolence' (stage 5) the difference is significant. (Significance of F-value = 0.05).

Comparison to Baseline:

At 'Twelve Months' (stage 7) the level of psychological symptoms shows a significant decrease for Females (2-tailed p=0.02) but not for Males (2-tailed p=0.96)*.
* Non- Parametric Wilcoxon Matched -Pairs Test.

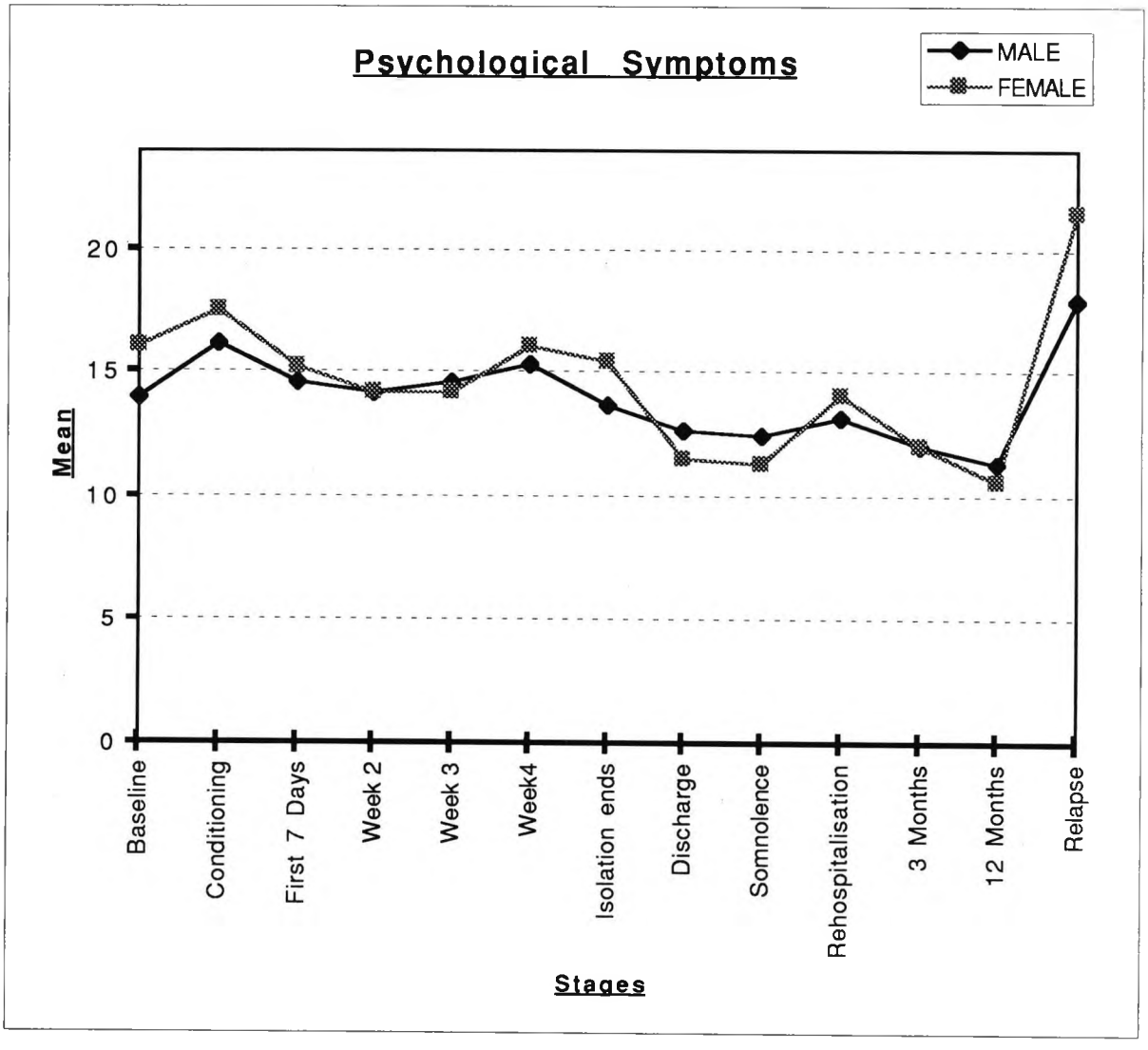
Table PS:6.4.2

RSCL Psychological Symptoms: The difference from the baseline of the mean scores for Males and Females at each stage.

Psychological	MALE			FEMALE			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**13.97**	3.6	35	**16.07**	5.2	27	0.15
Conditioning	+2.17	2.6	35	+1.41	5	22	0.6
First 7 Days	+0.70	3.8	33	-0.83	3.6	18	0.17
Week 2	+0.22	5.1	18	-1.83	4	12	0.25
Week 3	+0.64	3	11	-1.86	4.3	7	0.16
Week 4	+1.33	4.8	6	-	-	-	-
Isolation ends	-0.31	5.7	32	-0.59	5.4	17	0.74
Discharge	-1.32	4.7	19	-4.56	3.7	9	0.08
Somnolence	-1.50	4	18	-4.78	4.8	9	0.05
Rehospitalisation	-0.75	4	20	-2.00	7.1	10	0.54
3 Months	-1.94	3.3	18	-4.00	6.5	10	0.27
12 Months	-2.69	2.9	13	-5.50	3.6	6	0.1
Relapse	+4.00	6.1	6	+5.50	4.9	2	0.77

Figure PS:6.4.2

RSCL Psychological Symptoms: The mean scores for Males and Females at each stage.



PS:6.4.3 Comparison Between Patients At The Two Hospitals

The sample was divided into patients treated at the Royal Marsden Hospital and the Royal Free Hospital and compared. Results are shown on Table PS:6.4.3 and.

There is no significant difference between the two hospital at any stage.
There is, however, a trend at 'Week 2' (stage 3a) when patients treated at the Royal Free Hospital show a decrease in psychological symptoms and those at the Royal Marsden an increase. Compared to Baseline neither group show a significant difference at this stage.

Tested on the Non-Parametric Wilcoxon Matched-Pairs Test.

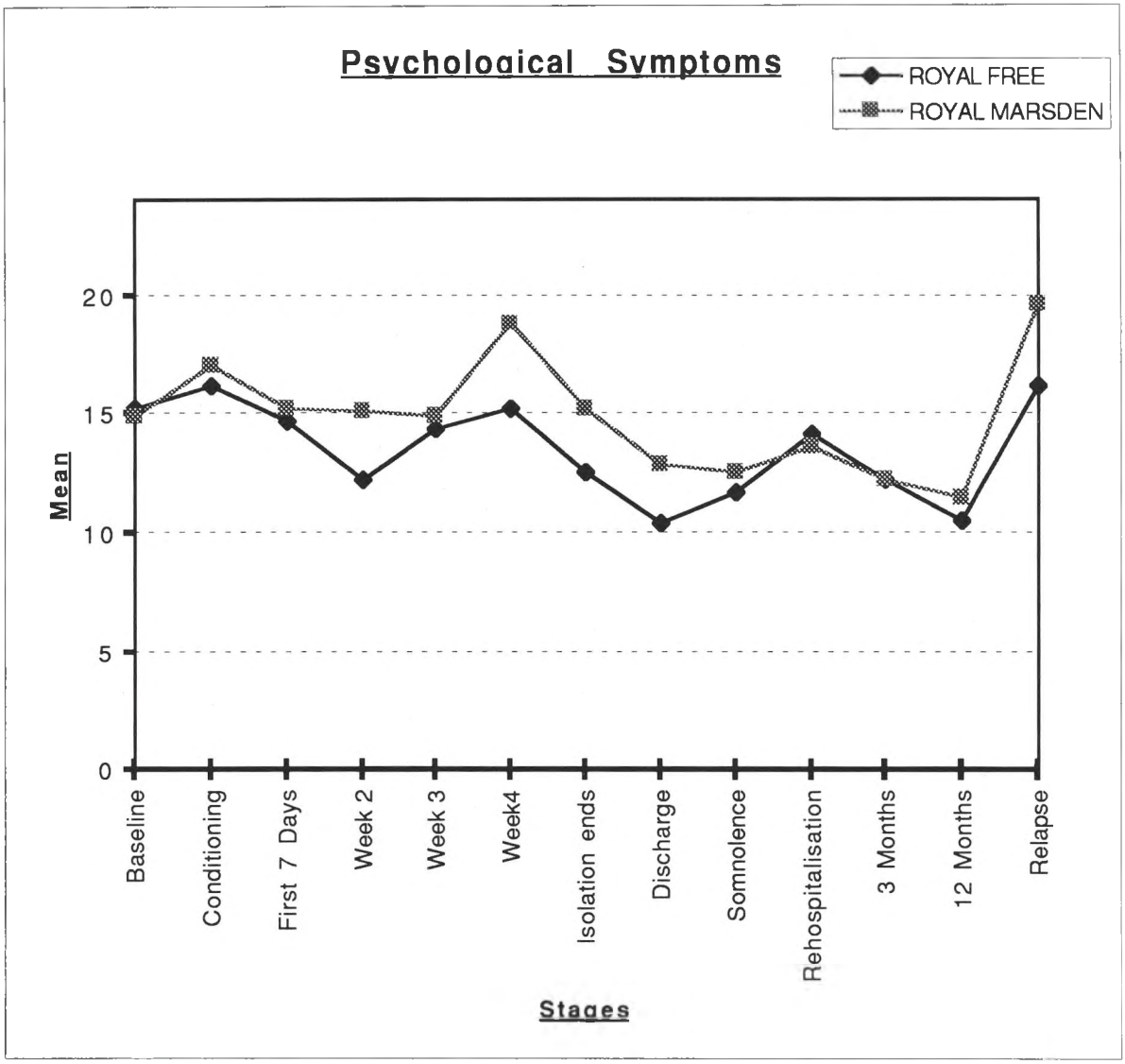
Table PS:6.4.3

RSCL Psychological Symptoms: The difference from the baseline of the mean scores for the two Hospitals at each stage.

PSYCHOLOGICA	ROYAL FREE			ROYAL MARSDEN			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**15.17**	4	12	**14.82**	4.6	50	0.62
Conditioning	+1.00	7.6	13	+2.14	4.5	44	0.5
First 7 Days	-0.55	5.3	11	+0.35	3.2	40	0.49
Week 2	-3.00	3.8	8	+0.27	4.8	22	0.09
Week 3	-0.87	2.9	8	+0.10	4.2	10	0.59
Week 4	+/- 0.00	5.3	4	+4.00	2.8	2	0.39
Isolation ends	-2.60	6.3	10	+0.38	5.3	39	0.13
Discharge	-4.75	7.3	4	-1.96	4.1	24	0.27
Somnolence	-3.50	5.8	6	-2.33	4.1	21	0.75
Rehospitalisation	-1.00	10	5	-1.20	3.9	25	0.94
3 Months	-3.00	3.5	6	-2.59	5	22	0.85
12 Months	-4.67	6.1	3	-3.38	2.8	16	0.59
Relapse	+1.00	-	1	+4.86	5.8	7	0.56

Figure PS:6.4.3

RSCL Psychological Symptoms: The mean scores for the two Hospitals at each stage.



PS:6.4.4 Comparison Between The Two Types Of Transplants

The sample was divided into patients who received allogeneic and those who received an autologeous transplant. The two groups were compared. Results are shown on Table PS:6.4.4.

There are no significant differences between the two groups at any stage. However when compared to baseline at 'Week 2' (stage 3a) Autografts show a significant decrease in psychological symptoms compared to 'Baseline' (stage 1). (2-tailed p=0.05).

Tested on the Non-Parametric Wilcoxon Matched Pairs Test.

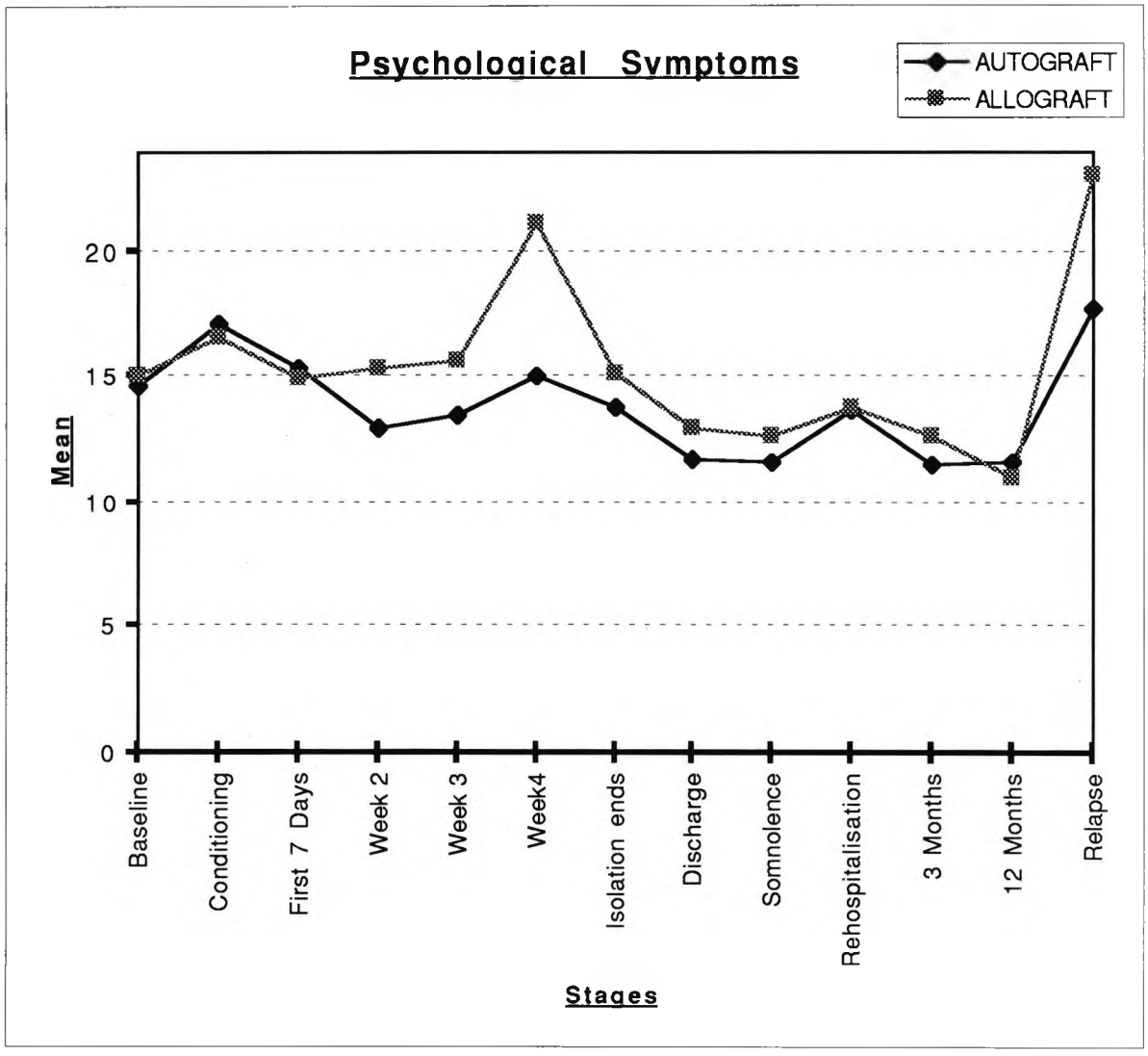
Table PS:6.4.4

RSCL Psychological Symptoms: The difference from the baseline of the mean scores (at each stage) for the two types of Transplant.

Psychological	AUTOGRAFT			ALLOGRAFT			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**14.6**	4.8	25	**15.08**	4.2	37	0.32
Conditioning	+2.52	5.6	21	+1.50	5.2	36	0.49
First 7 Days	+0.70	4	20	-0.19	3.7	31	0.42
Week 2	-1.64	3.3	14	+0.31	5.7	16	0.27
Week 3	-1.10	3.1	10	+0.62	4.2	8	0.33
Week 4	+0.40	4.7	5	+6.00	-	1	0.34
Isolation ends	-0.78	3.5	18	+0.10	6.5	31	0.6
Discharge	-2.88	3.7	8	-2.15	5	20	0.72
Somnolence	-3.00	3.5	8	-2.42	4.9	19	0.75
Rehospitalisation	-0.89	2.8	9	-1.29	6	21	0.85
3 Months	-3.09	5.1	11	-2.41	4.6	17	0.72
12 Months	-3.00	2.7	9	-4.10	3.9	10	0.42
Relapse	+3.16	3.2	6	+8.00	11.3	2	0.32

Table PS:6.4.4

RSCL Psychological Symptoms: The mean scores (at each stage) for the two types of Transplant.



PS:6.4.5 Comparison Between The Two Types Of Conditioning

The sample was divided into patients treated with chemotherapy alone and those treated with a combination of chemotherapy and Total Body Irradiation (TBI). The groups were then compared. Results are shown on Table PS:6.4.5.

Comparison between Groups

There are no significant differences between the two groups at any stage.

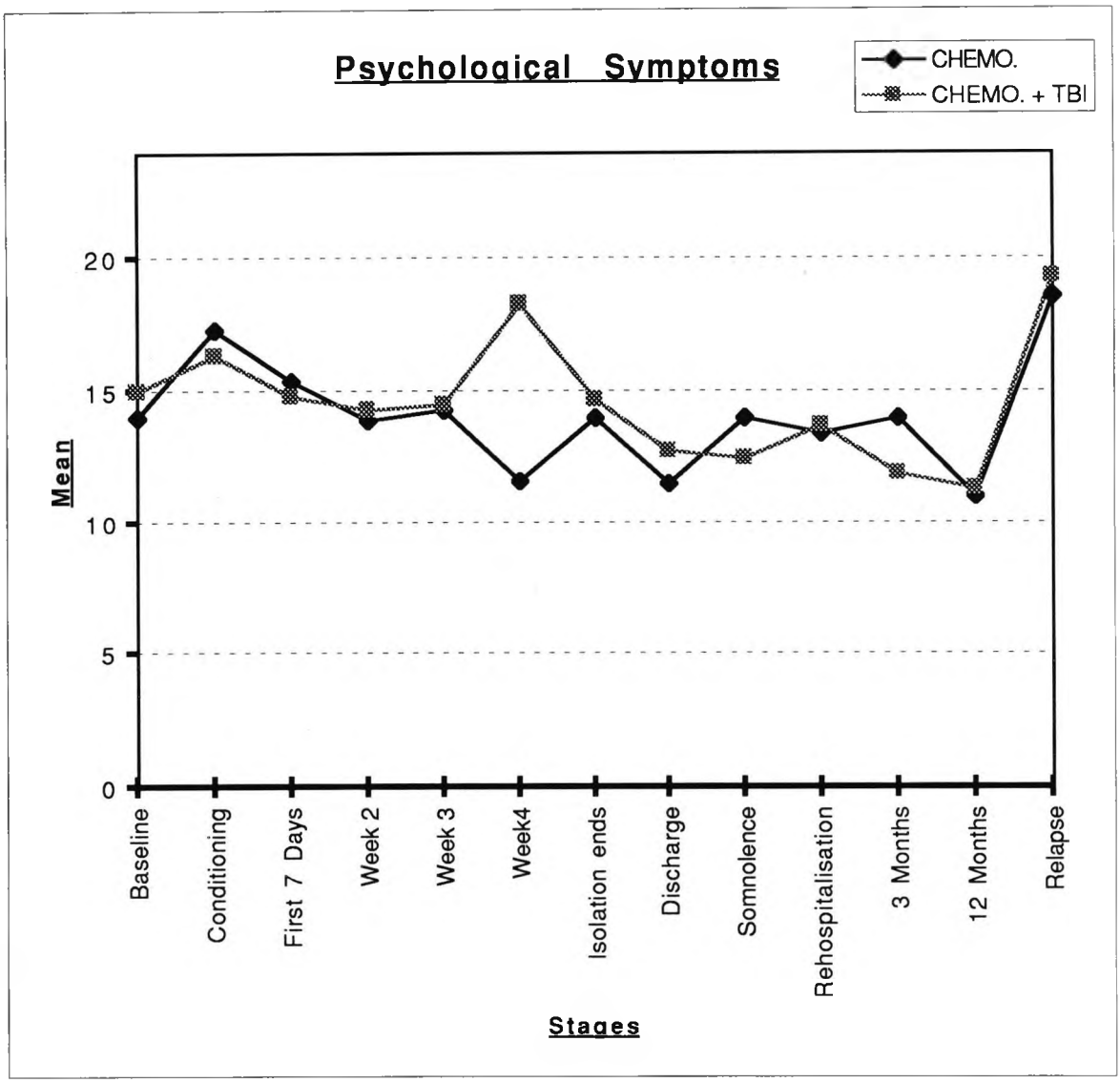
Table PS:6.4.5

RSCL Psychological Symptoms: The difference from the baseline of the mean scores (at each stage) for the two types of Pre-Treatment Conditioning.

PSYCHOLOGICAL	CHEMO.			CHEMO. + TBI			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**14.08**	3.4	13	**15.04**	4.8	45	0.65
Conditioning	+3.24	4.8	17	+1.30	5.5	40	0.21
First 7 Days	+1.31	2.7	13	-0.24	4.1	38	0.21
Week 2	-0.14	2	7	-0.74	5.3	23	0.78
Week 3	+0.25	2.8	4	-0.50	3.9	14	0.73
Week 4	-2.50	0.7	2	+3.25	4.9	4	0.19
Isolation ends	some	3.9	12	-0.30	6	37	0.87
Discharge	-2.60	1.1	5	-2.30	5.1	23	0.9
Somnolence	-	-	-	-2.58	4.6	26	-
Rehospitalisation	-0.60	4.4	5	-1.28	5.4	25	0.79
3 Months	+/- 0.00	7.3	4	-3.13	4.2	24	0.22
12 Months	-3.00	3.2	4	-3.73	3.4	15	0.86
Relapse	+4.50	6.4	2	+4.33	5.9	6	0.97

Figure PS:6.4.5

RSCL Psychological Symptoms: The mean scores (at each stage) for the two types of Pre-Treatment Conditioning.



PH:6.4 PHYSICAL SYMPTOMS SUBSCALE

PH:6.4 Results of the Physical Symptoms Subscale

Results are given in the following order:

PH:6.4.1 (i) Results for the whole sample
PH:6.4.2 (ii) Comparison between Males and Females
PH:6.4.3 (iii) Comparison between the two Hospitals
PH:6.4.4 (iv) Comparison between the two types of Transplants
PH:6.4.5 (v) Comparison between the two types of Conditioning

Results of the RSCL sub-scale Physical Symptoms are shown on Table PH:6.4.1 and Figure PH:6.4.1.

The Table PH:6.4.1 shows the mean of Physical Symptom scores at baseline and the differences from baseline for entire sample at all stages. It shows the number of patients for whom data are available and the statistical significance of the comparison of the difference from baseline of increases (+) and decreases (-) to baseline mean.

Table PH:6.4.1

RSCL Physical Symptoms: The difference from the baseline of the mean scores (for the entire sample) at each stage.

Stages	Differences from baseline mean	S.D.	n	Comparison -Baseline 2-tailed p*
Stage 1 Baseline	mean 8.53	5.7	72	n.a.
Stage 2 Conditioning	+8.47	6.9	57	≤0.001
Stage 3 First 7 days	+12.00	7.8	51	≤0.001
Stage 3a Week 2	+11.00	9.1	30	0.001
Stage 3b Week 3	+8.39	9.0	18	0.02
Stage 3c Week 4	+5.33	10.2	6	≤0.001
Stage 4 End of isolation	+9.52	9.3	49	≤0.001
Assessment I Discharge	+6.79	6.7	28	0.01
Stage 5 Somnolence	+8.19	5.8	27	0.001
Assessment II Rehospitalization	+7.60	6.4	30	0.29
Stage 6 3 months	+5.82	6.8	28	0.28
Stage 7 12 months	-0.22	5.16	18	0.02

*p=values are based on the statistical analysis of the differences to baseline on the Non-Parametric Wilcoxon Matched-Pairs Test.

PH:6.4.1 Comparison From Baseline

With the exception of stage 'Twelve Months' (stage 7) every stage shows an increase in the level of physical symptoms.

Compared to Baseline these increase are significant at stages:

2	(Conditioning)	2 tailed p< 0.001*
3	(First 7 Days)	2-tailed p<)0.001
3a	(Week 2)	2-tailed p=0.001
3b	(Week 3)	2-tailed p=0.02
3c	(Week 2)	2-tailed p<0.001
4	(End of Isolation)	2-tailed p=<0.001
I	(Discharge)	2-tailed p=0.005
5	(Somnolence)	2-tailed p=0.001

From these data it appears that physical symptoms increase after conditioning and remain high compared to 'Baseline' (stage 1) until the last assessment at 'Twelve Months' (stage 7) when physical symptoms show decreases from 'Baseline' (stage 1).

In addition it should be kept in mind that only those patients who felt well enough for interviews were actually assessed. This may have influenced the data and reduced the actual level of symptoms recorded. If patients who were too ill for assessment were included in these data the level of physical symptoms would probably be higher than here recorded.

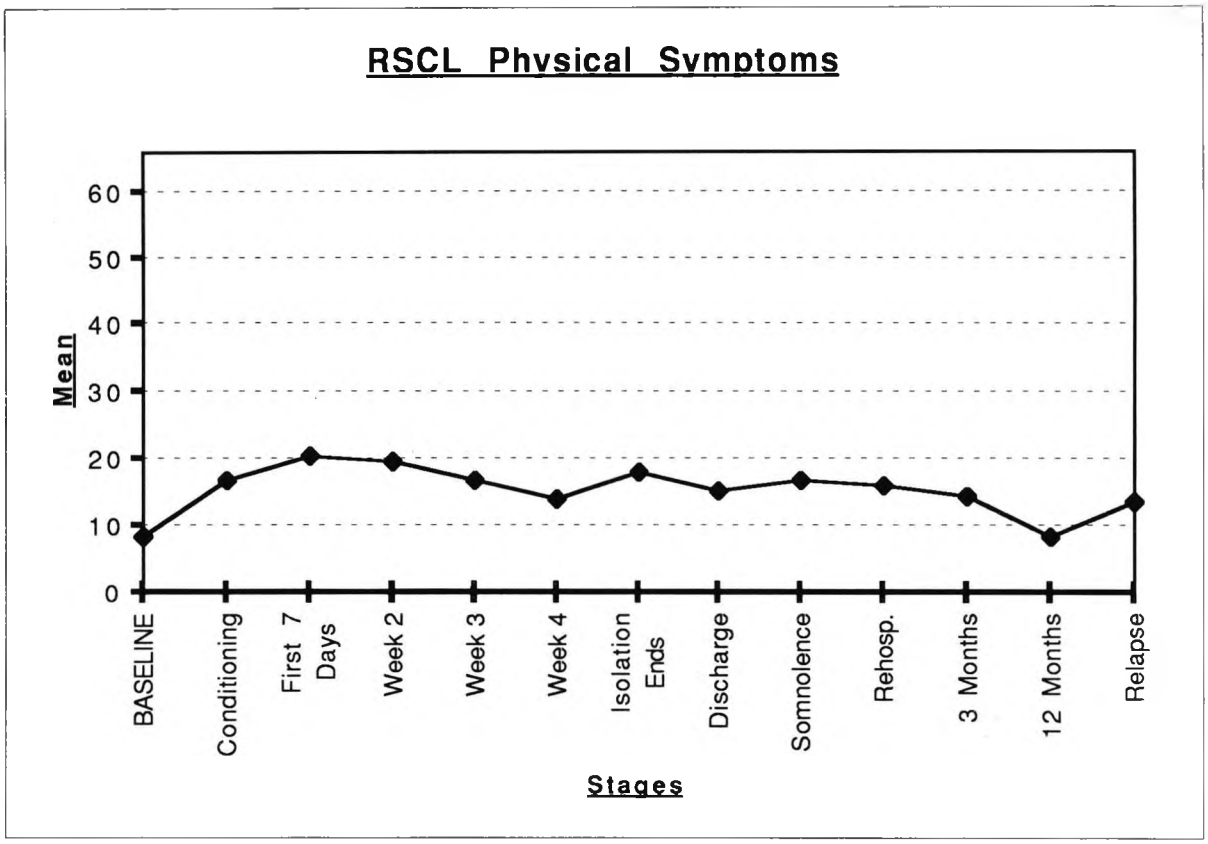
The above data confirm Hypothesis number two which says:

"The quality of life does not remain constant during the treatment. It is influenced by the changes in the treatment during the different stages."

* tested on the Non-Parametric Wilcoxon Matched Pair Test.

Figure PH:6.4.1

RSCL Physical Symptoms: The difference from the baseline of the mean scores (for the entire sample) at each stage.



PH:6.4.2 Comparison between Males and Females

The sample was divided into males and females and compared. Results are shown on Table PH:6.4.2.

At 'Baseline" (stage 1) there is no significant difference between the two groups. (Significance of F-value=0.66).

There is however, a significant difference at 'Week 3' (stage 3b) when Females score higher on physical symptoms than Males (significance of F-value = 0.03). From 'Baseline' (stage 1) the difference is significant for Females (2-tailed p=0.06) but not for Males (2-tailed p=0.18). Tested on the Non-Parametric Wilcoxon Matched-Pairs Test Signed Rank Test.

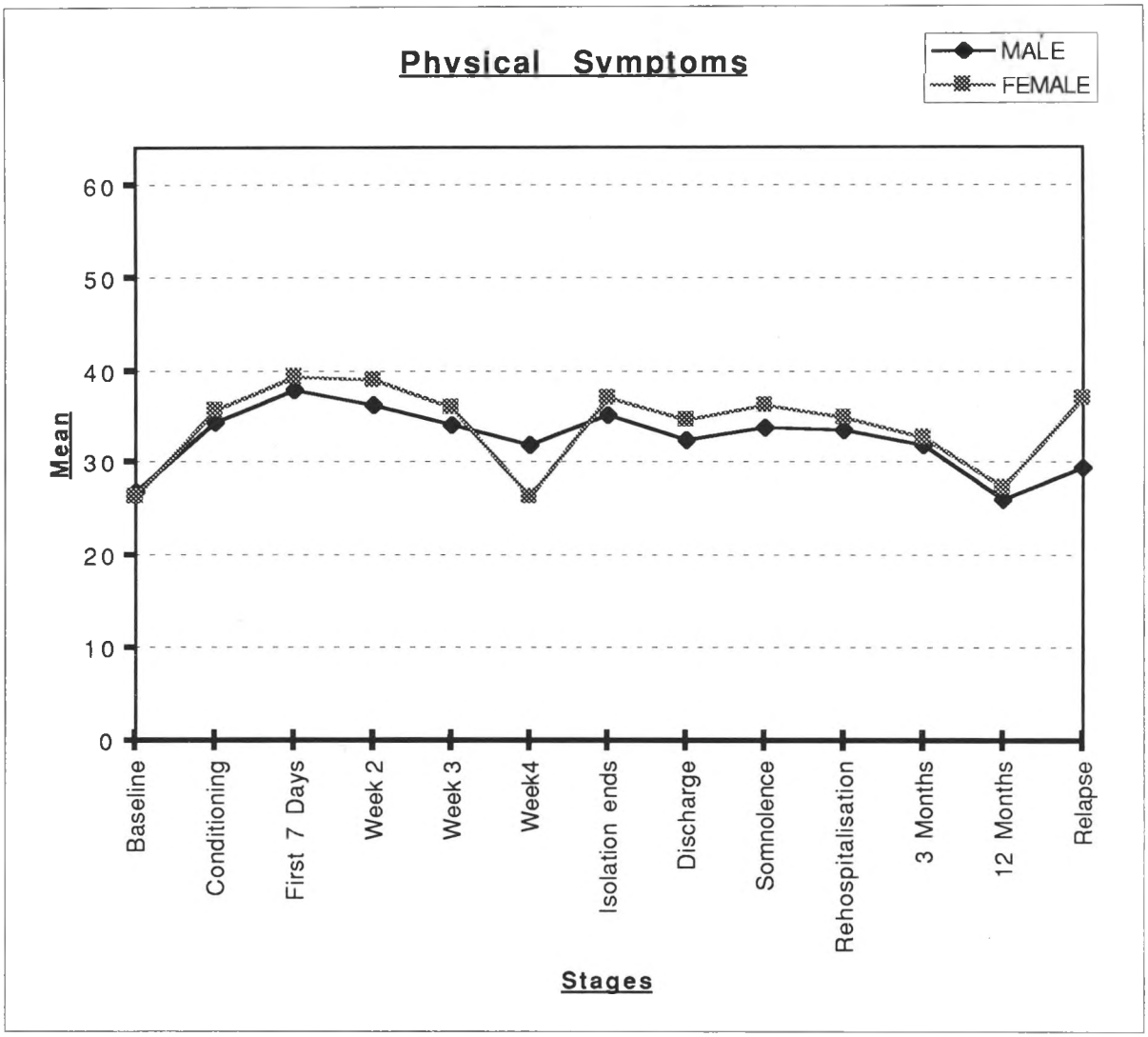
Table PH:6.4.2

RSCL Physical Symptoms: The difference from the baseline of the mean scores for Males and Females at each stage.

PHYSICAL	MALE			FEMALE			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**26.63**	6.3	35	**26.33**	4.7	27	0.66
Conditioning	+7.74	6.1	35	+9.64	8	22	0.32
First 7 Days	+11.33	7.9	33	+13.22	7.7	18	0.41
Week 2	+9.78	10.4	18	+12.83	6.8	12	0.38
Week 3	+7.55	7.7	11	+9.71	11.2	7	0.03
Week 4	+5.33	10.2	6	-	-	-	-
Isolation ends	+8.75	10	32	+10.94	7.6	17	0.44
Discharge	+6.00	7.2	19	+8.44	5.1	9	0.37
Somnolence	+7.17	5.9	18	+10.22	5.4	9	0.18
Rehospitalisation	+7.00	6.6	20	+8.80	6.2	10	0.48
3 Months	+5.39	7	18	+6.60	6.8	10	0.66
12 Months	-0.83	4.1	12	+1.00	7.1	6	0.49
Relapse	+3.00	8	6	+11.00	1.4	2	0.23

Figure PH:6.4.2

RSCL Physical Symptoms: The mean scores for Males and Females at each stage.



PH:6.4.3 Comparison Between Patients At The Two Hospitals

The sample was divided into patients treated at the Royal Marsden Hospital and the Royal Free Hospital and compared. Results are shown on Table PH:6.4.3.

At 'Baseline' (stage 1) there is a trend (Significance of F-value= 0.12) for patients at the Royal Free Hospital to record more physical symptoms than patients at the Royal Marsden Hospital. However, during isolation patients at the Royal Marsden Hospital show a greater increase in physical symptoms than patients at the Royal Free Hospital. At stages 'Week 2' (stage 3a) and 'End of Isolation' (stage 4) the difference between the hospitals is significant. At stages 'First 7 Days' (stage 3) and 'Week 3' (stage 3b) the differences are not significant, although there is a trend at both stages.

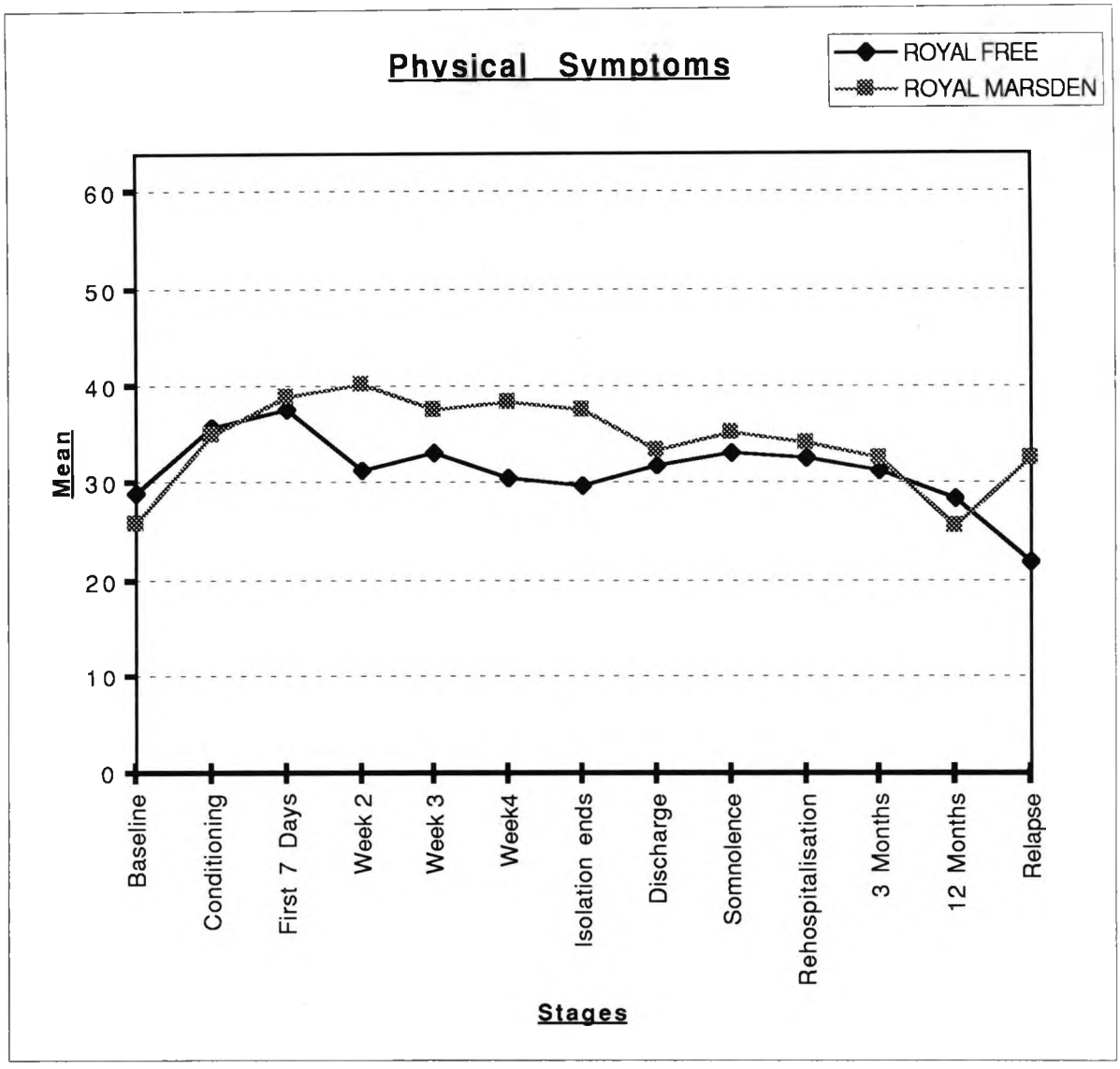
Table PH:6.4.3

RSCL Physical Symptoms: The difference from the baseline of the mean scores for the two Hospitals at each stage.

PHYSICAL	ROYAL FREE			ROYAL MARSDEN			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**28.92**	6.9	12	**25.92**	5.2	50	0.12
Conditioning	+6.85	6.2	13	+8.95	7	44	0.34
First 7 Days	+8.63	11.7	11	+12.93	6.2	40	0.11
Week 2	+2.38	8.7	8	+14.14	7.1	22	0.001
Week 3	+4.25	9.3	8	+11.70	7.5	10	0.8
Week 4	+1.75	8.5	4	+12.50	12	2	0.26
Isolation ends	+0.90	6.4	10	+11.72	8.6	39	0.001
Discharge	+3.00	6.3	4	+7.42	6.6	23	0.22
Somnolence	+4.17	5.3	6	+9.33	5.5	21	0.45
Rehospitalisation	+3.60	6.2	5	+8.40	6.3	25	0.13
3 Months	+2.50	5.7	6	+6.73	6.9	22	0.18
12 Months	-0.33	8.5	3	-0.20	4.7	15	0.97
Relapse	-7.00	-	1	+6.71	6.5	7	0.1

Figure PH:6.4.3

RSCL Physical Symptoms: The mean scores for the two Hospitals at each stage.



PH:6.4.4 Comparison Between The Two Types Of Transplants

The sample was divided into patients who received allogeneic and those who received an autologous transplants. The two groups were compared. Results are shown on Table PH:6.4.4.

At 'Baseline' (stage 1) both groups score similar levels in physical symptoms and the difference between the group is not significant. Significance of F-value =0.56.

During isolation patients who received allografts record more physical symptoms than patients who received autografts. At stages 'Week 3' (stage 3b) and 'End of Isolation' (stage 4) the differences are significant. At stages 'Week 2' (stage 3a) and 'Week 4' (stage 3c) there is a trend at both stages, but the differences are not significant. (See Table PH:6.4.4).

A comparison from 'Baseline' (stage 1) to stages during isolation for the two groups are shown on Table PH:6.4.4.b.

PH:6.4.4.b

STAGES	AUTOGRAFT	ALLOGRAFT
1-3a	2-tailed p=0.01*	2-tailed p=0.04
1-3b	2-tailed p=0.13	2-tailed p=0.07
1-3c	2-tailed p=0.03	2-tailed p=0.002
1-4	2-tailed p=0.04	2-tailed p=0.004

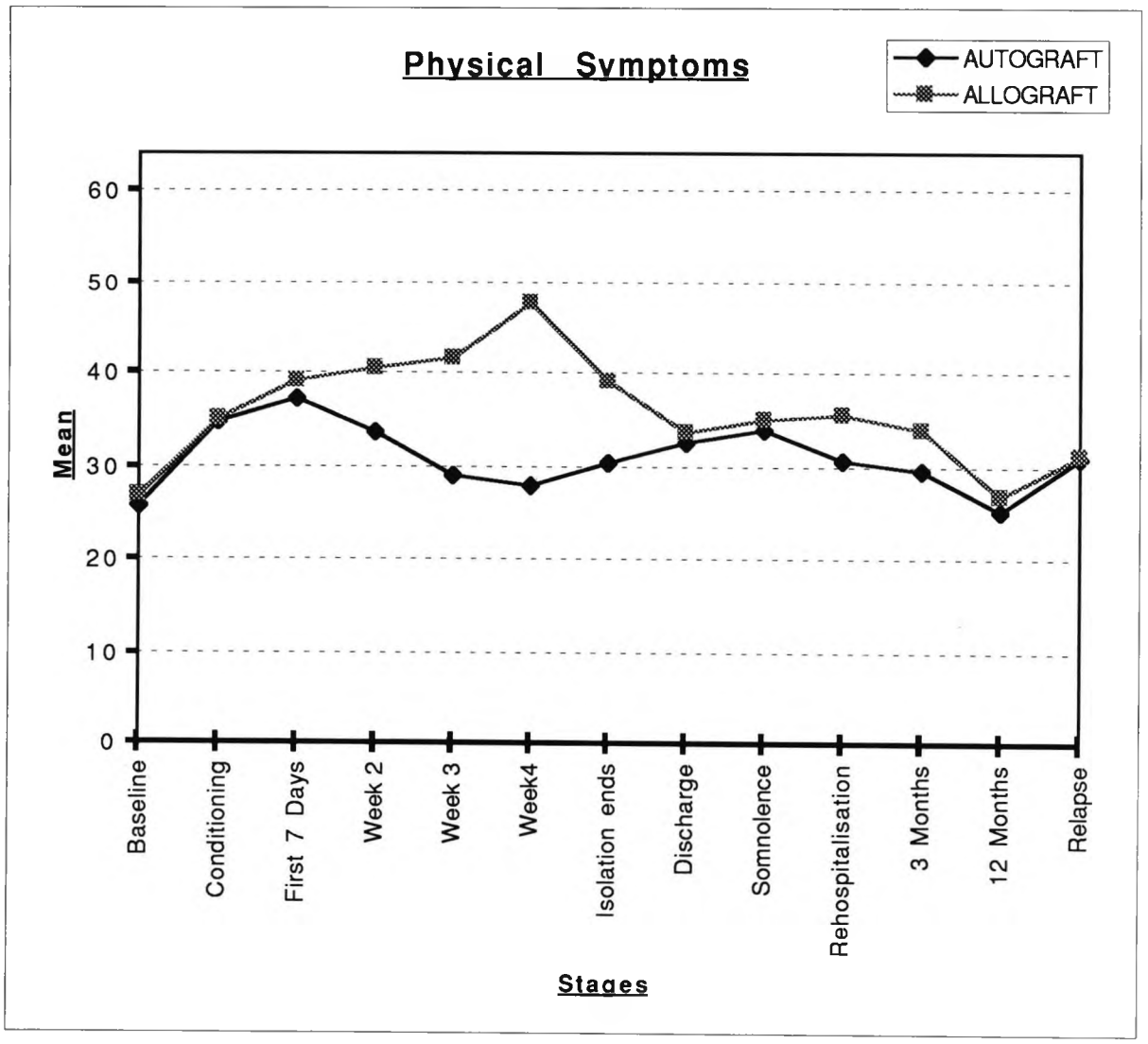
Table PH:6.4.4

RSCL Physical Symptoms: The difference from the baseline of the mean scores (at each stage) for the two types of Transplant.

PHYSICAL	AUTOGRAFT			ALLOGRAFT			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**25.92**	5.3	25	**26.89**	5.9	37	0.56
Conditioning	+9.05	6.7	21	+8.14	7.1	36	0.49
First 7 Days	+11.40	8.4	20	+12.39	7.5	31	0.66
Week 2	+7.93	7.2	14	+13.69	10	16	0.08
Week 3	+3.20	7.2	10	+14.88	6.5	8	0.002
Week 4	+2.20	7.5	5	+21.00	-	1	0.08
Isolation ends	+4.50	5.5	18	+12.42	9.8	31	0.003
Discharge	+6.63	3.9	8	+6.85	7.6	20	0.94
Somnolence	+8.25	6.5	8	+8.16	5.7	19	0.44
Rehospitalisation	+4.89	6.6	9	+8.76	6.1	21	0.13
3 Months	+3.82	5.3	11	+7.12	7.5	17	0.22
12 Months	-0.56	6.3	9	+0.11	4.1	9	0.79
Relapse	+5.17	8.9	6	+4.50	5	2	0.93

Table PH:6.4.4

RSCL Physical Symptoms: The mean scores (at each stage) for the two types of Transplant.



PH:6.4.5 Comparison Between The Two Types Of Conditioning

The sample was divided into patients treated with chemotherapy alone and those treated with a combination of chemotherapy + Total Body Irradiation (TBI). The groups were then compared. Results are shown on Table PH:6.4.5.

At 'Baseline" (stage 1) the group to be treated with chemotherapy alone shows a higher level of physical symptoms than the group of patients to be treated with chemotherapy + TBI. The difference between the group is not significant. Significance of F-value=0.2.

At the stage 'Conditioning' (Stage 2) the Chemotherapy group shows a greater increase in symptoms than the group treated with Chemotherapy + TBI. The difference is a not significant, although there is a trend. (Significance of F-value=0.085).

At 'Week 3' (stage 3b) patients in the Chemotherapy group show no increase in physical symptoms from 'Baseline' (stage 1), while the those in the Chemotherapy + TBI group show increases at this stage. The difference between the two groups is significant. (Significance of F-value=0.028).

Compared to 'Baseline' the increase is significant for the Chemotherapy + TBI group (2 tailed p=0.01) but not for the Chemotherapy group (2-tailed p=0.65). (tested on the Non-Parametric Wilcoxon Matched Pairs Test).

At 'Rehospitalization' (stage II) the Chemotherapy + TBI group shows greater increases from baseline than the Chemotherapy group. The difference between the two groups is not significant, although there is a trend. (Significance of F-value=0.079).

At the 'End of Isolation' (stage 4) the increase from Baseline in the number of physical symptoms is significant (2-tailed p=0.001) for the Chemotherapy + TBI group but not for the Chemotherapy group. (2-tailed p=0.29).

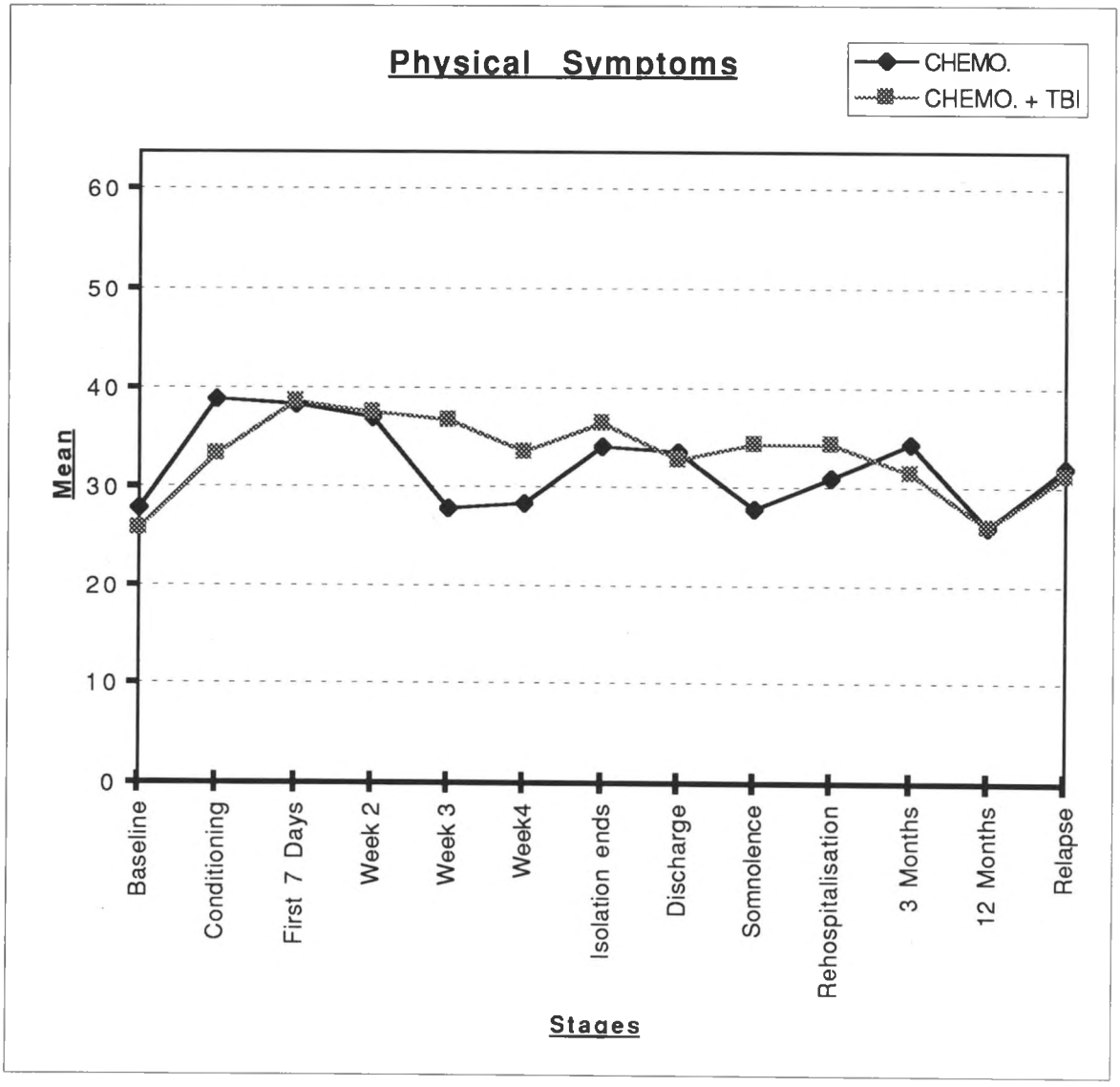
Table PH:6.4.5

RSCL Physical Symptoms: The difference from the baseline of the mean scores (at each stage) for the two Pre-Treatment conditionings.

PHYSICAL	CHEMO.			CHEMO. + TBI			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**28.08**	5.9	13	**25.96**	5.2	45	0.2
Conditioning	+10.88	7.9	17	+7.45	6.2	40	0.09
First 7 Days	+10.15	9.2	13	+12.63	7.3	38	0.33
Week 2	+8.86	6.9	7	+11.65	9.3	23	0.49
Week 3	+/- 0.00	5	4	+10.79	8.4	14	0.03
Week 4	+0.50	3.5	2	+7.75	12	4	0.47
Isolation ends	+6.08	6.8	12	+10.62	9.7	37	0.14
Discharge	+5.60	6.4	5	+7.04	6.8	23	0.67
Somnolence	-	-	-	+8.38	5.8	26	-
Rehospitalisation	+3.00	5.6	5	+8.52	6.3	25	0.08
3 Months	+6.50	5.5	4	+5.71	7.1	24	0.83
12 Months	-2.00	8.9	3	+0.13	4.5	15	0.53
Relapse	+4.00	8.5	2	+5.33	8.3	6	0.85

Figure PH:6.4.5

RSCL Physical Symptoms: The mean scores (at each stage) for the two Pre-Treatment conditionings.



6.5 MENTAL ADJUSTMENT TO CANCER SCALE (MAC)

6.5 Results Of The Mac Scale

The results of the MAC Scale are presented in the following order:

FS:6.5	Fighting Spirit Subscale
H:6.5	Helplessness Subscale
AP:6.5	Anxious Preoccupation Subscale
F :6.5	Fatalism Subscale

For each subscale, results are given in the following order:

6.5.1	(i)	Results for the whole sample
6.5.2	(ii)	Comparison between Males and Females
6.5.3	(iii)	Comparison between the two Hospitals
6.5.4	(iv)	Comparison between the two types of Transplants
6.5.5	(v)	Comparison between the two types of Conditioning

FS:6.5 FIGHTING SPIRIT SUBSCALE

The sub-scale's results are given in the following order:

FS:6.5.1	**(i)**	**Results for the whole sample**
FS:6.5.2	**(ii)**	**Comparison between Males and Females**
FS:6.5.3	**(iii)**	**Comparison between the two Hospitals**
FS:6.5.4	**(iv)**	**Comparison between the two types of Transplants**
FS:6.5.5	**(v)**	**Comparison between the two types of Conditioning**

Results of the MAC sub-scale Fighting Spirit are shown on Table FS:6.5.1.

The Table FS:6.5.1 shows mean scores of Fighting Spirit at Baseline and differences from baseline for entire sample at all stages. It shows the number of patients for whom data are available and statistical significance of the comparison of the difference from baseline of increases (+) and decreases (-) to baseline mean.

Table FS:6.5.1

MAC-Fighting Spirit: The difference from the baseline of the mean scores (for entire sample) at stages 1,2, 3, 4, 7, 8, I and II

Stages Baseline	Differences to baseline mean	S.D.	n	Comparison-2-tailed p *
Stage 1 Baseline	mean 52.31	6.7	72	n.a.
Stage 2 Conditioning	-O.88	5.5	56	0.08
Stage 3 First 7 days	-1.10	6.0	51	1.0
Stage 4 End of isolation	-0.6	6.3	49	0.62
Assessment I Discharge	+0.25	6.4	28	0.1
Assessment II Rehospitalization	-1.03	5.1	29	0.11
Stage 6 3 months	-0.31	7.4	29	0.69
Stage 7 12 months	+2.61	5.0	18	0.91

*p=values are based on the statistical analysis of the differences to baseline on the Non-Parametric Wilcoxon Matched-Pairs Test.

FS:6.5.1 Comparison From Baseline

At 'Baseline' (stage 1) Fighting Spirit scores (mean=52.31) are higher than those of the Normative sample of a mixed cancer group (mean=51.7) reported by Watson et al. (1989). The level of Fighting Spirit decreases from 'Baseline' (stage 1) at all stages except stages 'Discharge' (stage I) and 'Twelve Months' (stage 7). The decreases do not reach the level of statistical significance.

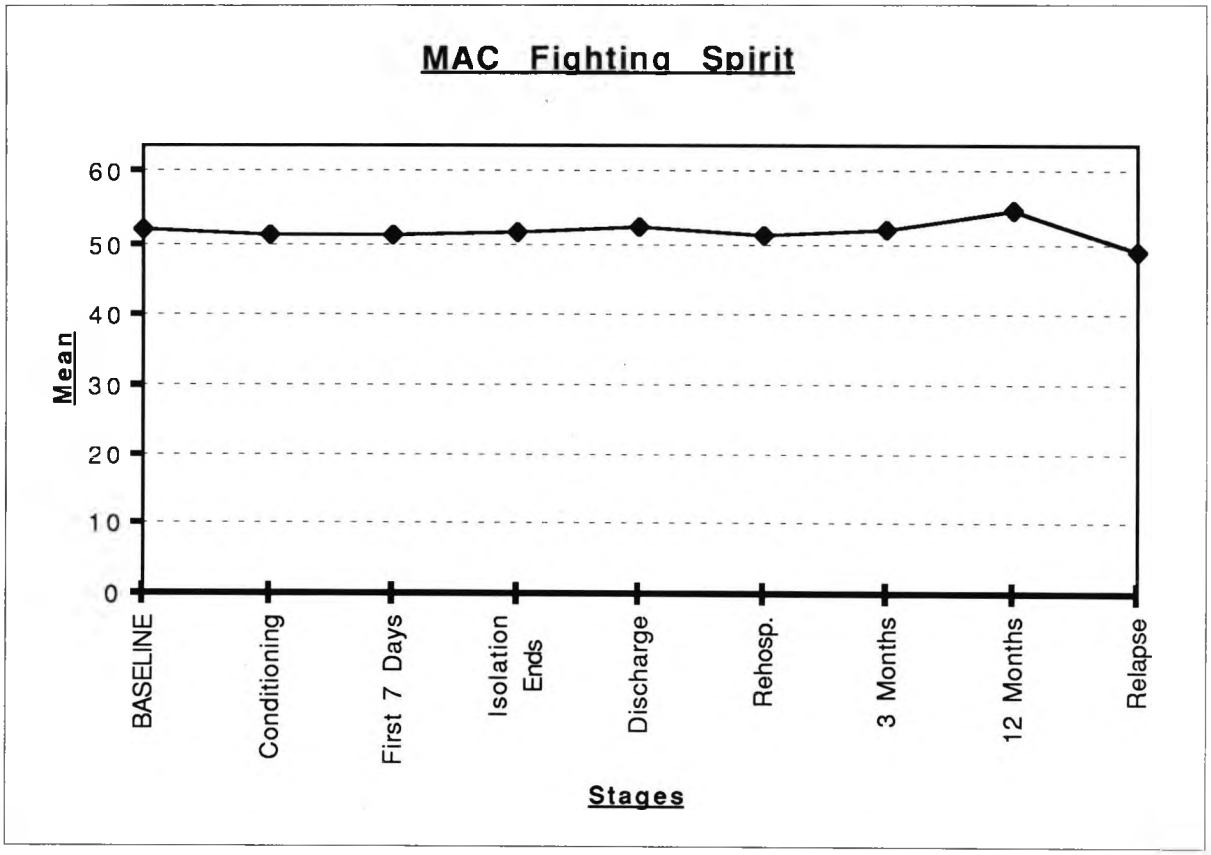
From these data it appears that Fighting Spirit decreases throughout transplant, but shows an increase at the time of Discharge (stage I) and at 'Twelve Months' (stage 7).

For the subscale Fighting Spirit data do not confirm Hypothesis number three which says:

"The patient's attitude towards cancer does not remain constant during treatment. It is influenced by changes in the treatment during the different stages."

Figure FS:6.5.1

MAC-Fighting Spirit: The mean scores (for entire sample) at stages ,2, 3, 4, 7, 8, I, II and III.



FS:6.5.2 Comparison Between Males And Females

The sample was divided into Males and Females and compared. Results are shown on Table FS:6.5.2.

There are no significant differences between the two genders any stage evaluated.

'Baseline' (stage 1), however, Females (mean=53.07) show higher scores than Males (mean=51.82). The difference is not significant, Significance of F value = 0.61, but the findings are in contrast to those reported by Watson et al. (1989). Their data show a higher Fighting Spirit score for males (mean = 52.2) than females (mean = 51.6).

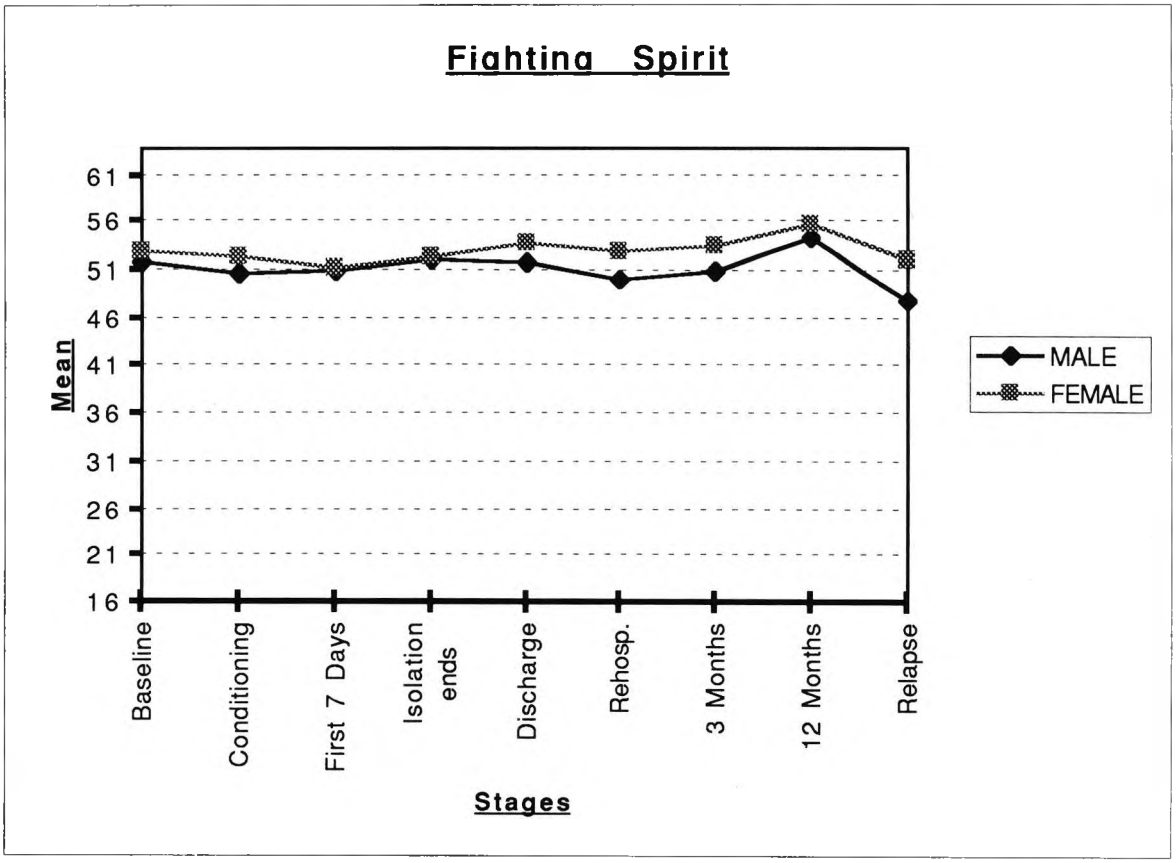
Table FS:6.5.2

MAC-Fighting Spirit: The difference from the baseline of the mean scores for Males and Females at stages 1, 2, 3, 4, 7, 8, II and III.

Fighting Spirit	MALE			FEMALE			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**51.82**	7.1	44	**53.07**	5.2	28	0.61
Conditioning	-1.09	5.8	35	-0.52	5.1	21	0.71
First 7 Days	-0.79	6.2	33	-1.67	4	18	0.69
Isolation ends	+0.19	6.5	32	-0.53	5.9	17	0.76
Discharge	+0.05	7.6	19	+0.67	2.1	9	0.82
Rehospitalisation	-1.53	5.6	19	-0.10	3.9	10	0.48
3 Months	-0.74	7.8	19	+0.50	6.7	10	0.67
12 Months	+2.58	5.3	12	+2.67	4.7	6	0.98
Relapse	-4.00	3.7	6	-1.00	5.7	2	0.41

Figure FS:6.5.2

MAC-Fighting Spirit: The mean scores for Male and Female patients at stages 1, 2, 3, 4, 7, 8, I, II and III.



FS:6.5.3 Comparison between patients at the two Hospitals

The sample was divided into patients treated at the Royal Marsden Hospital and the Royal Free Hospital and compared. Results are shown on Table FS:6.5.3.

There are no significant differences between the two hospitals at 'Baseline' (stage 1). (Significance of F value = 0.85).

At 'Twelve Months' (stage 7) patients in the Royal Free Hospital show a greater increase in Fighting Spirit than patients at the Royal Marsden Hospital. The difference is not significant although there is a trend. (Significance of F value = 0.095).

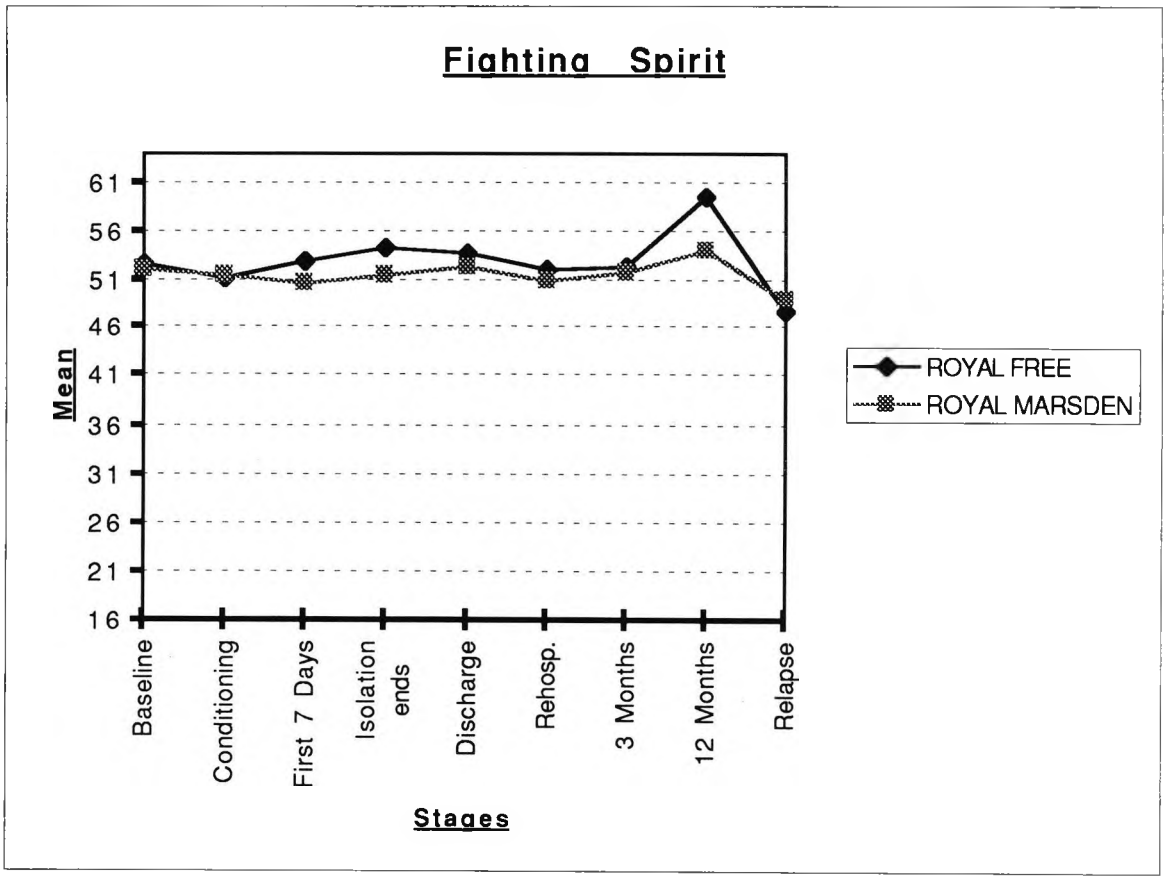
Table FS:6.5.3

MAC-Fighting Spirit: The difference from the baseline of the mean scores for the two Hospitals at stages 1, 2, 3, 4, 7, 8, I, II and III.

Fighting Spirit	ROYAL FREE			ROYAL MARSDEN			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**52.64**	7.5	14	**52.22**	6.5	58	0.85
Conditioning	-1.31	3.4	13	-0.74	6	43	0.75
First 7 Days	+0.36	4.7	11	-1.50	6.2	40	0.32
Isolation ends	+1.70	4.3	10	-0.51	6.6	39	0.3
Discharge	+1.25	4.5	4	+0.08	6.7	24	0.74
Rehospitalisation	-0.60	5.5	5	-1.13	5.1	24	0.84
3 Months	-0.17	3.9	6	-0.35	8.1	23	0.96
12 Months	+7.00	2.6	3	+1.73	4.9	15	0.09
Relapse	-5.00	-	1	-3.00	4.3	7	0.68

Figure FS:6.5.3

MAC-Fighting Spirit: The difference from the baseline of the mean scores for the two Hospitals at stages 1, 2, 3, 4, 7, 8, I, II and III.



FS:6.5.4 Comparison between the two types of transplant

The sample was divided into patients treated with Allogeneic Transplant alone and those treated with Autologous Transplant. The groups were then compared. Results are shown on Table FS:6.5.3.

There are no significant differences between the two treatment groups at 'Baseline' (stage 1). (Significance of F value = 0.38).

At 'First 7 Days' (stage 3) the Autograft group shows an increase in Fighting Spirit while the Allograft group shows a decrease. The difference between the two groups is significant. (Significance of F value = 0.05).

At 'End of Isolation' (stage 4) the Autograft group shows an increase in Fighting Spirit while the Allograft group shows a decrease. The difference is not significant, although there is a trend. (Significance of F value = 0.07).

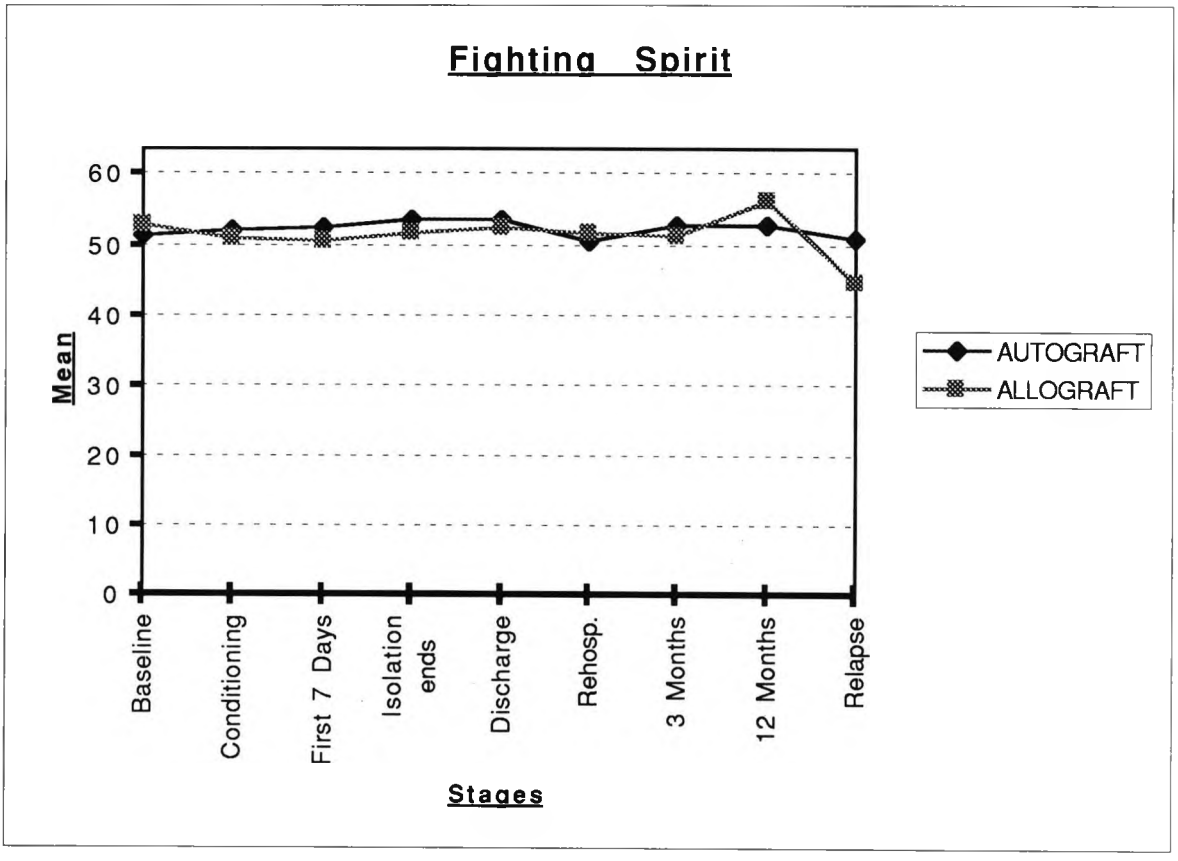
Table FS:6.5.4

MAC-Fighting Spirit: The difference from the baseline of the mean scores for the two types of Transplant at stages 1, 2, 3, 4, 7, 8, I, II and III.

Fighting Spirit	AUTOGRAFT			ALLOGRAFT			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**51.54**	6.9	28	**52.8**	6.5	44	0.38
Conditioning	+0.70	5.1	20	-1.75	5.6	36	0.11
First 7 Days	+0.80	6.4	20	-2.32	5.4	31	0.05
Isolation ends	+1.94	6.9	18	-1.23	5.6	31	0.07
Discharge	+2.00	10.3	8	-0.45	4	20	0.37
Rehospitalisation	-0.89	2.9	9	-1.10	5.9	20	0.92
3 Months	+1.33	8.7	12	-1.47	6.3	17	0.32
12 Months	+1.25	3.2	8	+3.70	6	10	0.31
Relapse	-0.67	3.1	6	-8.00	2.8	2	0.04

Figure FS:6.5.4

MAC-Fighting Spirit: The mean scores for the two types of Transplant at stages 1, 2, 3, 4, 7, 8, I, II and III.



FS:6.5.5 Comparison Between The Two Types Of Conditioning

The sample was divided into patients treated with Chemotherapy alone and those treated with a combination of Chemotherapy + Total Body Irradiation (TBI). The groups were then compared. Results are shown on Table FS:6.5.3.

There are no significant differences between the two treatment groups at 'Baseline' (stage 1). (Significance of F value = 0.73).

At 'Rehospitalisation' (stage II) the Chemotherapy group shows an increase in Fighting Spirit while the Chemotherapy + TBI group shows a decrease. The difference between the two groups is significant. (Significance of F value = 0.016).

Table FS:6.5.5 Comparison Between The Two Types Of Conditioning

MAC-Fighting Spirit: The difference from the baseline of the mean scores for the two Pre-Treatment Conditionings at stages 1, 2, 3, 4, 7, 8, I, II and III.

Fighting Spirit	CHEMO.			CHEMO. + TBI			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	53	5.6	18	52.22	7	50	0.73
Conditioning	+0.94	3.6	16	-1.60	6	40	0.11
First 7 Days	-0.15	4.3	13	-1.42	6.5	38	0.46
Isolation ends	+2.08	4.9	12	-0.76	6.6	37	0.16
Discharge	+2.60	2.1	5	-0.26	6.9	23	0.37
Rehospitalisation	+3.80	4.8	5	-2.04	4.6	24	0.02
3 Months	+1.80	7.1	5	-0.75	7.5	24	0.49
12 Months	+2.50	4.5	4	+2.64	5.3	14	0.96
Relapse	-2.50	3.5	2	-3.50	4.5	6	0.79

H:6.5 HELPLESSNESS/HOPELESSNESS SUBSCALE

H:6.5 Results Of The Helplessness/Hopelessness Subscale

Results are given in the following order:

H:6.5.1	**(i)**	**Results for the whole sample**
H:6.5.2	**(ii)**	**Comparison between Males and Females**
H:6.5.3	**(iii)**	**Comparison between the two Hospitals**
H:6.5.4	**(iv)**	**Comparison between the two types of Transplants**
H:6.5.5	**(v)**	**Comparison between the two types of Conditioning**

Results of the MAC sub-scale Helplessness are shown on Table H:6.5.1 and results of the combined T scores for Fighting Spirit and Helplessness/Hopelessness are shown on Table FSH-T:6.5.1 and Figure FSH-T:6.5.1.

The Table H:6.5.1 shows mean scores of Helplessness at Baseline and differences from baseline for entire sample at all stages. It shows the number of patients for whom data are available and statistical significance of the comparison of the difference from baseline of increases (+) and decreases (-) to baseline mean.

Figure H:6.5.1 shows mean scores of Helplessness/Hopelessness at stages 1,2, 3, 4, I, II, 6 and 7.

Table H:.5.1

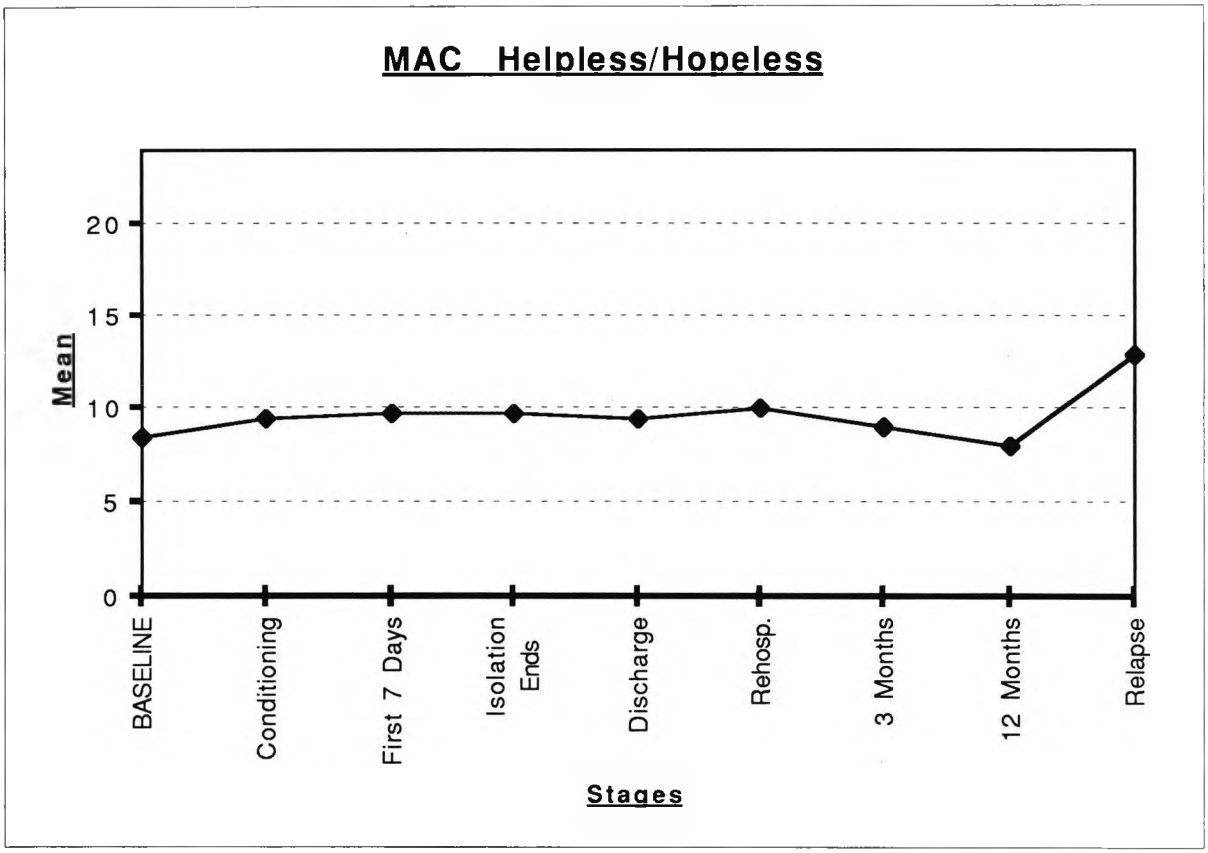
MAC-Helplessness/Hopelessness: The difference from the baseline of the mean scores (for entire sample) at stages 1, 3, 4, I, II, 6 and 7.

Stages Baseline	Differences from baseline mean	S.D.	n	Comparison-2-tailed p *
Stage 1 Baseline	mean 8.54	2.3	71	n.a.
Stage 2 Conditioning	+0.90	2.2	58	0.02
Stage 3 First 7 days	+1.26	2.2	50	0.69
Stage 4 End of isolation	+1.25	2.8	48	0.56
Assessment I Discharge	+0.96	2.3	28	0.05
Assessment II Rehospitalization	+1.48	2.7	29	0.11
Stage 6 3 months	+0.45	3.0	29	0.22
Stage 7 12 months	-O.47	2.4	19	0.71

*p=values are based on the statistical analysis of the differences to baseline on the Non-Parametric Wilcoxon Matched-Pairs Test.

Figure H:6.5.1

MAC-Helplessness/Hopelessness: The mean scores (for entire sample) at stages 1,2, 3, 4, I, II, 6 and 7.



H:6.5.1 Comparison From Baseline

At 'Baseline' (stage 1) Helplessness mean scores (mean=8.54) are similar to those of the Normative sample of a mixed cancer group (mean=8.6) reported by Watson et al. (1989). The level of Helplessness increases from 'Baseline' (stage 1) with the exception of stage 'Twelve Months' (stage 7) when Helplessness shows a small, non significant decrease from 'Baseline" (stage 1). (See Table H:6.5.1)

At stages 'Conditioning' (stage 2) and 'Discharge' (stage I) increases from 'Baseline' (stage 1) are significant. (Stage 2 :2-tailed p=0.02; stage I: 2-tailed p=0.05).

From these data it appears that Helplessness/Hopelessness increases throughout the transplant procedure and shows decreases at one year post-transplant.

These data confirm Hypothesis number three which says:

"The patient's attitude towards cancer does not remain constant during treatment. It is influenced by changes in the treatment during the different stages."

Table FSH-T:6.5.2

Mean T-Scores for FSH (for the entire sample) at stages 1, 2, 3, 4, 7, 8, I and II.

Stages	Mean Scores	SD	n	2-tailed p
Stage 1 Baseline	49.67	10.9	42	n.a.
Stage 2 Conditioning	52.58	9.5	52	0.02
Stage 3 First 7 days	52.00	10.5	10	0.11
Stage 4 End of Isolation	50.27	11.7	11	0.5
Assessment I Discharge	54.45	11.4	22	0.06
Assessment II Rehospitalization	65.33	11.0	3	not enough cases
Stage 6 3 months	48.25	10.2	16	0.79
Stage 7 12 months	52.50	10.7	19	0.33

*p=values are based on the statistical analysis of the differences from baseline on the Wilcoxon.

FSH-T:6.5.2 Comparison from Baseline

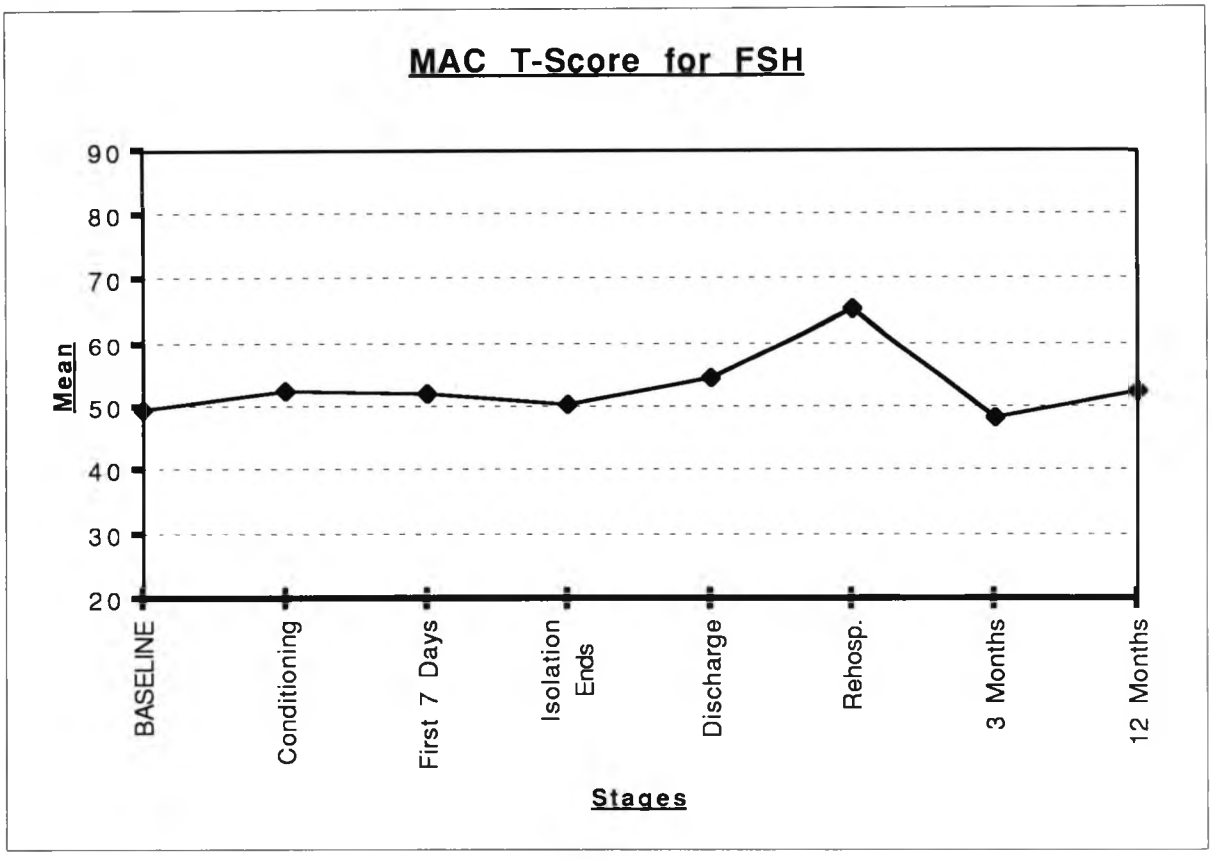
At 'Baseline' (stage 1) the combined T-scores for Fighting Spirit and Helplessness (FSH) are below the cut-off point (50 and above) qualifying as 'cases'. From 'Baseline' (stage 1) to 'Conditioning' (stage 2) there is a significant increase (2-tailed p=0.02) in the level of T scores and the mean for FSH is above the cut-off point. The mean remains elevated above the cut-off point until Three Months (stage 6), but raises again above at 'Twelve Months' (stage 7).

At 'Discharge' (stage I) the increase from baseline shows a trend (p=0.06) but the increase is not significant.

Tested on the Non-Parametric Wilcoxon Matched-Pairs Test.

Figure FSH-T:6.5.2

Mean T-Scores for FSH (for the entire sample) at stages 1, 2, 3, 4, 7, 8, I and II.



H:6.5.2 Comparison between Males and Females

The sample was divided into Males and Females and compared. Results are shown on Table H:6.5.2.

There are no significant differences between the two genders at Baseline (Significance of F value = 0.91) or at any of the later stages.

Table H:6.5.2

MAC-Helplessness/Hopelessness: The difference from the baseline of the mean scores Males and Females at stages: 1, 2, 3, 4, 7, 8, I, II and III.

HELPLESSNESS	MALE			FEMALE			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**8.51**	2.3	43	**8.57**	2.4	28	0.91
Conditioning	+1.03	2.4	36	+0.68	1.9	22	0.6
First 7 Days	+1.38	2.6	32	+1.06	1.4	18	0.63
Isolation ends	+1.10	2.4	31	+1.53	3.4	17	0.61
Discharge	+0.84	2.5	19	+1.22	1.7	9	0.69
Rehospitalisation	+1.63	2.6	19	+1.20	3.1	10	0.69
3 Months	+0.21	2.9	19	+0.90	3.2	10	0.56
12 Months	-0.92	2.4	13	+0.50	2.1	6	0.23
Relapse	+4.83	3.3	6	+3.00	1.4	2	0.49

Figure H:6.5.2

MAC-Helplessness/Hopelessness: The mean scores for Males and Females at stages: 1, 2, 3, 4, 7, 8, I, II and III.

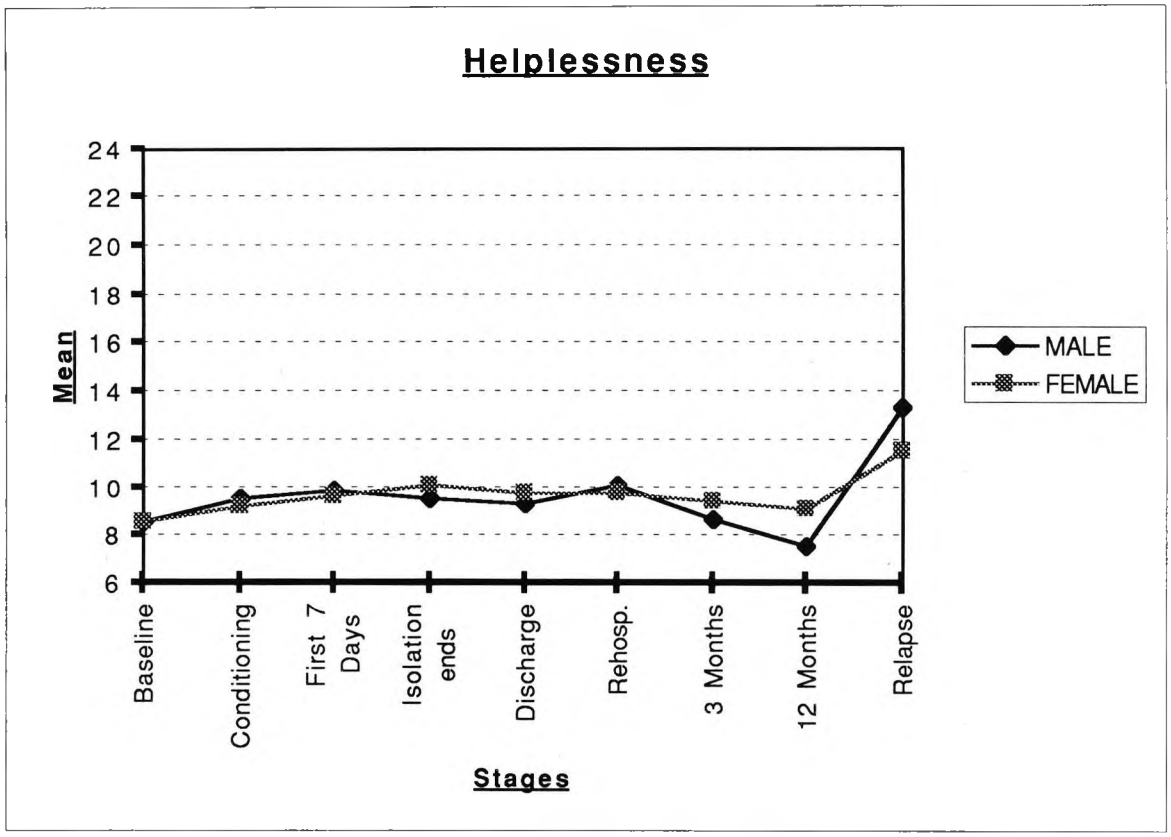


Table FSH-T:6.5.2

Mean T-Scores for FSH for Males and Females at stages: 1, 2, 3, 4, 7, 8, I and II.

Mean T-Scores for FSH (MAC)						
	MALE			FEMALE		
STAGES	Mean	S.D.	n	Mean	S.D.	n
Baseline	48.33	10.11	24	51.44	11.85	18
Conditioning	52.45	8.98	33	52.79	10.58	19
First 7 Days	48.25	7.52	8	67.00	5.66	2
Isolation ends	45.86	9.51	4	58.00	12.30	4
Discharge	48.91	8.80	11	46.80	13.77	5
Rehospitalisation	51.82	9.60	13	53.57	13.23	7
3 Months	54.00	9.73	14	55.25	14.63	8
12 Months	65.33	11.02	3	-	-	-

H:6.5.3 Comparison Between Patients At The Two Hospitals

The sample was divided into patients treated at the Royal Marsden Hospital and those at the Royal Free Hospital and compared. Results are shown on Table H:6.5.3.

There are no significant differences between the two hospitals at 'Baseline' (stage 1). (Significance of F value = 0.38).

At 'Conditioning' (stage 2) patients in the Royal Free show a decrease in Helplessness while those in the Royal Marsden Hospital show an increase. The difference between the two groups is significant. (Significance of F value = 0.01).

Compared to 'Baseline' (stage 1) the increase at 'Conditioning' (stage 2) is significant for the Royal Marsden group (2-tailed p=0.01) but the decrease is not significant for the Royal Free Hospital group. (2-tailed p=0.87).

At 'First 7 Days' (stage 3) patients in the Royal Free show a smaller increase in Helplessness than those in the Royal Marsden Hospital. The difference between the two groups is significant. (Significance of F value = 0.05).

Table H:6.5.3

MAC-Helplessness/Hopelessness: The difference from the baseline of the mean scores for the two Hospitals at stages 1, 2, 3, 4, 7, 8, I, II and III.

HELPLESSNESS	ROYAL FREE			ROYAL MARSDEN			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**9.07**	2.6	14	**8.4**	2.3	57	0.38
Conditioning	-0.38	2.1	13	+1.27	2.1	45	0.01
First 7 Days	+0.09	2.4	11	+1.59	2.1	39	0.05
Isolation ends	+0.50	1.4	10	+1.45	3	38	0.34
Discharge	+0.25	1.5	4	+1.08	2.4	24	0.51
Rehospitalisation	+2.60	1.8	5	+1.25	2.9	24	0.32
3 Months	+0.50	0.19	6	+0.43	3.2	23	0.96
12 Months	+1.00	2.6	3	-0.75	2.3	16	0.25
Relapse	+5.00	3.8	1	+4.29	3.2	7	0.84

Figure H:6.5.3

MAC-Helplessness/Hopelessness: The mean scores for the two Hospitals at stages: 1,2, 3, 4, 7, 8, I, II and III.

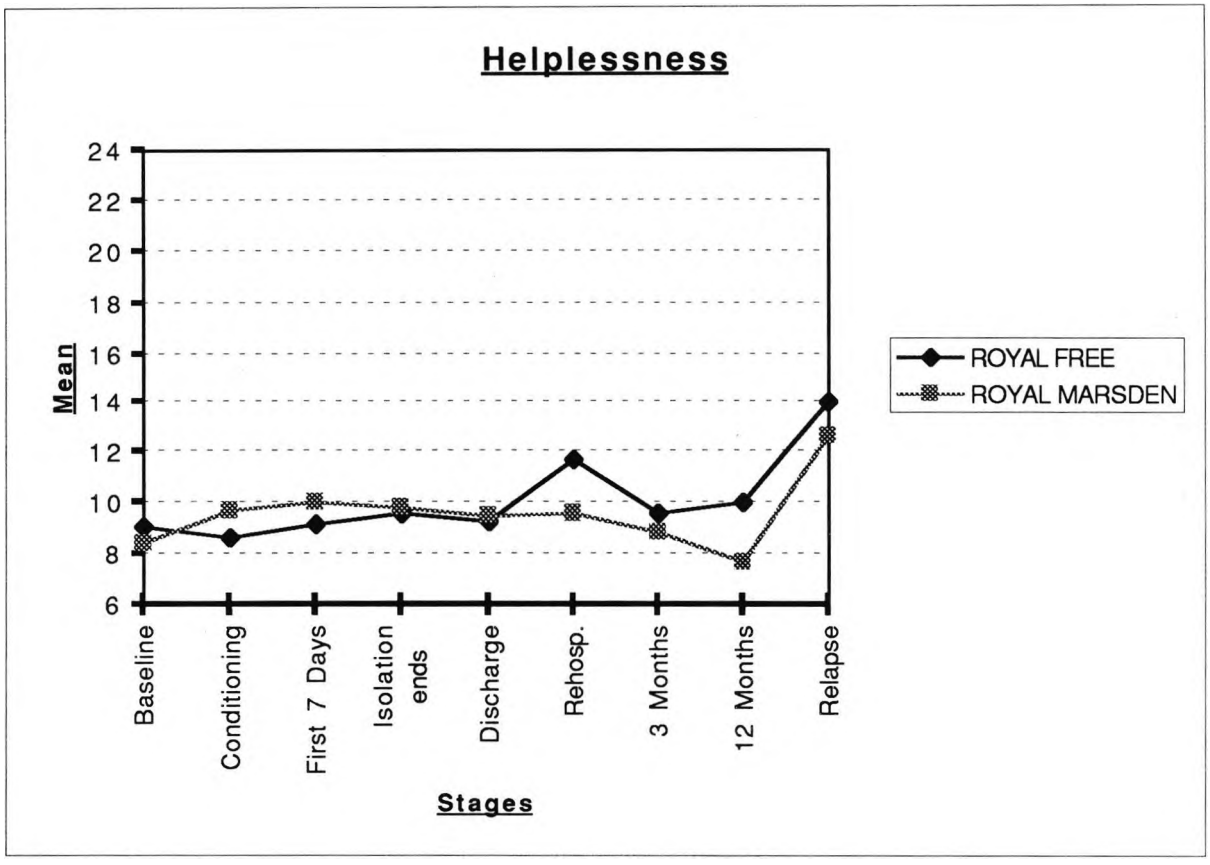


Table FSH-T:6.5.3.a

Mean T-Scores for FSH for the two Hospitals at stages: 1, 2,3,4,7,8,I and II.

	ROYAL FREE			ROYAL MARSDEN		
STAGES	Mean	S.D.	n	Mean	S.D.	n
Baseline	49.43	12.88	7	49.71	10.63	35
Conditioning	49.45	11.99	11	53.41	8.69	41
First 7 Days	51.00	0.00	1	52.11	11.12	9
Isolation ends	44.00	0.00	1	50.90	12.15	10
Discharge	48.33	17.90	3	48.23	8.70	13
Rehospitalisation	57.25	11.67	4	51.31	10.48	16
3 Months	63.80	10.38	5	51.71	10.43	17
12 Months	60.00	0.00	1	68.00	14.14	2

H:6.5.4 Comparison Between The Two Types Of Transplant

The sample was divided into patients treated with Allogeneic Transplant and those treated with Autologous Transplant. The groups were then compared. Results are shown on Table H:6.5.3.

There are no significant differences between the two treatment groups at 'Baseline' (stage 1). (Significance of F value = 0.51).

At 'Conditioning' (stage 2) the Allograft group shows a greater increase in Helplessness than the Autograft group. The difference between the two groups is significant. (Significance of F value = 0.05).

Table H:6.5.4

MAC-Helplessness/Hopelessness: The difference from the baseline of the mean scores for the two types of Transplant at stages: 1, 2, 3, 4, 7, 8, I, II and III.

HELPLESSNESS	AUTOGRAFT			ALLOGRAFT			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**8.29**	2.2	28	**8.7**	2.4	43	0.51
Conditioning	+0.14	2.1	21	+1.32	2.2	37	0.05
First 7 Days	+0.70	2.4	20	+1.63	2.1	30	0.15
Isolation ends	+0.44	1.5	18	+1.73	3.2	30	0.12
Discharge	+1.25	1.9	8	+0.85	2.4	20	0.68
Rehospitalisation	+1.78	1.9	9	+1.35	3.1	20	0.7
3 Months	+1.25	2.3	12	-0.12	3.3	17	0.23
12 Months	+/- 0.00	1.7	9	-0.90	2.9	10	0.45
Relapse	+3.17	1.3	6	+8.00	4.2	2	0.03

Figure H:6.5.4

MAC-Helplessness/Hopelessness: The mean scores for the two types of Transplant at stages: 1, 2, 3, 4, 7, 8, I, II and III.

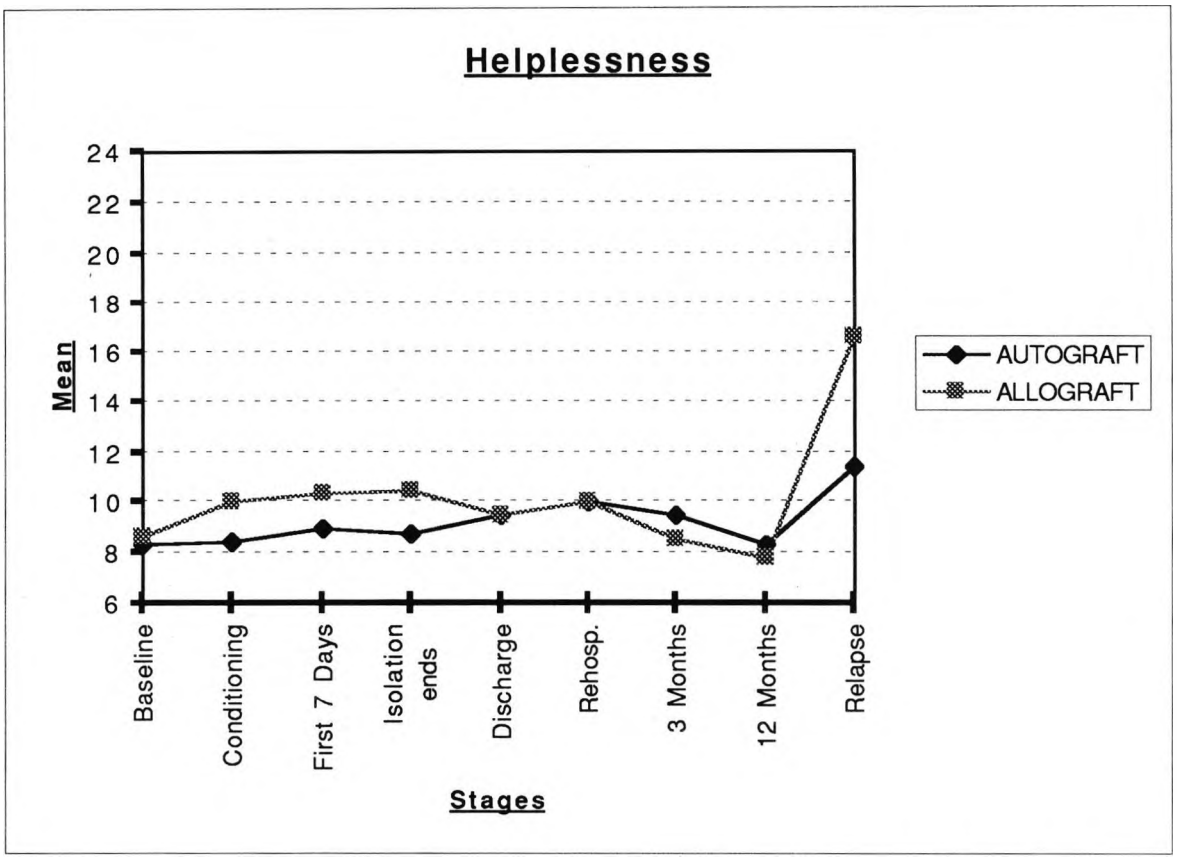


Table FSH-T:6.5.4.a

Mean T-Scores for FSH for the two types of Transplant at stages: 1, 2 ,3, 4, 7, 8, I and II.

Mean T-Scores for FSH (MAC)						
	AUTOGRAFT			ALLOGRAFT		
STAGES	Mean	S.D.	n	Mean	S.D.	n
Baseline	48.41	8.82	17	50.52	12.16	25
Conditioning	50.86	9.33	21	53.74	9.57	31
First 7 Days	52.75	7.85	4	51.50	12.66	6
Isolation ends	54.43	10.18	7	43.00	11.80	4
Discharge	48.13	10.86	8	48.38	10.17	8
Rehospitalisation	56.50	6.46	4	51.50	11.44	16
3 Months	54.00	5.48	4	54.56	12.47	18
12 Months	59.00	1.41	2	78.00	0.00	1

H:6.5.5 Comparison Between The Two Types Of Conditioning

The sample was divided into patients treated with Chemotherapy alone and those treated with a combination of Chemotherapy + Total Body Irradiation (TBI). The groups were then compared. Results are shown on Table H:6.5.5.

There are no significant differences between the two treatment groups at 'Baseline' (stage 1). (Significance of F value = 0.75).

Compared to 'Baseline' (stage 1) at 'Rehospitalization' (stage II) the Chemotherapy + TBI group shows a significant increase (2-tailed p=0.02) while the Chemotherapy group does not. (2-tailed p=0.56).

Table H:6.5.5

MAC-Helplessness/Hopelessness: The difference from the baseline of the mean scores for the two Pre-Treatment Conditionings at stages: 1, 2, 3, 4, 7, 8, I, II and III.

HELPLESSNESS	CHEMO.			CHEMO. + TBI			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**8.44**	2.5	18	**8.57**	2.3	49	0.75
Conditioning	+0.35	1.8	17	+1.12	2.3	41	0.25
First 7 Days	+0.38	2.4	13	+1.57	2.1	37	0.1
Isolation ends	+0.17	2.3	12	+1.61	2.8	36	0.12
Discharge	+0.60	1.3	5	+1.04	2.4	23	0.7
Rehospitalisation	+0.60	3.5	5	+1.67	2.6	24	0.44
3 Months	+1.40	4.7	5	+0.25	2.6	24	0.44
12 Months	-0.25	3.7	4	-0.53	2.1	15	0.82
Relapse	+4.00	0	2	+4.50	3.5	6	0.86

Figure H:6.5.5

MAC-Helplessness/Hopelessness: The mean scores for the two Pre-Treatment Conditionings at stages: 1, 2, 3, 4, 7, 8, I, II and III.

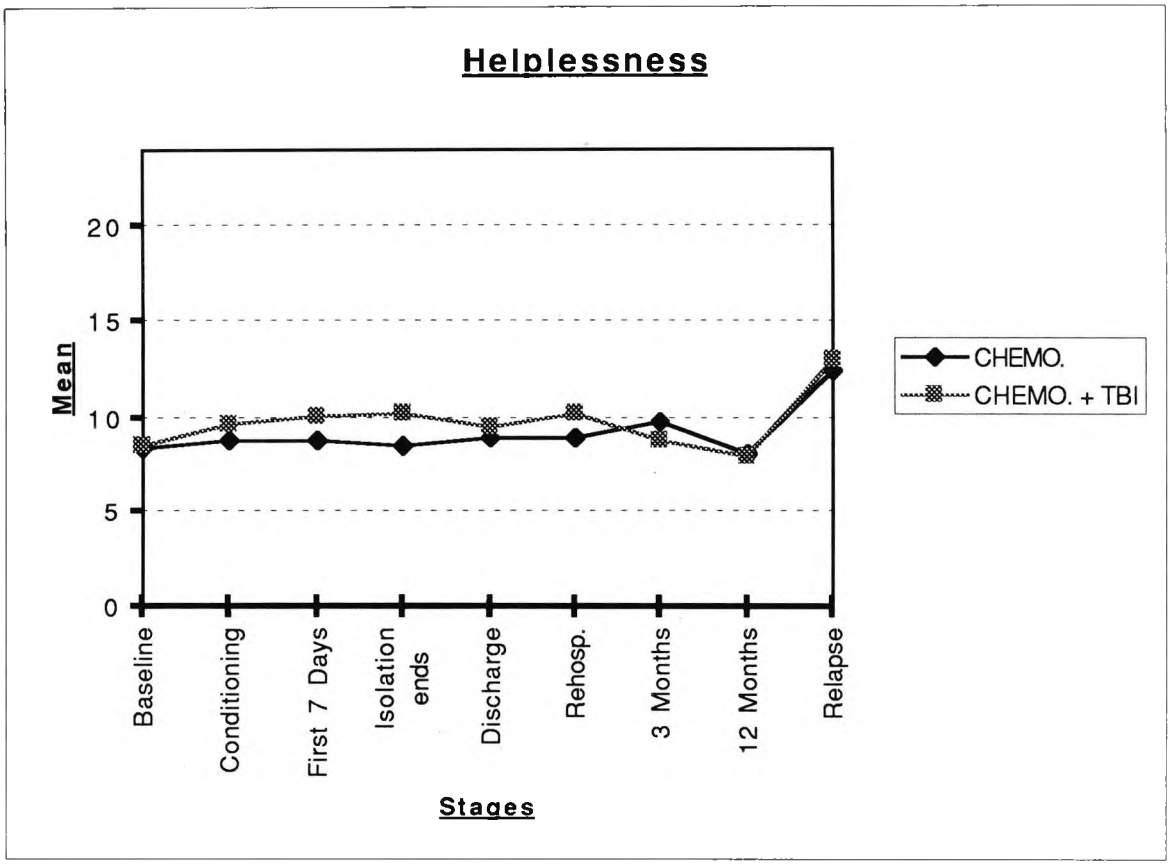


Table FSH-T:6.5.5.a

Mean T-Scores for FSH for the two types of Conditioning at stages: 1, 2, 3, 4, 7, 8, I and II.

Mean T-Scores for FSH (MAC)						
	CHEMO.			CHEMO. + TBI		
STAGES	Mean	S.D.	n	Mean	S.D.	n
Baseline	46.93	9.90	15	51.19	11.26	27
Conditioning	51.46	9.51	13	52.95	9.58	39
First 7 Days	52.00	10.54	3	52.00	11.31	7
Isolation ends	55.00	12.12	3	48.50	11.87	8
Discharge	42.50	9.54	4	50.17	10.00	12
Rehospitalisation	34.67	8.08	3	55.65	7.57	17
3 Months	37.25	1.50	4	58.28	8.68	18
12 Months	-	-	-	65.33	11.02	3

AP:6.5 ANXIOUS PREOCCUPATION SUBSCALE

The sub-scale's results are given in the following order:

AP:6.5.1	**(i)**	**Results for the whole sample**
AP:6.5.2	**(ii)**	**Comparison between Males and Females**
AP:6.5.3	**(iii)**	**Comparison between the two Hospitals**
AP:6.5.4	**(iv)**	**Comparison between the two types of Transplants**
AP:6.5.5	**(v)**	**Comparison between the two types of Conditioning**

Results of the MAC sub-scale Anxious Preoccupation are shown on Table AP:6.5.1.

The Table AP:6.5.1 shows mean scores of Anxious Preoccupation at Baseline and differences from baseline for entire sample at all stages. It shows the number of patients for whom data are available and statistical significance of the comparison of the difference from baseline of increases (+) and decreases (-) to baseline mean.

Figure AP:6.5.1 shows mean scores of Anxious Preoccupation at stages: 1, 2, 3, 4, I, II, 6 and 7.

Table AP:6.5.1

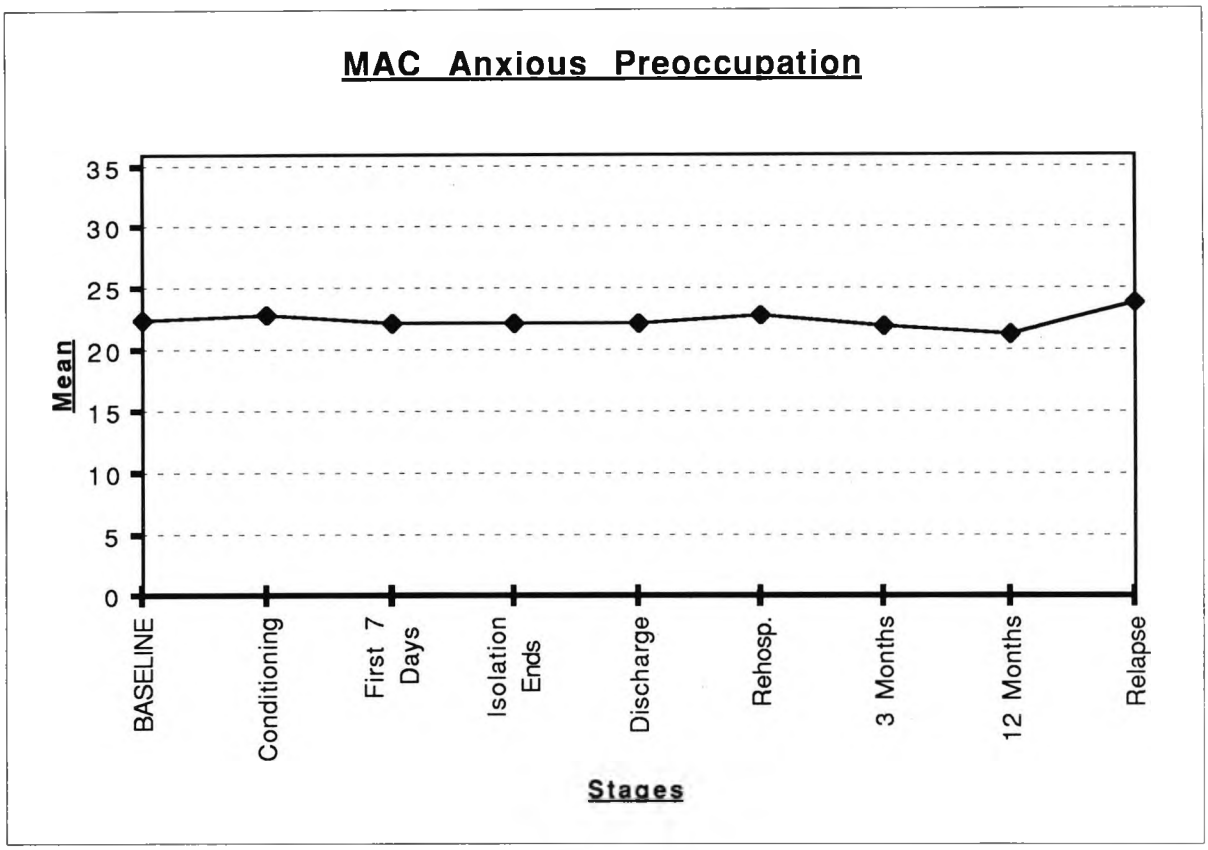
MAC-Anxious Preoccupation: The difference from the baseline of the mean scores (for the entire sample) at stages: 1, 2, 3, 4, 7, 8, I, II and III.

Stages Baseline	Differences from baseline mean	SD	Comparison- n	2-tailed p *
Stage 1 Baseline	mean 22.44	4.0	71	n.a.
Stage 2 Conditioning	+0.42	3.3	57	0.4
Stage 3 First 7 days	-0.28	2.7	50	0.12
Stage 4 End of isolation	-0.23	3.1	48	0.44
Assessment I Discharge	-0.32	3.2	28	0.82
Assessment II Rehospitalization	+0.38	2.9	29	0.11
Stage 6 3 months	-0.52	3.0	29	0.84
Stage 7 12 months	-1.42	2.6	19	0.79

*p=values are based on the statistical analysis of the differences to baseline on the Wilcoxon ...

Figure AP:6.5.1

Mean scores of Anxious Preoccupation for (the entire sample) at stages:1, 2, 3, 4, I, II, 6 and7.



AP:6.5.1 Comparison From Baseline

At 'Baseline' (stage 1) Anxious Preoccupation mean scores (mean=22.44) are higher than the mean of a normative sample of a mixed cancer group (mean = 20.6) reported by Watson et al. (1989). The level of Anxious Preoccupation shows an increase at 'Conditioning' (stage 2) and decreases thereafter with the exception of stage 'Rehospitalization' (stage II). The changes from 'Baseline' do not reach the level of statistical significance. (See Table AP:6.5.1).

For Anxious Preoccupation data do not confirm Hypothesis number three which says:

"The patient's attitude towards cancer does not remain constant during treatment. It is influenced by changes in the treatment during the dfferent stages."

Table AP-T:6.5.1

Mean T-Scores for Anxious Preoccupation (for the entire sample) at stages 2, 3, 4, 7, 8, I and II.

Stages cases in	Mean	SD	n	2-tailed p
Stage 1 Baseline	54.29	7.3	42	n.a.
Stage 2 Conditioning	52.34	8.1	53	0.67
Stage 3 First 7 days	47.30	11.7	10	0.59
Stage 4 End of Isolation	50.17	15.2	12	0.07
Assessment I Discharge	53.59	7.8	22	0.73
Assessment II Rehospitalization	55.00	10.5	3	0.11
Stage 6 3 months	51.69	7.2	16	0.68
Stage 7 12 months	53.70	8.2	19	0.93

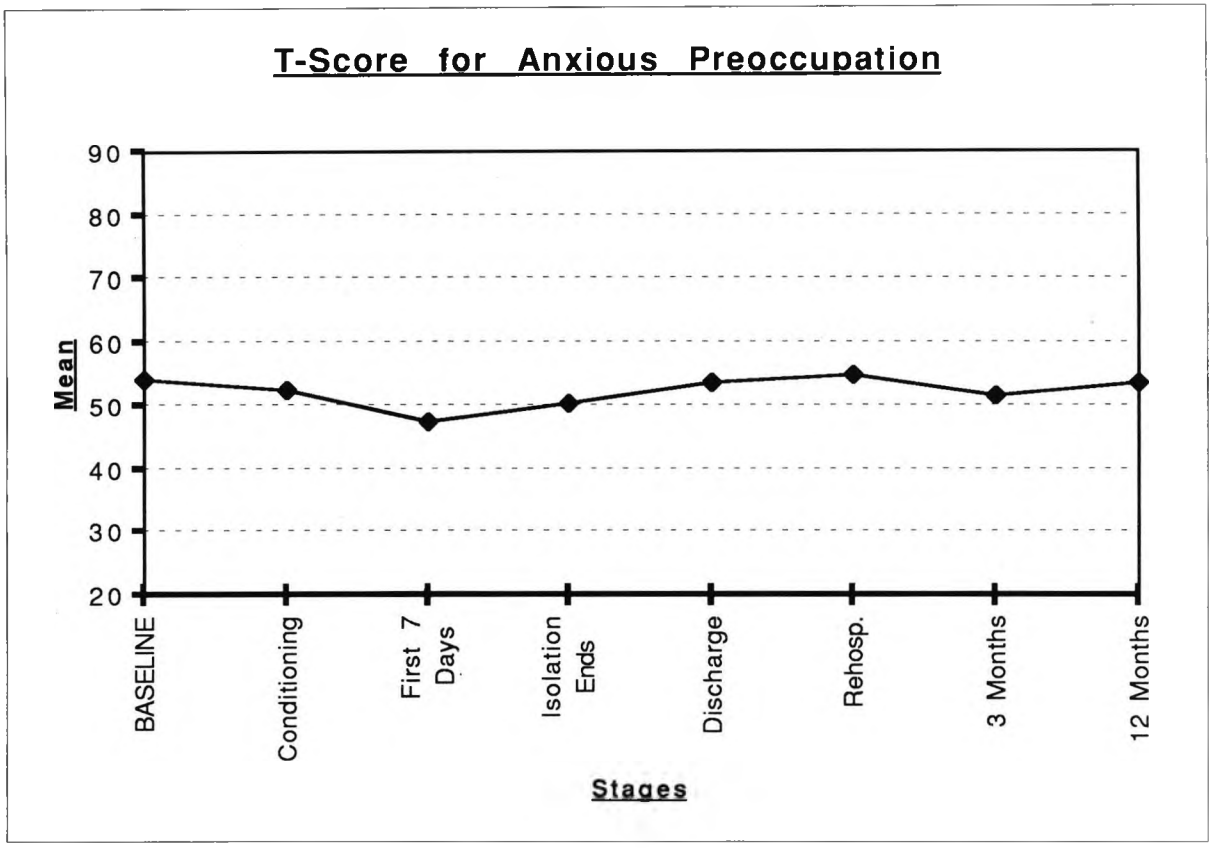
Tested on the Non-Parametric Wilcoxon Matched-Pairs Test.

AP-T:6.5.1 Comparison from Baseline

The mean T-scores for Anxious Preoccupation fall only once below the cut-off point (50) for "caseness". This is at 'First 7 Days' (stage 3). They remain above the cut-off point at all other stages throughout transplant.

Figure AP-T:6.5.2

Mean T-Scores for Anxious Preoccupation (for the entire sample) at stages 1, 2, 3, 4, 7, 8, I and II.



AP:6.5.2 Comparison Between Males And Females

The sample was divided into Males and Females and compared. Results are shown on Table AP:6.5.2.

At 'Baseline' (stage 1) the mean scores for Anxious Preoccupation for Females are higher than those for Males. The difference is significant. (Significance of F value = 0.03). This result corresponds with the result found by Watson et al. 1989 for their normative sample of a mixed cancer group. In this group Females scored significantly higher scores on Anxious Preoccupation than Males. (p=0.002).

At 'Conditioning' (stage 2) Females show a decrease in Anxious Preoccupation while Males show an increase. The difference between the groups is significant. (Significance of F value = 0.03).

At 'Rehospitalization' (stage II) Females show a decrease in Anxious Preoccupation while Males show an increase. The difference is not significant, although there is a trend. (Significance of F value = 0.06).

Table AP:6.5.2

MAC-Anxious Preoccupation: The difference from the baseline of the mean scores Males and Females at stages: 1, 2, 3, 4, 7, 8, I, II and III.

Anxious Preoccupation	MALE			FEMALE			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**21.49**	3.5	43	**23.89**	4.3	28	0.03
Conditioning	+1.17	3.4	36	-0.86	2.6	21	0.03
First 7 Days	-0.47	2.8	32	+0.06	2.6	18	0.52
Isolation ends	+0.26	3	31	-1.12	3.1	17	0.14
Discharge	+0.32	3.2	19	-1.67	2.8	9	0.12
Rehospitalisation	+1.11	2.5	19	-1.00	3.1	10	0.06
3 Months	-0.32	2.8	19	-0.90	3.3	10	0.62
12 Months	+1.00	2.6	13	-2.33	2.5	6	0.26
Relapse	+1.83	1.3	6	some	5.7	2	0.42

Figure AP:6.5.2

MAC-Anxious Preoccupation: The mean scores Males and Females at stages: 1, 2, 3, 4, 7, 8, I, II and III.

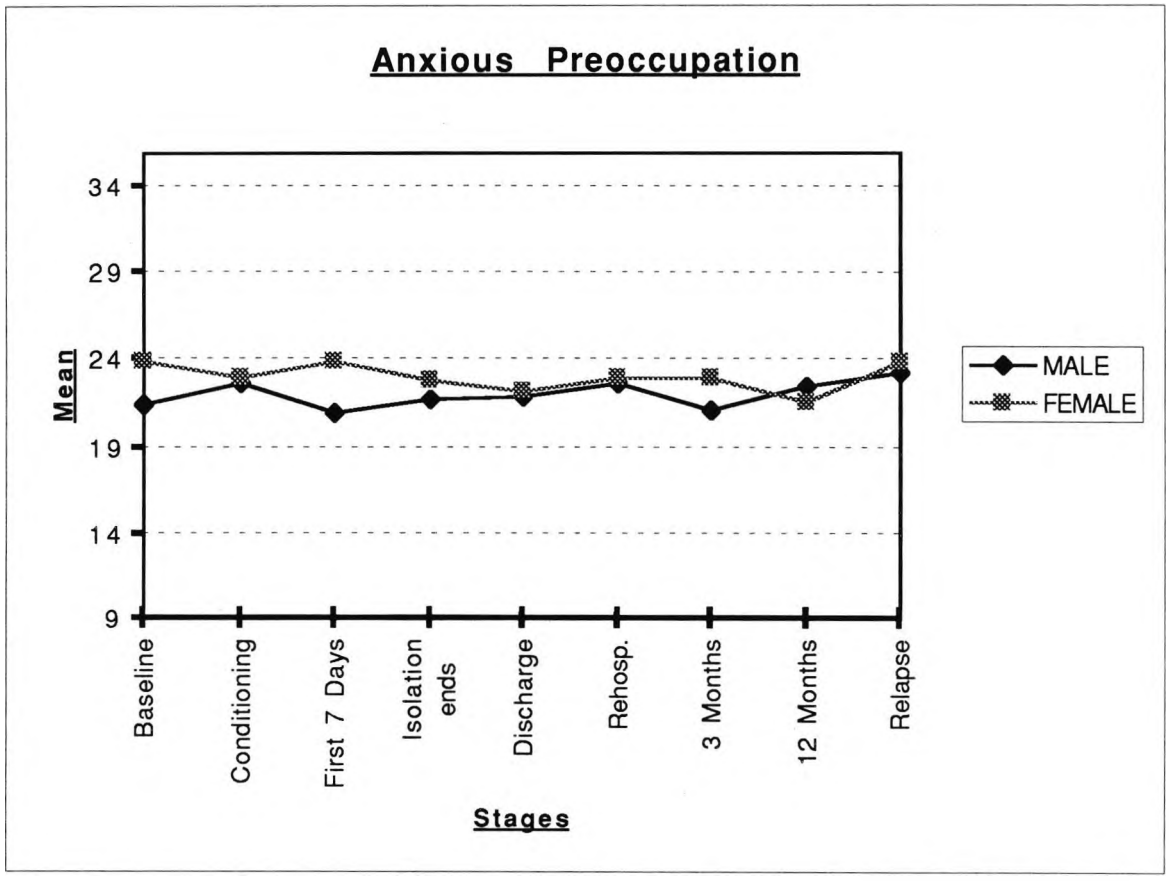


Table AP-T:6.5.2.a

Mean T-Scores for Anxious Preoccupation for Males and Females at stages: 1, 2, 3, 4, 7, 8, I and II.

	MALE			FEMALE		
STAGES	Mean	S.D.	n	Mean	S.D.	n
Baseline	52.33	7.12	24	56.89	6.82	18
Conditioning	50.64	7.85	33	55.15	8.02	20
First 7 Days	47.38	12.85	8	47.00	8.49	2
Isolation ends	43.38	10.10	8	63.75	15.50	4
Discharge	50.82	7.74	11	53.60	6.27	5
Rehospitalisation	53.62	7.90	13	53.86	9.48	7
3 Months	53.64	5.10	14	53.50	10.74	8
12 Months	55.00	10.54	3	-	-	-

AP:6.5.3 Comparison Between Patients At The Two Hospitals

The sample was divided into patients treated at the Royal Marsden Hospital and the Royal Free Hospital and compared. Results are shown on Table AP:6.5.3.

There are no significant differences between the two hospitals at 'Baseline' (stage 1). (Significance of F value = 0.84) and no significant differences at any other stage.

Table AP:6.5.3

MAC-Anxious Preoccupation: The difference from the baseline of the mean scores for the two Hospitals at stages: 1, 2, 3, 4, 7, 8, I, II and III.

Anxious Preoccupation	ROYAL FREE			ROYAL MARSDEN			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**22.71**	3.3	14	**22.37**	4.2	57	0.84
Conditioning	-0.69	2.6	13	+0.75	3.4	44	0.15
First 7 Days	-0.91	2.3	11	-0.10	2.8	39	0.39
Isolation ends	-0.80	3	10	-0.08	3.1	38	0.51
Discharge	-0.25	3.4	4	-0.33	3.2	24	0.96
Rehospitalisation	-1.20	3	5	+0.71	2.8	24	0.18
3 Months	-1.00	2.3	6	-0.39	3.2	23	0.66
12 Months	-1.00	2	3	-1.50	2.7	16	0.82
Relapse	+3.00	-	1	2.67	2.7	7	0.54

Figure AP:6.5.3

MAC-Anxious Preoccupation: The mean scores for the two Hospitals at stages: 1, 2, 3, 4, 7, 8, I, II and III.

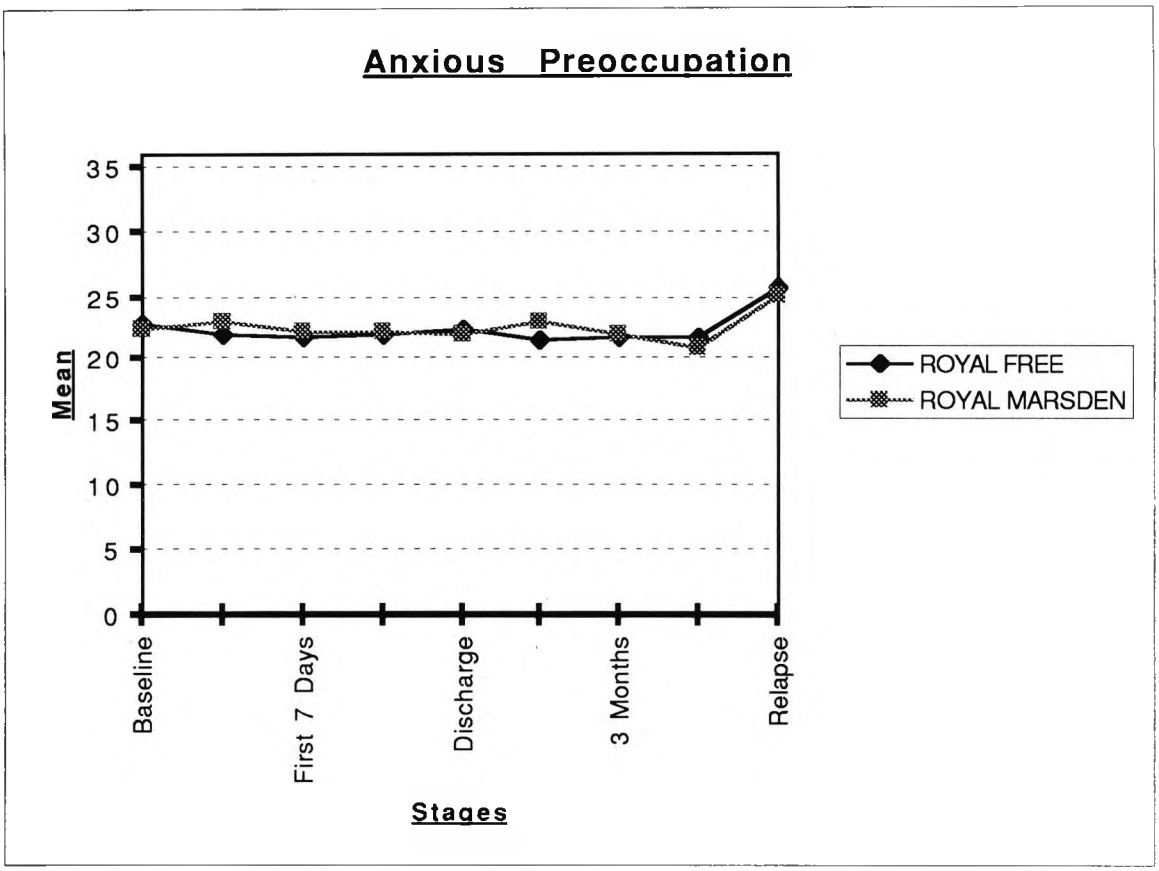


Table AP-T:6.5.3.a

Mean T-Scores for Anxious Preoccupation for the two Hospitals at stages: 1, 2, 3, 4, 7, 8, I and II.

Mean T-Scores for Anxious Preoccupation (MAC)						
	ROYAL FREE			ROYAL MARSDEN		
STAGES	Mean	S.D.	n	Mean	S.D.	n
Baseline	51.14	7.49	7	54.91	7.17	35
Conditioning	51.36	7.70	11	52.60	8.32	42
First 7 Days	41.00	0.00	1	48.00	12.17	9
Isolation ends	40.00	0.00	1	51.09	15.59	11
Discharge	51.33	5.77	3	51.77	7.73	13
Rehospitalisation	56.00	5.42	4	53.13	8.85	16
3 Months	52.20	4.02	5	54.00	8.65	17
12 Months	56.00	0.00	1	54.50	14.85	2

AP:6.5.4 Comparison Between The Two Types Of Transplant

The sample was divided into patients treated with Allogeneic Transplant and those treated with Autologeous Transplant. The groups were then compared. Results are shown on Table AP:6.5.3.

There are no significant differences between the two transplant groups at 'Baseline' (stage 1). (Significance of F value = 0.97).

At 'Conditioning' (stage 2) the Allograft group shows an increase in Anxious Preoccupation while the Autograft group shows a decrease. The difference between the two groups is not significant, but there is a trend. (Significance of F value = 0.09).

At 'First 7 Days' (stage 3) the Allograft group shows an increase in Anxious Preoccupation while the Autograft group shows a decrease. The difference between the two groups is significant. (Significance of F value = 0.04).

At 'Rehospitalization' (stage II) the Allograft group shows an increase in Anxious Preoccupation while the Autograft group shows a decrease. The difference between the two groups is not significant, but there is a trend. (Significance of F value = 0.06).

Table AP:6.5.4

MAC-Anxious Preoccupation: The difference from the baseline of the mean scores for the two types of Transplant at stages: 1, 2, 3, 4, 7, 8, I, II and III.

Anxious Preoccupation	AUTOGRAFT			ALLOGRAFT			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**22.82**	5	28	**22.17**	3.2	43	0.97
Conditioning	-0.65	3	20	+1.00	3.3	37	0.09
First 7 Days	-1.25	2.2	20	+0.37	2.9	30	0.04
Isolation ends	-0.94	2.9	18	+0.20	3.2	30	0.22
Discharge	-0.50	3.6	8	-0.25	3.1	20	0.86
Rehospitalisation	+1.89	2.2	9	-0.30	3	20	0.06
3 Months	-0.17	2.7	12	-0.76	3.2	17	0.6
12 Months	-1.78	2.3	9	-1.10	2.9	10	0.69
Relapse	+1.33	2.9	6	+1.50	2.1	2	0.94

Figure AP:6.5.4

MAC-Anxious Preoccupation: The difference from the baseline of the mean scores for the two types of Transplant at stages: 1, 2, 3, 4, 7, 8, I, II and III.

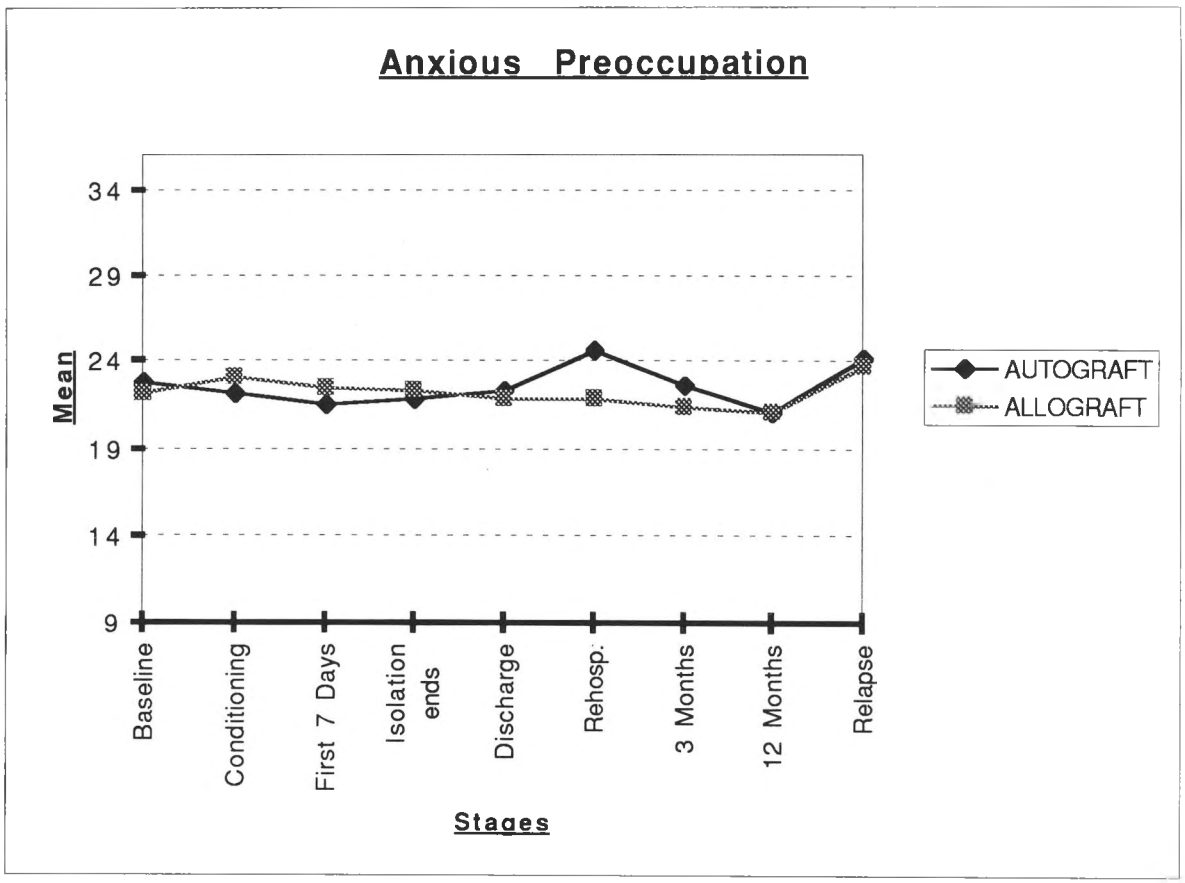


Table AP-T:6.5.4.a

Mean T-Scores for Anxious Preoccupation for the two types of Transplant at stages: 1, 2, 3, 4, 7, 8, I and II.

Mean T-Scores for Anxious Preoccupation (MAC)						
	AUTOGRAFT			ALLOGRAFT		
STAGES	Mean	S.D.	n	Mean	S.D.	n
Baseline	51.88	8.51	17	55.92	5.93	25
Conditioning	49.62	8.00	21	54.13	7.85	32
First 7 Days	44.50	5.92	4	49.17	14.63	6
Isolation ends	51.38	17.23	8	47.75	11.95	4
Discharge	50.88	6.98	8	52.50	7.86	8
Rehospitalisation	54.50	10.85	4	53.50	7.88	16
3 Months	54.75	10.24	4	53.33	7.49	18
12 Months	50.00	8.49	2	65.00	0.00	1

AP:6.5.5 Comparison Between The Two Types Of Conditioning

The sample was divided into patients treated with Chemotherapy alone and those treated with a combination of Chemotherapy + Total Body Irradiation (TBI). The groups were then compared. Results are shown on Table FS:6.5.3.

There are no significant differences between the two treatment groups at 'Baseline' (stage 6). (Significance of F value = 0.87).

At 'Three Months' (stage 6) the Chemotherapy group shows an increase in Anxious Preoccupation while the Chemotherapy + TBI group shows a decrease. The difference is not significant but there is a trend. (Significance of F-value = 0.08).

Table AP:6.5.5

MAC-Anxious Preoccupation: The difference from the baseline of the mean scores for the two Pre-Treatment Conditionings at stages: 1, 2, 3, 4, 7, 8, I, II and III.

Anxious Preoccupation	CHEMO.			CHEMO. + TBI			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**22.28**	3.2	18	**22.33**	4.3	49	0.87
Conditioning	+0.13	3.8	16	+0.54	3.7	41	0.8
First 7 Days	+0.15	2.9	13	-.043	2.7	37	0.51
Isolation ends	-0.83	3.9	12	-0.03	2.8	36	0.44
Discharge	-0.20	3.8	5	-0.35	3.1	23	0.93
Rehospitalisation	+1.40	2.1	5	+0.17	3	24	0.4
3 Months	+1.60	2.6	5	-0.96	2.9	24	0.08
12 Months	-0.50	3.4	4	-1.67	2.4	15	0.49
Relapse	-0.50	5	2	+2.00	1.6	6	0.26

Figure AP:6.5.5

MAC-Anxious Preoccupation: The difference from the baseline of the mean scores for the two Pre-Treatment Conditionings at stages: 1, 2, 3, 4, 7, 8, I, II and III.

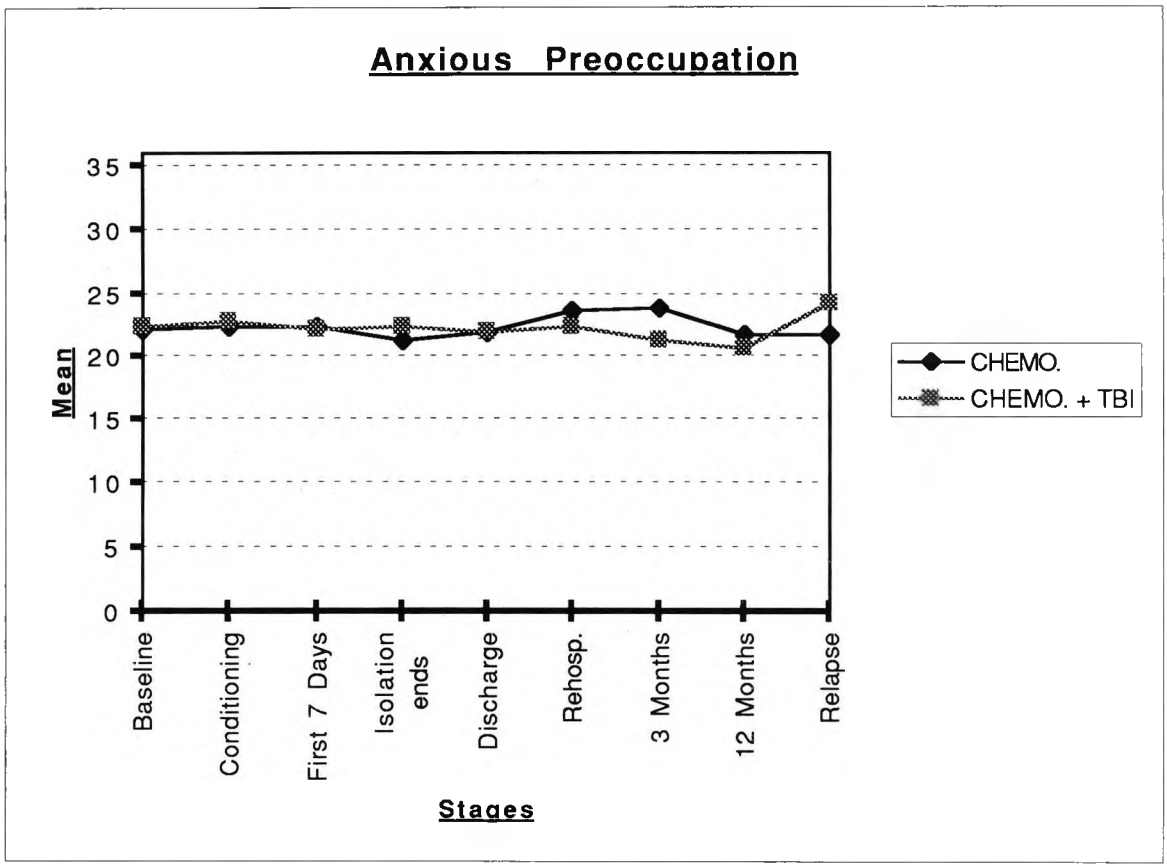


Table AP-T:6.5.5.a

Mean T-Scores for Anxious Preoccupation for the two types of Conditioning at stages: 1, 2, 3, 4, 7, 8, I and II.

Mean T-Scores for Anxious Preoccupation (MAC)						
	CHEMO.			CHEMO. + TBI		
STAGES	Mean	S.D.	n	Mean	S.D.	n
Baseline	52.67	6.17	15	55.19	7.78	27
Conditioning	53.31	7.30	13	52.03	8.46	40
First 7 Days	46.00	6.25	3	47.86	13.80	7
Isolation ends	48.00	8.00	3	50.89	17.30	9
Discharge	52.50	5.26	4	51.41	7.96	12
Rehospitalisation	56.33	3.51	3	53.24	8.80	17
3 Months	55.50	2.89	4	53.17	8.51	18
12 Months	-	-	-	55.00	10.54	3

F:6.5 FATALISM SUBSCALE

F:6.5 Results Of The Fatalism Subscale

Results are given in the following order:

F:6.5.1	**(i)**	**Results for the whole sample**
F:6.5.2	**(ii)**	**Comparison between Males and Females**
F:6.5.3	**(iii)**	**Comparison between the two Hospitals**
F:6.5.4	**(iv)**	**Comparison between the two types of transplants**
F:6.5.5	**(v)**	**Comparison between the two types of conditioning**

Results of the MAC sub-scale Fatalism are shown on Table F:6.5.1. Results for T-scores for Fatalism are shown on Table F-T:6.5.1 and Figure F-T:6.5.1.

The Table F:6.5.1 shows mean scores of Fatalism at Baseline and differences from baseline for entire sample at all stages. It shows the number of patients for whom data are available and the statistical significance of the comparison of the difference from baseline of increases (+) and decreases (-) to baseline mean.

Table F:6.5.1

MAC-Fatalism: The difference from the baseline of the mean scores (for the entire sample) at stages: 1, 2, 3, 4, 7, 8, I, II and III.

Stages	Differences from baseline mean	SD	n	Comparison-Baseline 2-tailed p *
Stage 1 Baseline	mean 17.39	3.5	71	n.a.
Stage 2 Conditioning	+0.11	2.5	57	0.1
Stage 3 First 7 Days	+0.30	2.81	50	0.25
Stage 4 End of Isolation	+0.10	3.1	48	1.0
Assessment I Discharge	+0.29	3.2	28	0.04**
Assessment II Rehospitalization	+0.72	3.4	29	0.11
Stage 6 3 Months	+0.48	4.1	29	0.18
Stage 7 12 Months	-1.05	2.9	19	0.31
Assessment III Relapse	+4.0	4.1	8	

*p=values are based the Non-Parametric Wilcoxon Matched-Pairs Test.

F:6.5.1 Comparison from Baseline

At 'Baseline' (stage 1) Fatalism scores (mean=17.39) are lower than the mean of the Normative sample of a mixed cancer group (mean = 17.7) reported by Watson et al. (1989). The level of Fatalism shows a continuous increase throughout stages with one exception. At 'Twelve Months' (stage 7) the level of Fatalism decreases. The decrease from 'Baseline' (stage 1) is not significant. (2-tailed p=0.31))
At 'Discharge' (stage II) the increase from 'Baseline' (stage 1) iis significant. (2-tailed p=0.04).

These data confirm Hypothesis number three which says:

"The patient's attitude towards cancer does not remain constant during treatment. It is influenced by changes in the treatment during the different stages."

Figure F:6.5.1

MAC-Fatalism: The mean scores (for the entire sample) at stages: 1, 2, 3, 4, 7, 8, I, II and III.

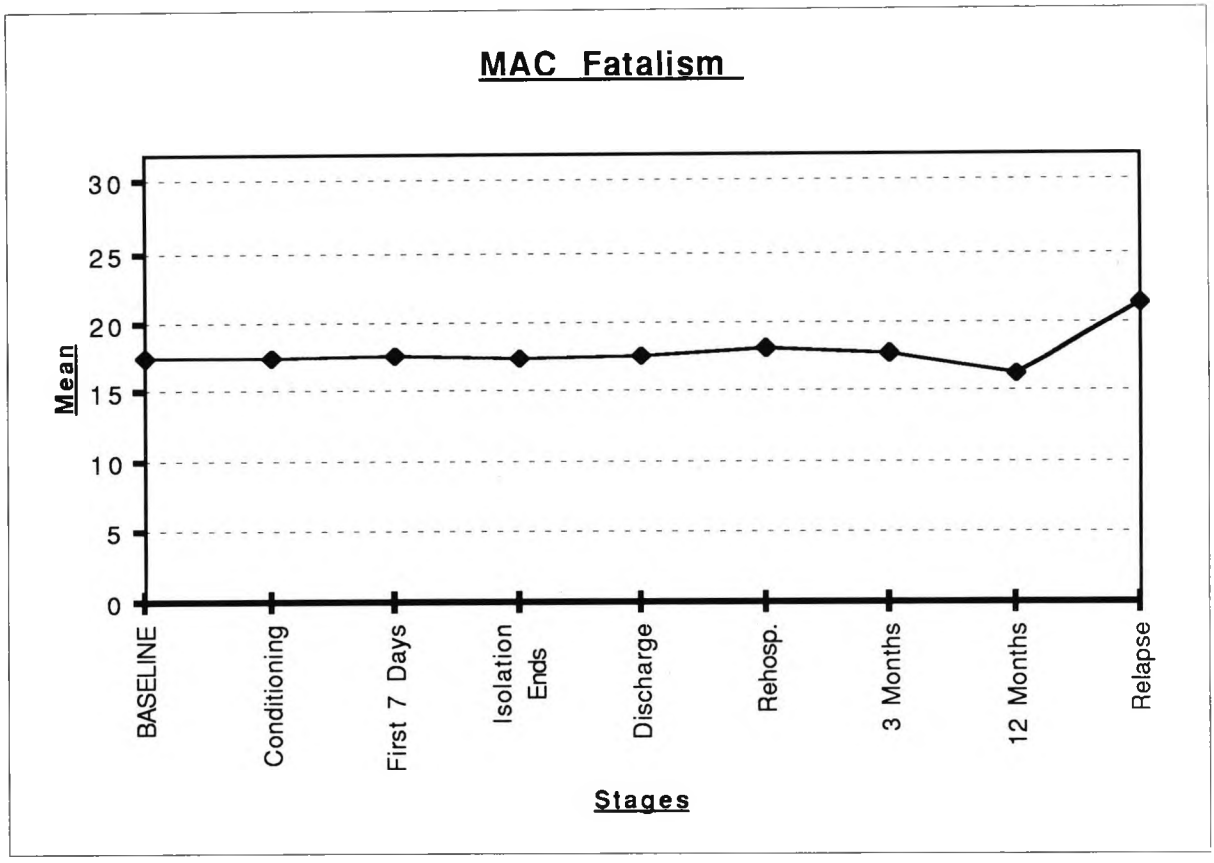


Table F-T:6.5.1

Mean T-Scores for Fatalism for the entire sample at stages 2, 3, 4, 7, 8, I and II.

Stages	Mean	SD	n	2-tailed p
Stage 1 Baseline	49.05	8.4	42	n.a.
Stage 2 Conditioning	49.40	8.8	53	0.50
Stage 3 First 7 days	48.50	11.5	10	0.32
Stage 4 End of isolation	45.33	10.6	12	0.35
Assessment I Discharge	49.91	6.3	22	0.12
Assessment II Rehospitalization	59.33	14.7	3	0,11
Stage 6 3 months	46.69	7.8	16	0.40
Stage 7 12 months	49.25	7.2	19	0.40

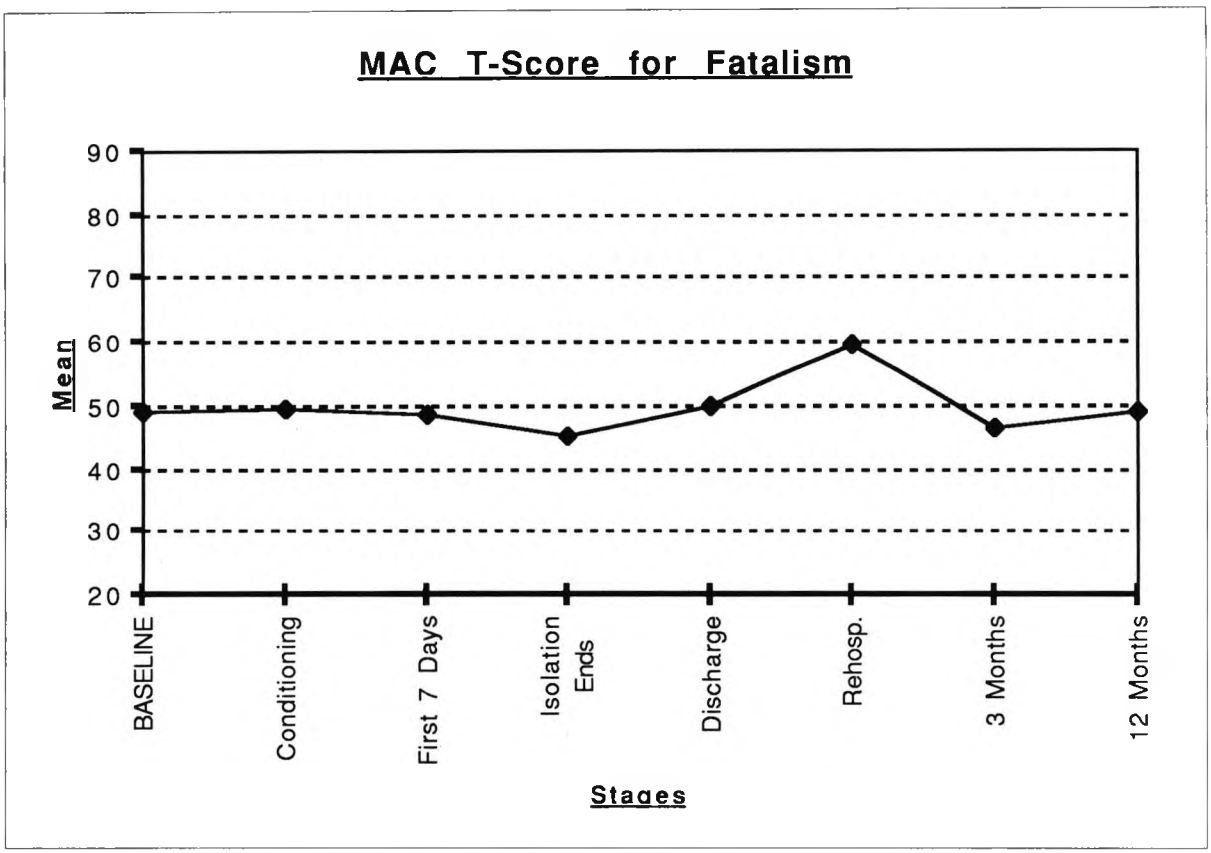
*p=values are based the Non-Parametric Wilcoxon Matched-Pairs Test.

F-T:6.5.1 Comparison T Scores For Fatalism

The mean for the Fatalism T-scores rises above the cut-off point (50) for 'cases' only once at 'Rehospitalisation' (stage II). The increase was not significant.

Figure F-T:6.5.1

Mean T-Scores for Fatalism at stages: 1, 2, 3, 4, 7, 8, I and II.



F:6.5.2 Comparison Between Males And Females

The sample was divided into Males and Females and compared. Results are shown on Table F:6.5.2.

There is no difference between mean scores for Fatalism for Females and Males at 'Baseline' (stage 1). (Significance of F value = 0.85).

Throughout transplant there are no significant differences between the two gender.

Table F:6.5.2

MAC-Fatalism: The difference from the baseline of the mean scores Males and Females at stages:1, 2, 3, 4, 7, 8, I, II and III.

FATALISM	MALE			FEMALE			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**17.49**	3.9	43	**17.25**	2.9	28	0.85
Conditioning	+0.11	2.7	36	+0.70	2.2	21	0.82
First 7 Days	+0.38	3.2	32	+0.17	1.9	18	0.8
Isolation ends	+0.13	3.5	31	+0.59	2.5	17	0.94
Discharge	+0.11	3.6	19	+0.67	2.1	9	0.67
Rehospitalisation	+1.05	3	19	+0.10	4.2	10	0.49
3 Months	+0.32	4.6	19	+0.80	3.1	10	0.77
12 Months	-1.31	3.2	13	-0.50	2.2	6	0.59
Relapse	+4.17	4.6	6	+3.50	3.5	2	0.86

Figure F:6.5.2

MAC-Fatalism: The mean scores for Males and Females at stages: 1, 2, 3, 4, 7, 8, I, II and III.

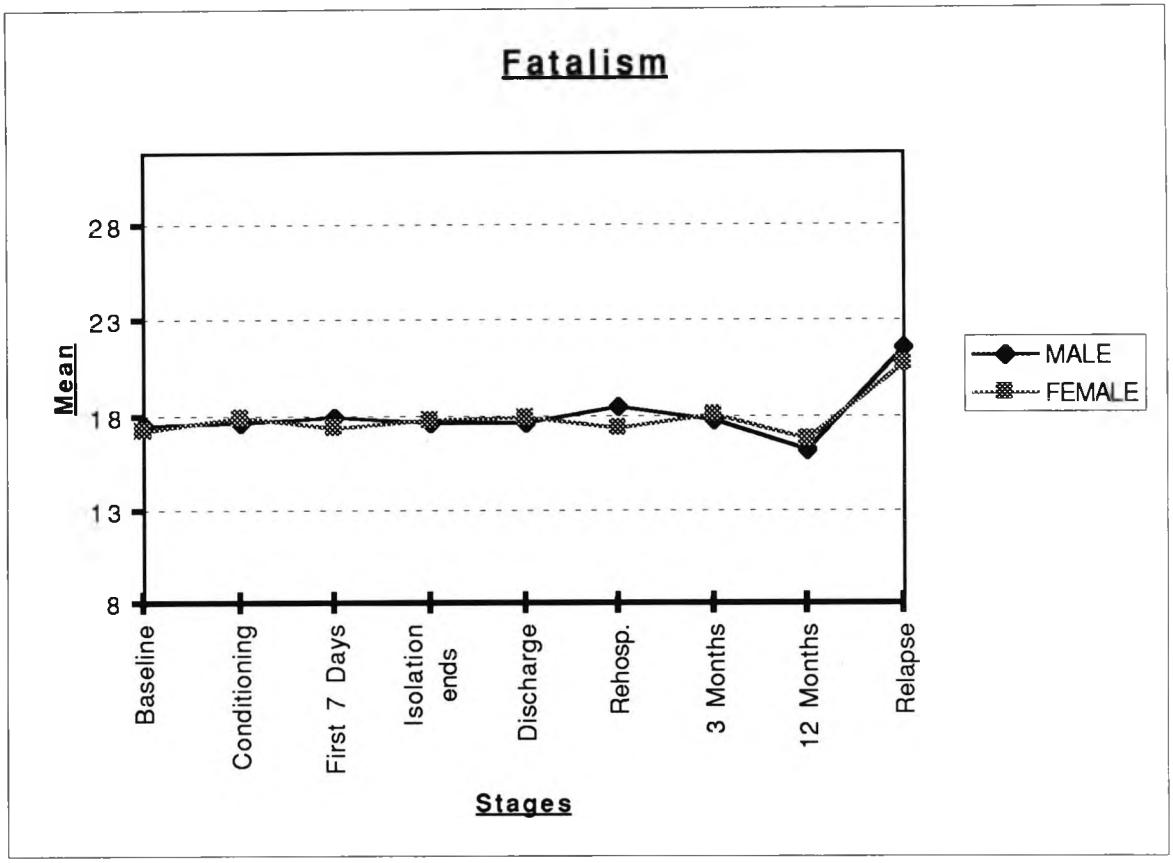


Table F-T:6.5.2.a

Mean T-Scores for Fatalism for Males and Females at stages: 1, 2, 3, 4, 7, 8, I and II.

Mean T-Scores for FATALISM (MAC)						
	MALE			FEMALE		
STAGES	Mean	S.D.	n	Mean	S.D.	n
Baseline	49.13	10.00	24	48.94	5.72	18
Conditioning	49.27	8.85	33	49.60	8.95	20
First 7 Days	47.25	12.37	8	53.50	7.78	2
Isolation ends	40.25	8.99	8	55.50	4.20	4
Discharge	48.73	7.18	11	42.20	7.79	5
Rehospitalisation	50.31	6.52	13	47.29	8.56	7
3 Months	51.64	4.43	14	46.88	8.10	8
12 Months	59.33	14.74	3	-	-	-

F:6.5.3 Comparison Between Patients At The Two Hospitals

The sample was divided into patients treated at the Royal Marsden Hospital and the Royal Free Hospital and compared. Results are shown on Table F:6.5.3.

There are no significant differences between the two hospitals at 'Baseline' (stage 1). (Significance of F value = 0.82)

Throughout transplant there are no significant differences between the two hospital groups.

Table F:6.5.3

MAC-Fatalism: The difference from the baseline of the mean scores for the two Hospitals at stages: 1, 2, 3, 4, 7, 8, I, II and III.

FATALISM	ROYAL FREE			ROYAL MARSDEN			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**17.29**	3.2	14	**17.42**	3.6	57	0.82
Conditioning	-0.69	2.8	13	+0.34	2.3	44	0.22
First 7 Days	-0.73	3	11	+0.59	2.7	39	0.17
Isolation ends	-0.70	4.1	10	+0.32	2.9	38	0.37
Discharge	-1.25	4	4	+0.54	3	24	0.3
Rehospitalisation	+1.20	2.6	5	+0.62	3.6	24	0.74
3 Months	+0.17	4	6	+0.57	4.2	23	0.84
12 Months	-2.00	1	3	-0.88	3.1	16	0.56
Relapse	+5.00	-	1	+3.86	4.4	7	0.82

Figure F:6.5.3

MAC-Fatalism: The difference from the baseline of the mean scores for the two Hospitals at stages: 1, 2, 3, 4, 7, 8, I, II and III.

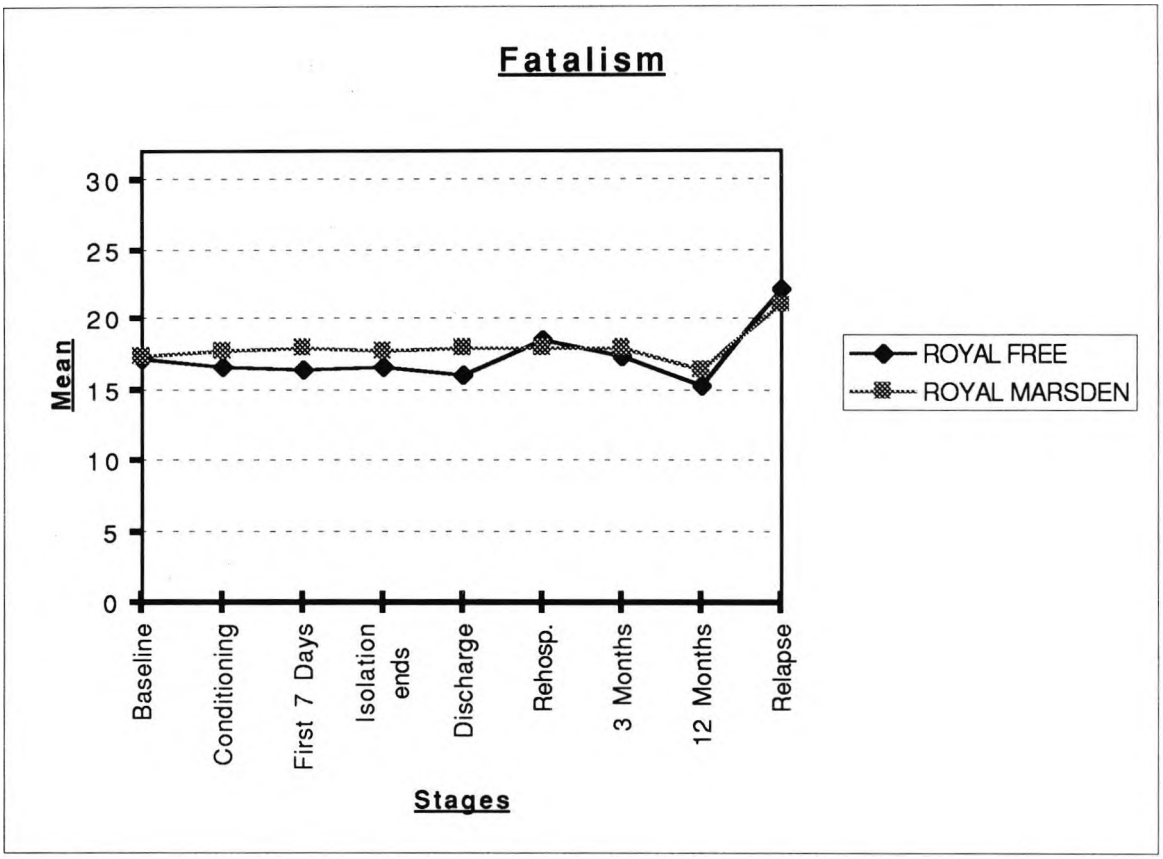


Table F-T:6.5.3.a

Mean T scores for Fatalism for the two Hospitals at stages: 1, 2, 3, 4, 7, 8, I and II.

Mean T-Scores for FATALISM (MAC)						
	ROYAL FREE			ROYAL MARSDEN		
STAGES	Mean	S.D.	n	Mean	S.D.	n
Baseline	47.29	7.06	7	49.40	8.63	35
Conditioning	47.27	7.70	11	49.95	9.07	42
First 7 Days	43.00	0.00	1	49.11	12.05	9
Isolation ends	35.00	0.00	1	46.27	10.59	11
Discharge	43.67	7.02	3	47.38	8.03	13
Rehospitalisation	49.50	1.73	4	49.19	8.09	16
3 Months	50.40	3.91	5	49.76	6.92	17
12 Months	54.00	0.00	1	62.00	19.80	2

F:6.5.4 Comparison Between The Two Types Of Transplant

The sample was divided into patients treated with Allogeneic Transplant and those treated with Autologous Transplant. The groups were then compared. Results are shown on Table F:6.5.3.

At 'Baseline' (stage 1) the groups Allograft shows higher levels of Fatalism than the Autograft group. The difference is not significant. (Significance of F value = 0.2).

Throughout transplant there are no significant differences between the two types of transplants.

Table F:6.5.4

MAC-Fatalism: The difference from the baseline of the mean scores for the two types of Transplant at stages: 1, 2, 3, 4, 7, 8, I, II and III.

FATALISM	AUTOGRAFT			ALLOGRAFT			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	**16.64**	3.3	28	**17.88**	3.6	43	0.2
Conditioning	-0.05	2.3	20	+0.19	2.6	37	0.57
First 7 Days	+0.20	2.4	20	+0.37	3.1	30	0.84
Isolation ends	-0.06	3.1	18	+0.20	3.2	30	0.79
Discharge	+0.88	1.8	8	+0.05	3.6	20	0.54
Rehospitalisation	+1.89	2.6	9	+0.20	3.7	20	0.23
3 Months	+0.17	2.6	12	+0.76	5	17	0.73
12 Months	-1.00	2.1	9	-1.10	3.5	10	0.95
Relapse	+2.67	2.3	6	+8.00	7.1	2	0.12

Figure F:6.5.4

MAC-Fatalism: The mean scores for the two types of Transplant at stages: 1, 2, 3, 4, 7, 8, I, II and III.

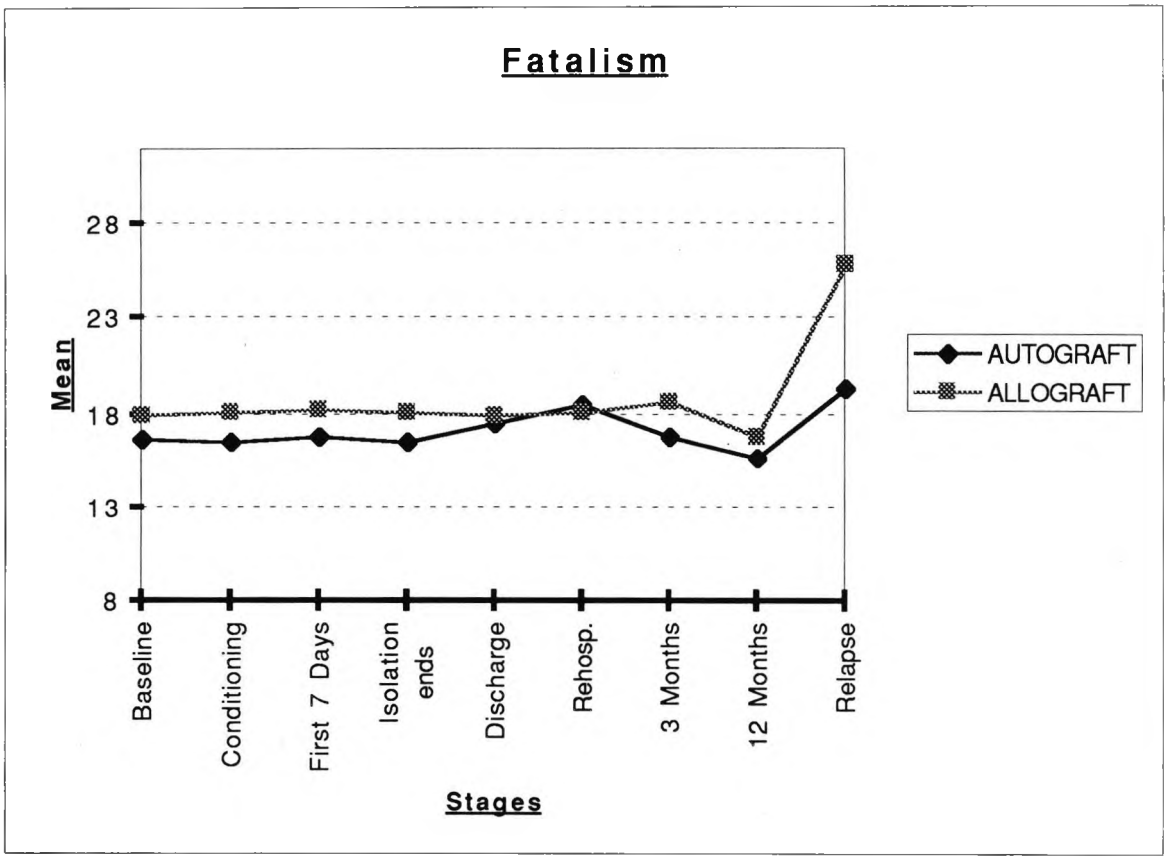


Table F-T:6.5.4.a

Mean T-Scores for Fatalism for the two types of Transplant at stages: 1, 2,3,4,7,8,I and II.

Mean T-Scores for FATALISM (MAC)						
	AUTOGRAFT			ALLOGRAFT		
STAGES	Mean	S.D.	n	Mean	S.D.	n
Baseline	47.41	6.43	17	50.16	9.39	25
Conditioning	47.33	9.44	21	50.75	8.22	32
First 7 Days	38.00	9.63	4	55.50	6.02	6
Isolation ends	44.88	12.76	8	46.25	5.62	4
Discharge	46.00	9.10	8	47.38	6.74	8
Rehospitalisation	51.00	10.42	4	48.81	6.59	16
3 Months	51.50	6.25	4	49.56	6.42	18
12 Months	51.00	4.24	2	76.00	0.00	1

F:6.5.5 Comparison Between The Two Types Of Conditioning

The sample was divided into patients treated with Chemotherapy alone and those treated with a combination of Chemotherapy + Total Body Irradiation (TBI). The groups were then compared. Results are shown on Table F:6.5.3.

There are no significant differences between the two treatment groups at 'Baseline' (stage 1). (Significance of F value = 0.69).

Throughout transplant there are no significant differences between the two types of conditioning.

Table F:6.5.5

MAC-Fatalism: The difference from the baseline of the mean scores for the two Pre-Treatment Conditionings at stages: 1, 2, 3, 4, 7, 8, I, II and III.

FATALISM	CHEMO.			CHEMO. + TBI			Significance
STAGES	Mean	S.D.	n	Mean	S.D.	n	of F Value
Baseline	17	2.5	18	17.5	3.9	49	0.69
Conditioning	+0.13	2.8	16	+0.1	2.4	41	0.83
First 7 Days	+0.77	2.4	13	+0.38	3	37	0.74
Isolation ends	-0.50	3	12	+0.31	3.2	36	0.45
Discharge	+/- 0.00	1.2	5	+0.35	3.5	23	0.83
Rehospitalisation	+0.40	1.3	5	+0.79	3.7	24	0.82
3 Months	+1.60	1.1	5	+0.25	4.5	24	0.51
12 Months	-2.25	3	4	-0.73	2.8	15	0.37
Relapse	+1.50	0.7	2	+4.83	4.5	6	0.36

Figure F:6.5.5

MAC-Fatalism: The mean scores for the two Pre-Treatment Conditionings at stages: 1, 2, 3, 4, 7, 8, I, II and III.

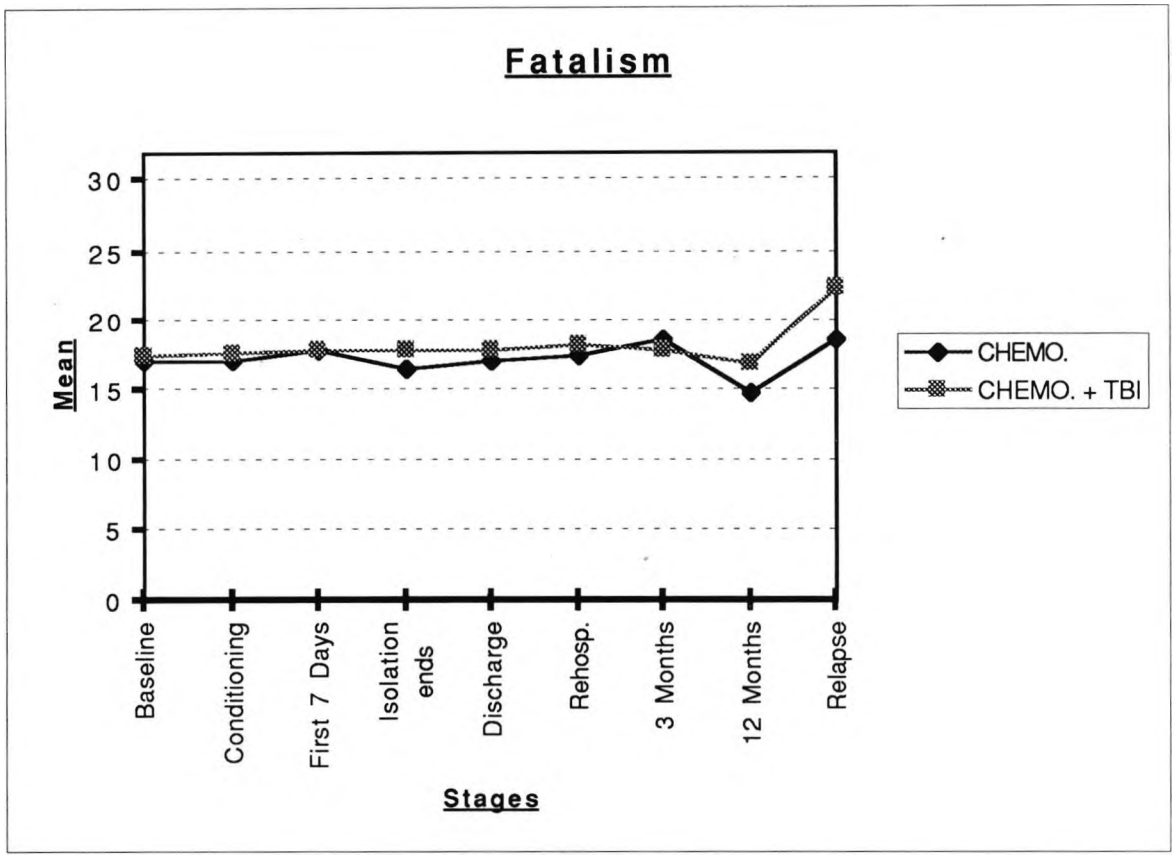


Table F-T:6.5.5.a

Mean T-Scores for Fatalism for the two Pre-Treatment Conditionings at stages: 1, 2,3,4,7,8,I and II.

Mean T-Scores for FSH (MAC)						
	CHEMO.			CHEMO. + TBI		
STAGES	Mean	S.D.	n	Mean	S.D.	n
Baseline	46.93	9.90	15	51.19	11.26	27
Conditioning	51.46	9.51	13	52.95	9.58	39
First 7 Days	52.00	10.54	3	52.00	11.31	7
Isolation ends	55.00	12.12	3	48.50	11.87	8
Discharge	42.50	9.54	4	50.17	10.00	12
Rehospitalisation	34.67	8.08	3	55.65	7.57	17
3 Months	37.25	1.50	4	58.28	8.68	18
12 Months	-	-	-	65.33	11.02	3

6.6 CANCER LOCUS OF CONTROL (CLOC) SCALE

6.6 Results Of The CLOC Scale

The results of the CLOC Scale are presented in the following order:

6.6.1 (i) Results for the whole sample

Results of the Cancer Locus of Control Scale are shown on Table .6.1 and Figure A:.6.1.

The Table A:6.6.1 shows mean scores of Cancer Locus of Control at 'Baseline' (stage 1) and differences from baseline for entire sample at all stages. It shows the number of patients for whom data are available and the statistical significance of the comparison of the difference from baseline of increases (+) and decreases (-) to baseline mean.

Table CLOC:6.6.1

CLOC: The difference from the baseline of the mean scores (for entire sample) at stages 1, 4, I, II, 7 and 8.

Stages	Differences from baseline mean	SD	n	Comparison-Baseline 2-tailed p *
Stage 1 Baseline	mean 24.03	3.5	69	n.a.
Stage 4 End of isolation	+0.88	2.8	17	0.50
Assessment I Discharge	+1.50	2.1	6	1.0
Assessment II Rehospitalization	+0.57	3.9	23	0.29
Stage 6 3 months	+0.12	3.1	25	n.e.c.
Stage 7 12 months	+0.88	3.8	16	n.e.c.

*p=values are based on the Non-Parametric Wilcoxon Matched-Pairs Test.

Comparison of Stages

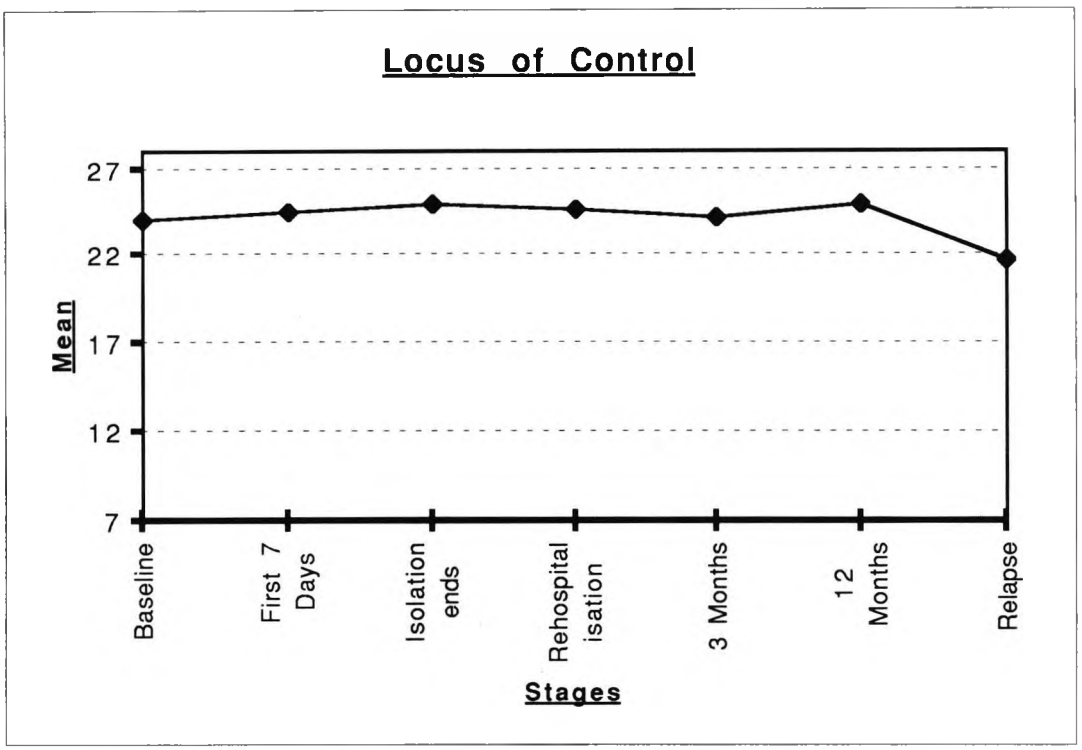
At baseline the mean scores for CLOC are 24.03 out of 28. Throughout transplant the level of mean scores does not significantly increase or decrease at any stage from baseline. There are no significant increases or decreases throughout transplant on this measure. Data suggest that the Locus of Control over the course of the disease is stable throughout the transplant procedure.

Data do not confirm Hypothesis number four which says:

" Perception of control does not remain constant during the treatment. It is influenced by the changes in the treatment during different stages.

Figure CLOC:6.6.1

CLOC: The mean scores (for entire sample) at stages 4, 5, I, II, 7 and 8.



6.7 RELAPSE DATA

Results of the data collected for relapsed patients are shown on Table 6.7.
Data are available for n=8.
The Table 6.7 shows differences from 'Baseline' (stage 1) to stage 'Relapse' (stage III) for all measures. It shows the comparison of the difference from baseline of increases (+) and decreases (-) to baseline mean. The number of patients was too small to allow statistical analysis.

6.7 Comparison From Baseline

At 'Relapse' (Stage III), the patients' psychological states show deterioration from 'Baseline' on all measures used in this study.

Table 6.7

Relapse Data for all measures.

Variables	Difference to Baseline Mean	S D	n
Hospital Anxiety and Depression Scale			
Anxiety	+4.5	6.5	n=8
Depression	+4.88	4.8	n=8
Mental Adjustment to Cancer Scale			
Fighting Spirit	-3.50		n=8
Helplessness	+4.38	3.0	n=8
FSH-T scores			n=8
Anxious Preoccupation	+1.38	2.6	n=8
APT- scores			n=8
Fatalism	+ 4.00	4.1	n=8
FT-scores			n=8
Locus of Control Scale			
LOC	- 2.33	4.8	n=6
The Rotterdam Symptom Checklist			
Psychological Symptoms	+4.38	5.5	n=8
Physical Symptoms	+5.00	7.8	n=8

6.8 INTERVIEWS

6.8.0 Data from the Interviews

Data will be presented in the following order:

6.8.1 Questions presented at the 'Baseline' (stage 1) only.

6.8.2 Questions presented at other stages except 'Baseline'.

These other stages are listed below:

'Conditioning' (stage 2)
'First 7 Days' (stage 3)
'End of Isolation' (stage 4)
'Discharge' (stage I)
'First Rehospitalization' (stage II)
'Three Months" (stage 6)
'Twelve Months' (stage 7)
'Relapse' (stage III).

6.8.1 Stage 1 - Decision For Transplant

Question No. 1:

When was Bone-Marrow-Transplantation (BMT) offered to you as a treatment option?

Responses:

Categories	Percentages
At the time of diagnosis	50%
At the time of remission	17%
At the time of relapse	21%
Others*	13%

* This includes patients who investigated this option themselves. This applies particularly to patients with the chronic leukaemias.

BMT was introduced to half of this group (50%) at the time of their diagnosis almost as the next step in their outlined treatment plan.

Only 13 % were offered the treatment after relapse.

Question No. 2:

Did you have a choice between BMT and other treatment options?

Responses:

Categories	Percentages
Yes, choice	27%
No choice	73%

Seventy-three percent of those interviewed at baseline did not perceive a choice in this matter.

Question No 3:

Why did you go ahead with BMT?

Responses:

Categories	Percentages
In order to live	27%
No real choice	31%
To be cured	13%
Only option	19%
Better chance	4%
Others	6%

Although 31% explained that there was no real choice, 27% went ahead in order to live and 13 % to be cured.

Question No 4:

Did you discuss BMT with somebody outside the hospital? If so, with whom?

Responses:

Categories	Percentages
Nobody	29%
With partner	33%
With family	20%
With General Practitioner	5%
With a long-term survivor	5%
With a friend	4%
Others	4%

One third (33%) discussed BMt with their partner and 20% with their family; that is 53% discussed BMT with their family, but 29% did not discuss with someone outside the hospital.

Question No. 5:

Did anybody influence your decision?

Responses:

Categories	Percentages
Consultant	43%
Nobody	41%
General Practitioner	4%
Family	4%
Partner	4%
Others	4%

Forty-three percent cited the consultant in charge as the one who influenced their decision, but 41% said they were not influenced by anybody.

The family appears to have influenced very few patients in their decision. When they did, it was indirectly e.g. the fact that they were needed by their small children.

Question No. 6

You have decided to go ahead with BMT. What are your expectations regarding the outcome of this treatment?

Responses:

Categories	Percentages
To be cured	62%
I shall get better	27%
To lead a normal life	11%

Sixty-two percent of those questioned expected to be cured and 11% to lead a normal life after transplant. This implies that almost three-quarter of those interviewed expected to be able to live after transplant without any further residue of their illness and their treatment.

6.8.2 Results Of The Interviews At Other Stages (see below)

'Conditioning' (stage 2)
'First 7 Days' (stage 3)
'End of Isolation' (stage 4)
'Discharge' (stage I)
'First Rehospitalization' (stage II)
'Three Months" (stage 6)
'Twelve Months' (stage 7)
'Relapse' (stage III).

Question No.1:

From the time I saw you last to the present what events caused you to feel upset?

Responses:

STAGES

CATEGORIES	2	3	4	I	II	6	7	III
Leaving hospital	0	0	0	14%	0	0	6%	0
Lack of sympathy	4%	3%	2%	0	0	0	0	0
Death of fellow patient	8%	3%	10%	0	0	9%	31%	0
Treatment related problems*	**33%**	11%	25%	18%	11%	23%	19%	13%
Isolation related problems	14%	19%	19%	5%	0	0	0	0
Disease/treatment side effects**	22%	**41%**	15%	14%	0	**36%**	19%	0
(Re-)hospitalisation	0	0	0	9%	**78%**	9%	6%	0
Relapse	0	0	0	0	0	0	0	**63%**
No upset	14%	24%	25%	**41%**	11%	23%	19%	0
Others	6%	0	4%	0	0	0	0	25%

*includes Chemotherapy, TBI
**pain, nausea

During isolation*** treatment and disease related problems were the main source for patients' upset and were still upsetting 32% at 'Discharge' (stage I). By 'Rehospitalisation" (stage II) 11% reported that treatment and disease related problems were upsetting, but to 78% it was rehospitalisation.
*** (stage 2-54%; stage 3-52%; stage 4-40%)

At Stage 6 (3 Months) the number of patients quoting treatment and disease related problems as upsetting rose to 59%. Patients often quoted the length of time it took for medical problems to resolve as upsetting.

At 'Twelve Months' (stage 7), a year post-transplant, 31% named the death of a fellow patient as upsetting. (See question no. 2)

At 'Relapse' the fact that patients did relapse was experienced as upsetting.

Question No. 2:

What was the most upsetting event?

Responses:

STAGES

CATEGORIES	2	3	4	I	II	6	7	III
Leaving Hospital	0	0	0	6%	0	0	0	0
Lack of Sympathy	0	3%	0	0	0	0	0	0
Death of fellow patient	2%	3%	10%	0	0	10%	40%	0
Treatment related problems	45%	14%	20%	24%	20%	29%	27%	0
Isolation related problems	14%	17%	20%	6%	0	0	0	0
Disease/treatment side effects	14%	38%	15%	6%	0	19%	7%	0
(Re-)hospitalisation	2%	0	0	0	60%	10%	7%	17%
Relapse	0	0	0	6%	0	10%	0	67%
No Upset	16%	24%	27%	41%	10%	24%	20%	0
Others	5%	0	5%	12%	17%	0	0	17%

*includes Chemotherapy, TBI
**pain, nausea

At 'Rehospitalisation' (stage II) 60 % named this event as the most upsetting.

At 'Twelve Months' (stage 7) the most upsetting event quoted by 40% of patients was the death of a fellow patient. This is in accordance with the literature (Patenaude & Rappeport, 1982) reporting that the death of a fellow patient is the most difficult time during isolation reawakening the fear of patients' own death. During isolation only a minority of patients in this study quoted the death of a fellow patient as most upsetting event. One could speculate that patients were only able to admit to the impact of this event from the safe distance of a year post-transplant .

Question No.3:

How long did you feel upset?

Responses:

STAGES

CATEGORIES	2	3	4	I	II	6	7	III
Less than an hour	9%	7%	4%	0	7%	9%	0	0
A few hours	23%	13%	7%	**33%**	29%	9%	0	50%
A day	18%	0	22%	22%	21%	0	0	0
A few days	28%	4%	22%	11%	0	**36%**	**37%**	50%
A week	0	0	4%	0	0	9%	0	0
Longer than a week	6%	7%	14%	22%	14%	**36%**	**37%**	0
On and off	16%	**33%**	28%	11%	29%	0	25%	0

The experienced upset tended to last at least a day, often a few days, but surprisingly at stages 'Three Months' (stage 6)) and 'Twelve Months' (stage 7) patients reported to have felt upset for periods longer than a week.

Question No. 4

Since I saw you last have you experienced an incident, a period of time and or a treatment procedure as discouraging?

Responses:

STAGES

CATEGORIES	2	3	4	I	II	6	7	III
Less than an hour	0.09	0.07	0.04	0	0.07	0.09	0	0
A few hours	0.23	0.13	0.07	0.33	0.29	0.09	0	0.5
A day	0.18	0	0.22	0.22	0.21	0	0	0
A few days	0.28	0.4	0.22	0.11	0	0.36	0.37	0.5
A week	0	0	0.04	0	0	0.09	0	0
Longer than a week	0.06	0.07	0.14	0.22	0.14	0.36	0.37	0
On and off	0.16	0.33	0.28	0.11	0.29	0	0.25	0

Throughout transplant the majority did not experience discouragement. When it was experienced it was mainly disease and treatment related.

However, this is not true for 'Relapse' (stage III). Discouragement at this stage came from a variety of sources.

Question No. 5

Was there a time when you felt scared?

Responses:

STAGES

CATEGORIES	2	3	4	I	II	6	7	III
During medical procedures	**32%**	7%	5%	0	5%	0	0	0
Fear of infections	0	0	0	6%	5%	6%	7%	0
During isolation	5%	0	0	0	0	0	0	0
When due for an appointment	2%	0	0	0	0	0	14%	0
Medical complications	11%	4%	10%	0	5%	11%	7%	20%
Leaving hospital	0	0	3%	6%	0	0	0	0
Fear of relapse	0	0	0	0	0	11%	14%	20%
Fear of dying	5%	4%	3%	0	0	0	0	0
No fear	**36%**	**79%**	**69%**	**83%**	**80%**	**67%**	**43%**	20%
Others	9%	7%	8%	6%	5%	6%	14%	**40%**

During the conditioning procedure at 'Conditioning' (stage 2) a third of all patients interviewed experienced fear, particularly during Total Body Irradiation. However, during all subsequent stages the majority did not experience fear. When patients were scared it was during medical complications.

After the 'Three Months' (stage 6) stage the fear of relapse was named by 11% and this number increased to 14% at 'Twelve Months' (stage 7).

Question No. 6

What kind of support helped you most to manage difficult times?

Responses:

STAGES

CATEGORIES	2	3	4	I	II	6	7	III
FRIENDS	5%	8%	7%	10%	3%	10%	0	17%
PARTNER	20%	**30%**	**36%**	**34%**	**38%**	**52%**	**43%**	**33%**
STAFF	22%	**36%**	25%	7%	13%	10%	0	0
FAMILY	**39%**	25%	27%	**38%**	**40%**	28%	**36%**	**33%**
RELIGION	3%	0	4%	7%	3%	0	7%	0
FELLOW PATIENTS	5%	0	0	0	0	0	0	0
THINKING POSITIVELY	3%	0	0	3%	3%	0	14%	17%
DENIAL	2%	0	0	0	0	0	0	0

Throughout transplant the family plays an important supportive role. Partners and the family are quoted as the main source for the patient's support.

However, during isolation support from the staff, particularly the nursing staff, plays an important role. This role becomes less vital when the patient has been discharged, although during rehospitalisation its importance increased once again.

When relapsed, 'thinking positively' became an important source of self-help, quoted by 17% of the patients who had relapsed, but it remained the family's role to support the relapsed patient in 66% of all cases.

Question No. 7:

Have you developed a method to cope at these times?

Responses:

STAGES

CATEGORIES	2	3	4	I	II	6	7	III
TAKING DAY BY DAY	5%	9%	7%	22%	5%	5%	7%	0
RELIGIOUS BELIEFS	7%	6%	5%	0	10%	5%	0	0
TRUST IN DOCTORS	7%	3%	5%	11%	10%	10%	0	25%
BEING PATIENT	2%	3%	10%	6%	20%	10%	0	0
TAKING CONTROL	11%	9%	12%	22%	15%	0	7%	25%
TRYING TO KEEP BUSY	14%	34%	21%	0	10%	15%	14%	0
POSITIVE ATTITUDE	23%	9%	10%	17%	5%	15%	**29%**	0
NONE	11%	6%	14%	11%	15%	25%	**29%**	25%
OTHERS	21%	22%	17%	11%	10%	15%	14%	25%

Coping strategies changed with changing stages and reflect a flexibility on the patient's side to adapt to changing demands. During conditioning a 'positive attitude' was the most often quoted coping style.

In isolation the coping strategy most often employed was 'trying to keep busy'; when discharged, the patient coped by retaking control; when rehospitalised by 'being patient'. At 'Three Months' (stage 6) and 'Twelve Months" (stage 7) a 'positive attitude' or/and no 'coping style' were predominant.

At 'Relapse' (stage III) 'trust in doctors' emerges at the first time as major coping strategy.

Question No. 8:

Did your religious beliefs help you to cope better?

Responses:

STAGES

CATEGORIES	2	3	4	I	II	6	7	III
YES/DID HELP	42%	36%	58%	47%	35%	47%	54%	40%
NO/DID NOT HELP	58%	64%	42%	53%	65%	53%	46%	60%

During treatment until stage 7 (3 Months) the majority of patient did not find religion helpful. However, the results reversed at 'End of Isolation' (stage 4), 'Twelve Months' (stage 7) and 'Relapse' (stage III) when more patients found religion helpful. (58%,54% and 60%).

Question No. 9:

What are your expectations regarding the outcome of the BMT treatment?

Responses:

STAGES

CATEGORIES	2	3	4	I	II	6	7	III
CURE	**43%**	**65%**	**45%**	**61%**	**44%**	**59%**	**38%**	0
A Normal Life	12%	12%	26%	11%	**22%**	12%	**31%**	0
IMPROVED HEALTH	**45%**	23%	29%	28%	**34%**	29%	**31%**	**100%**

Expectations during the transplant procedure fluctuated but did not really change. At the beginning of the transplant procedure 45% expected an improved status of health, the rest to be cured and able to lead a normal life. The latter expectations, i.e. to be cured and a normal life, increased with time after transplant, but experienced a set-back during 'First Rehospitalization' (Stage II).

At 'Relapse' (stage III) patients expected to achieve an improvement in their health by further treatment.

Question No. 10:

Have your expectations changed?

Responses:

STAGES

CATEGORIES	2	3	4	I	II	6	7	III
CONSIDERABLY WORSE	0	0	0	0	0	0	0	**67%**
SLIGHTLY FOR THE WORSE	6%	3%	3%	0	12%	6%	0	0
REMAINED THE SAME	**76%**	**94%**	**78%**	**83%**	**71%**	**88%**	**82%**	**33%**
SLIGHTLY BETTER	15%	3%	14%	O	0%	6%	9%	0
CONSIDERABLY	3%	0	6%	17%	18%	0	9%	0

Up to the 'Relapse' (stage III) patients perceived their expectations as unchanged and stable. However, at 'Relapse' 67% of those relapsed reported that their expectations had changed considerably for the worse.

Question No. 11:

Have you had enough information ?

Responses:

STAGES

CATEGORIES	2	3	4	I	II	6	7	III
YES	83%	100%	96%	91%	75%	89%	83%	100%
NO	17%	0	4%	9%	25%	11%	17%	0

Generally patients did feel well informed, even at 'Relapse' (stage III) when all the patients interviewed (100%) declared that they had had enough information. However, the number of patients was only 8 at this stage.

At the 'End of Isolation' (stage 4) patients felt best informed, and only 4% said that they did not have enough information. However, during 'Conditioning' (stage 2) 17% did not have enough information and at 'First Rehospitalization' (stage II) 25% did not have enough information.

CHAPTER Seven: RELATIVES

7.1 Introduction

The Impact Of Bone Marrow Transplantation (BMT) On The Families

It has been repeatedly emphasised that BMT is a very demanding procedure for the patient and for the involved family. (Cohen et al., 1977; Popkin & Moldow, 1977; Lesko, 1989; Pot Mees, 1989). The Patient's medical and emotional difficulties during transplant, repeated disappointments during the treatment as well as the uncertainty of the future are shared by the family. (Lesko, 1989).

However, very few authors define their concept of 'family'. One of the few exceptions is Lesko (1989). For her the concept 'family' includes parents, spouses, siblings and children. Bluglass (1991) argues that this 'family' may not only involve the immediate family but should be extended to include the extended family as well as the care-givers. Care-givers need not necessarily be members of the patient's family. A care-giver is someone who is continuously involved with the patient during the patient-career. Care-givers may be a neighbour, a friend , a homosexual partner or a distant relative, (Bluglass, 1991). For Ell et al. (1989), however, this care giving individual is the closest relative whom they call the 'significant other'. Rait & Lederberg's (1989) name for the closest person is 'primary caretaker'.

In this discussion about the impact of BMT upon families the terminology 'family' has been kept. This global concept may refer to a group of people, parents and siblings; to an individual, the patient's spouse;. to a relative, such as a child or to a close individual such as a friend.

In BMT the family is "inevitably a participant in every phase", (Cohen et al., 1977). Alby (1991) confirms this . BMT demands the family's involvement. Nonetheless in most of the reports this participation is ill-defined. Rait & Lederberg, (1989) define the role of the family as one of providing emotional support for the patient. "They are expected by others - medical staff especially - and by themselves to be able to contain their feelings and function supportively toward the patient".(op. cit) The need for the family's support is acknowledge (Tebbi et al., 1985; Rait & Lederberg, 1989), although the form and content of this support have rarely been elaborated.

Tebbi et al. (1985) asked a group of adolescents about the most important source of their support. The group did not quote the staff, nor their peers but their families, mostly their mothers "as best source of support". Rait & Lederberg (1989) report that this support takes the form of collecting information at times of decision making when the patient is unable to manage. During these times the family takes over the decision making process.

The support provided may be practical in the form of nursing after discharge from hospital when the patient may still be on medication or in need of other nursing care. (Rait & Lederberg, 1989).

The involvement and the need to provide support even at times when the family members may be shattered themselves by bad news (Rait & Lederberg ,1989) puts these members into "a highly stressful situation" (Cohen et al. ,1977). Bluglass (1991) argues that the degree of stress experienced is related to and influenced by disease type. The cycle of relapse and remission causes a different sort of stress than slowly progressing solid tumours.,

How much is the degree of stress influenced by the phase of the treatment? Bluglass (1991) emphasises that different phases present different issues to the family and require a different approach. This is particularly true in leukaemia presenting cycles of relapse and remission.
The patient being discharged will experience different challenges and problems from the patient who has just relapsed. There is some evidence that relapse will be differently experienced from remission. Sanders & Kardinal (1977) report on the particular difficulties experienced by patients in remission. The families of these patients tended to keep them in the sick role and kept referring to them as being sick. These families found it difficult to adjust to the patients new status and remained illness oriented. Alby (1991) finds the decision for transplant a particularly stressful phase for the family as it is one which makes "good decision-making impossible". (Alby, 1991). For Pot-Mees (1989) the time around discharge is very stressful. She observed ambivalent feelings in the family at this time. On the one hand families were looking forward to normality, on the other hand they feared the loss of medical support.

Families of BMT patients are closely involved, (Cohen et al., 1977; Pot-Mees, 1989; Alby 1991). However, this does not mean that families are well informed and integrated into the treatment. Families may still feel like outsiders and become helpless spectators, (Alby, 1991).
Farkas-Patenaude et al., (1979) argue that other factors beside type of disease and disease phase influence the degree of stress experienced by families. These other factors are: "the medical course", "the individual" and "the family balance of strength and weaknesses". The latter factor contains three components. These are; "previous illness", "geographic dislocation"* and "other emotional problems". (Farkas-Patenaude et al., 1979).

The influence of the medical course and physical state on the families' emotional well-being has been acknowledged by other authors. (Chodoff et al., 1963; Popkin et al. ,1977;Ell et al., 1989).

Ell et al. (1989) emphasise that stress increases when patients' conditions are poor. Looking at different groups of relatives, they observed that when patients experienced a high number of physical complaints, then their relatives suffered more distress. This relationship has been confirmed by Chodoff et al., (1963). This research group observed parents of children with Leukaemia on the ward. When a death occurred on the ward the "parent became more vulnerable to the emotional impact of the fact that his child was really going to die". (Chodoff et al., 1963). Popkin et al. (1977) extend this relationship between the medical state of the patient and the stress experienced by the family to the psychological state of the patient and the response by the family. In their case history they report that "the patient's wife was a direct 'barometer' of his emotional states. When the patient was doing well and relaxed, she proved quite verbal; at times when his anxiety rose, she said little."

The observed responses to those multiple stressors include feelings of claustrophobia, mental and physical fatigue. (Pot-Mees,1989). Fatigue tends to increase with increasing time spent in the hospital. Another coping response observed by Cohen et al. (1977) is denial. They found that families in BMT tended to accept the diagnosis but denied the prognosis.

The opinions about what aspects contribute to successful coping in BMT differ. For Cohen et al. (1977) these aspects involve planning and seeking information. The gained information will prepare the family "for all probable

difficulties". This view is shared by Alby (1991). She expresses her view by saying " patients and families need to be carefully prepared for hospitalisation". However, Farkas-Patenaude et al. (1979) express the lack of knowledge and the inconclusiveness of available research with "it is not altogether clear why some individuals and some families cope better than others with the transplant experience".

Families have to provide support at a time when they themselves are overwhelmed and under considerable stress. (Rait & Lederberg, 1989). Manos & Chritakis (1985) warn about the danger that families who are unable to tolerate stress may abandon the patient. These families need support. Alby (1991) argues that all families need to be helped to stay close to the sick relative. They should be allowed to express their anxieties, their anger and their ambivalent emotions. They should also be allowed to question.

Magni et al. (1986) argue that social support will have a buffering effect for these families. For the BMT families social support is often restricted. Restriction may arise from the families 'dislocation' to the place of transplant or from the difficulties of 'sharing' this unusual experience. 'Sharing' involves lengthy explanation to the uninformed outsider. Social support may be thus limited, even though the family remains in its home environment.

Farkas-Patenaude et al. (1979) talks about 'social isolation' of these families created by the particulars of BMT. They write:

> "The nature of the transplant experience is unique and complex making it difficult to communicate with family and friends about the patient's daily states. The burdens of home and hospital visits leave little time and energy for lengthy explanations to ' outsiders '.

Alby (1991) stresses that psychological and social support for these families should be an integral part of the patient's care and should be provided throughout transplant. She stresses that support 'must begin before transplantation and last until a total physical and psychological recovery is achieved'.

When we talk about a family we do not talk about one 'entity' with uniform needs, but a group of individuals. Different family members will have different needs at different times.

For these reasons several writers (Cohen et al., 1977; Alby, 1991; Bluglass, 1991) advocate that any psychological intervention should be provided by a multidisciplinary team including professionals from various psychosocial disciplines.

7.2 -Method
Study Of BMT-Relatives

7.2.1. BACKGROUND

Close contact on the ward with the involved relatives of BMT patients revealed that these care giving relatives were experiencing and reporting considerable stress. However, their role on the ward was that of support to the patient. They welcomed and sought out conversations with the researcher, if only to talk to somebody about their difficulties. These conversations tended to start off with voiced concern about the patient. From there the questioners would move to issues about the patient's mood, behaviour and/or distress. Only very gradually did the conversation move to the questioners themselves, as if their own feelings had to be pushed firmly into the background and the patient had to came first.

From these observations and conversations the following study was developed. It was decided to inquire into the difficulties they experienced and the support that was available to them.

7.2.2 Timing:

The inquiry was restricted to one retrospective assessment of the closest relative.

A three months period was chosen because:

1. The time period coincided with the patient's assessment at stage 6 (3 Months post-transplant).

2. The time was still close enough to the transplant procedure to allow the relative to recollect the feelings he or she had experienced. At the same time it was distant enough to allow an overview over the period of transplant, avoiding the recency effect.

7.2.3. Subjects

Subjects for this study were the relatives of patients of at the Royal Free Hospital and the Royal Marsden Hospital undergoing BMT who were alive at the time of assessment. Relatives of dead and dying patients were not approached. It was decided to restrict subjects to relatives of patients participating in the main study.

7.2.4 Selection Criteria

Inclusion criteria were as follows:

1. Subjects needed to be aged eighteen and over

2. Subjects needed to be fluent in English

3. Subjects needed to be continuously involved with the patient.

Identification of this closest relative was based in the Royal Free on questioning of the patient and observations by staff and by the researcher.

In the Royal Marsden the rule is that only the closest relative is allowed into the patient's room during the isolation period. Identification was based on this rule. The relative who attended to the patient during isolation was invited to participate.

In two cases there was no relative attending to the patient. In both cases the 'spouses' had remained home outside London to look after the mutual children and could only intermittently visit their partners. They were not included in the study.

7.2.5 Dependent Variables:

1. **Information**
2. **Support**
3. **Distress**
4. **Involvement**
5. **Treatment Benefit**

7.2.6 Materials

A questionnaire was developed by the researcher to investigate the above five variables. (Copy is in Appendix III).

There are eighteen questions in this questionnaire.

(i) Six of these refer to the following three areas of information.

1. Satisfaction with the information provided, (e.g. was it sufficient);

2. Effectiveness of information, (e.g. was it presented in a way to be understood);

3. Access to information (e.g. was the medical staff willing to provide information).

(ii) Four questions refer to support.

1. Whether support was needed or not;

2. Whether support was available or not ;

3. Who provided support.

4. Whether relatives would make use of provided professional support if available.?

(iii) Two questions refer to distress experienced by the relatives.

1. One of these looks at twelve events in the BMT patient's career, e.g. 'waiting for transplant' and 'chemotherapy'.

2. The second at eleven physical side-effects of the treatment, (e.g. vomiting and hairloss) and negative psychological states of the patient, (e.g. 'feeling hopeless' and 'feeling low').

(iv) Two questions refer to areas relating to the relatives involvement in the patient's care.

1. The degree of involvement, (e.g. in terms of participation in the original discussion about BMT);

(v) Two questions were designed to encourage relatives to discuss their own feelings during the treatment procedure and to communicate any comments they might have.

(vi) One question was added at the suggestion of the consultant, who voiced his concern that all questions inquired after negative consequences of BMT and none addressed a possible positive effect on the lives of these relatives.

7.2.7 Scoring

Answers to questions were categorised and the numbers of answers in each category were displayed in percentages.

7.3. Procedure

7.3.1 Timing:

The questionnaire was administered once, at three months post-transplant.

7.3.2 Approach of Relatives:

One of the inclusion criteria was continuous involvement of the relative with the patient. This meant that the researcher and the relative had met long before the assessment was due, and relatives were aware of the existence of this questionnaire. The questionnaire was introduced early during the transplant meeting in conversation with the relative. At the time of the three-month assessment of the patient, the questionnaire for the relative was either handed to the relative or sent by post to the relative's home.

Compliance was extraordinarily good and all approached relatives returned the answered questionnaire.

7.4. Pilot Study:

7.4.1 Issues To Be Examined

The questionnaire was piloted on two subjects.
The aims of this pilot study were as follows:

1. **Feasibility of the study;**
2. **Acceptability to relatives and patient;**
3. **Testing of the newly developed questionnaire.**

7.4.2 Results of Pilot Study:

The study was feasible, and acceptable to relatives. The relatives were willing to participate and the study did not interfere with the relative's life. None reported to be unnecessarily reminded of a difficult period, but rather welcomed the opportunity to discuss their experience with an understanding professional. One relative told me, that these 'questions' reflected understanding. She said 'this is how I had felt, you must know these feelings very well.'

The pilot study revealed some shortcomings of the questionnaire. Answers to the questions consisting of forced choices 'yes' and 'no' did not allow any differentiation. It was therefore decided to offer more informative responses to these two choices.(e.g. if the answer was "yes' offer three of four graded answers). Furthermore the original twenty questions were reduced to eighteen questions.

7.5 RESULTS

5.5 Demographic Data

7.5.1 Data Collection:

The data collection for this study took place from May, 1988 (when the first relative for the pilot-study was interviewed), until May 1990 when the last patient reaching the three months follow up was assessed and the relative invited to fill in the questions.

7.5.2 Demographic Data.

Twenty five relatives were approached. Compliance was extraordinarily good and twenty four agreed to participate. One refused. The relative who refused had remained with her small children outside London and was not involved in her partner's care. Of these twenty four eight were males; sixteen were females.

7.5.3 Distribution of Gender

The final distribution of the sample according to gender was:

Males	**n = 8**
Females	**n = 16**

7.5.4 Relationship to Patients

Table 7.5.4

Relationship	partner	sibling	offspring	parent
Frequency	15	-	-	9

Of the nine parents eight were mothers, only one was the patient's father. This one father had taken over the care of the patient when his wife was called away by an unexpected death in the family. It appears that in times of illness the care-giving remains the mother's role. In the Royal Marsden, where families had to choose the one member who was allowed to enter the patient's room, none of the parents interviewed resisted or objected to the limited access given to the other partner.

7.5.5 Distribution Of Age

Table 7.5.5

Age-group	20-30	31-40	41-50	51-60	61-70
Frequency	4	6	10	3	1

The age group 40-50 years was the largest group represented. This may be partly due to the number of parents involved in looking after patients.

7.5.6 The Relative's Involvement:

Information about the frequency of contact between relative and patient during hospitalisation was obtained from 23 relatives:

Table 7.5.6

every day	twice a week	once a week
n= 20 (87%)	n=1 (4%)	n=2 (9%)

The majority (87%) of relatives visited the patient every day. This implies close contact with the patient and the unfolding treatment procedure.

7.6 Results From Questions

7.6. 1
Questions 1-6
Access to and Availability of Information for the Relative.

7.6.1-1 Question No: 1

Were you able to be present at the time of the discussion about BMT?

Table 8.6.1-1

Categories	Numbers	Percentages
YES	21	88%
NO	3	12%

88 % of all interviewed relatives attended the initial discussion about BMT between consultant and patient.

of the 3 (12%) who did not attend the initial discussion the reasons quoted for not attending were:

one relative was not invited;
two relatives provided no explanation.

Of those attending, 20 answered the sub-question No. 1b. (See below).

7.6.1-1b Question No: 1b

Were you satisfied with the way in which your questions were answered during the discussion?

Table 7.6.1-1b

Categories	Numbers	Percentages
Completely Satisfied	10	50%
Satisfied	8	40%
Not Really Satisfied	1	5%
Left with Unanswered Questions	1	5%

Ninety percent of the sample was satisfied with the way their questions were answered during that initial discussion, but 10% were not really satisfied and 5% were left with unanswered questions.

8.6.1-2 Question No: 2

Would you have liked more time spent discussing the treatment and the effect it had upon your relative?

Table 8.6.1-3

Response Category	Numbers	Percentages
YES	6	26%
NO	17	74%

Seventy-four percent of the interviewed relatives implied that the time spent on discussing BMT was sufficient.

Of those who would have liked to spend more time discussing BMT the topics they would have liked to discuss further are listed below:

7.6.1-2b List of Topics Relatives would have liked to spend more Time on:

1. **Unexpected side-effects**
2. **Severity of side-effect**
3. **Exact plan of management**
4. **Emotional issues (concerning the patient)**
5. **Personal issues (concerning the relative)**

7.6.1-3 Question No: 3

When Bone-Marrow-Transplantation was explained to you, could you understand it:

Table 7.6.1-3

Response Category	Numbers	Percentages
Fully Understood	17	74%
Not Enough Understanding	6	26%
No Clear Idea	0	0
No Understanding	0	0

The majority of relatives (74%) stated that they fully understood the complex treatment Bone Marrow Transplantation when it was explained to them. However, a quarter (26%) left the discussion with not enough understanding.

Table 7.6.1-4 Question No: 4

Were the possible side effects of the treatment explained to you?

Table 7.6.1-4

Response Category	Numbers	Percentages
YES	21	88%
NO	3*	12%

Despite 26% of the relatives being left with incomplete understanding (see previous question) only 12% reported that possible side effects were not explained.

*all three relatives answering with "No" were present at the initial discussion.

Table 7.6.1-4b Question No 4b

Can you state what side effects you expected?

Table 7.6.1-4b

Response Category	Numbers	Percentages
Hairloss	13	54%
Sore Mouth	7	29%
Vomiting	5	21%
Sterility	5	21%
Diarrhoea	5	21%
Infections	4	16%
Loss Of Appetite	4	16%
GvHD	4	16%
Nausea	4	16%
Depression	3	12%
Feeling Low	1	4%

It appears that physical side-effects such as 'Hairloss', 'Vomiting' and 'Diarrhoea' were expected by the majority of the relatives, but emotional side-effects such as 'Depression' and 'Feeling Low' were only expected by a minority.

7.6.1-5 Question No.: 5

Were there any unexpected side-effects?

Table 7.6.1-5

Response Category	Numbers	Percentages
YES	13	54%
NO	11	46%

This result is surprising considering that only 12% had stated that possible side effects were not explained (see question no. 4). Fifty-four percent came across unexpected side effects during the treatment of their relative.

When asked which side-effects were unexpected, relatives quoted the following:

Table 7.6.1-5b

Response Category	Numbers	Percentages
GvHD	4	33%
Skin Rash	3	25%
Cataracts	1	8%
Infertility	1	8%
Variable Blood Cell Counts	1	8%
Brittle Nails	1	8%
Burning (from TBI)	1	8%

Graft-versus-Host Disease (GvHD) and Skin Rash (the latter is a manifestation of the GvHD-Syndrome) were quoted by 48% as unexpected side effects. This result does not tally with relatives earlier response of 74% having fully understood the complex treatment Bone Marrow Transplantation when it was explained to them (See question no. 3).

This raises the question whether information was provided and if it was comprehensive enough, understandable and repeatedly given.

7.6.1-6 Question No.: 6

Did you feel free to ask questions when problems arose during the transplant period until now?

Table 7.6.1-6

Response Category	Numbers	Percentages
Most Of The Time	13	56%
Frequently	3	13%
Sometimes	6	26%
Not At All	0	0

Half of the interviewed relatives (56%) felt that they could ask questions most of the time, however 46% did not.

7.6.2 Questions 7 to 10

Issues of Support for the Relatives:

7.6.2-1 Question No.: 7

Did you feel that you yourself needed emotional support during your relative's, the patient, Bone-Marrow-Transplantation?

Table 7.6.2-1

Response Category	Numbers	Percentages
YES	18	75%
NO	6	25%

Seventy-five percent of the interviewed relatives reported that they needed support during this period. Surprisingly, there was no difference between males and females. (See Table 7.6.2-1b)

7.6.2-1b Gender of Subjects

Responses to Question No. 7 divided according to gender.

Response Category	Males	Females
YES	7 (78%)	12 (80%)
NO	2 (22%)	3 (20%)

7.6.2-2 Questions No. 8

Did you find such support?

Table 7.6.2-2

Response Category	Numbers	Percentages
YES	16	89%
NO	2	11%

Eighty-nine percent found the needed support, but eleven percent did not.

7.6.2-3 Question No :9

Who gave you emotional support?

Table 7.6.2-3

Response Category	Numbers	Percentages
Family	13	36%
Friend	10	28%
Church	6	17%
Social Worker	4	11%
Family Doctor	3	8%

Answers to the above question refers to the 89% who found support. (See question no. 8).

Support was provided by: the family of the relative for 36%; friends for 28% and organisations and professionals for 36%.

7.6.2-4 Question No: 10

If qualified counsellors were available for you to consult regarding any problems, would you use this service?

Table 7.6.2-4

Response Category	Numbers	Percentages
YES	17	74%
NO	6	26%

When asked whether relatives would make use of qualified professionals if the hospitals were to provide them, 74% said that they would. In view of the 11% of relatives who had no support and the 36% who were supported by organisations and professionals there is a need for professional support on the ward.

7.6.3 Questions Nos. 11 And 12

Experienced Distress

7.6.3-1 Question No.: 11

Can you name the most stressful events during your relative's Bone-Marrow Transplantation?

Table 7.6.3-2

The three most frequently named distressful events during the patient's treatment were:

Response Category	Numbers	Percentages
The Diagnosis	20	45%
Waiting for Transplant	13	30%
Infections	11	25%

Relatives named two pre-transplant events as the most stressful. These are the original diagnosis and waiting for transplant.

Infections have the potential of being life-threatening and were named by relatives as very stressful events during the transplant procedure.

7.6.3-3 Question No.: 12

The three most frequently named distressful aspects of the patient's quoted were:

Response Category	Numbers	Percentages
Feeling Low	16	37%
Pain	15	34%
Vomiting	12	28%

Emotional distress shown by the patient during transplant was experienced by relatives as the most distressing aspect of the patient's care. However, this is the one side effect relatives expected least. (see question no. 4b).

7.6.4 Questions Nos. 13 and 14

Positive Aspects of the Patient's care and Benefits for the Patient

7.6.4-1 Question No.: 13

Were you pleasantly surprised by any aspect of the patient's care and if so, by what?

There were 34 responses. The three areas repeatedly referred to were:

Response Category	Numbers	Percentages
Nursing Care	23	68%
Treatment (medical)	6	18%
Medical Care	3	9%
Others	2	5%

Ninety-five percent refer to nursing and treatment related care provided by the staff as the aspects they were pleasantly surprised by.

7.6.4-2 Question No.: 14

What positive benefits have you observed at this stage for the patient?

There were 34 responses and these referred to the following areas:

1. Future ,
e.g. lease of life, hope for the future;

2. Relationships;
e.g. improved relationship with family and with partner;

3. Being alive:
e.g. patient is still alive, children still have a parent;

4. State of Health;
e.g. return to health, being cured, looking well;

5. Change of priorities:
e.g. priorities made clear;

6. Change in personality:
e.g. more positive attitude, more outgoing

Table 7.6.4-2

Response Category	Numbers	Percentages
Future	7	21%
Alive	7	21%
Relationship	6	18%
Health	5	15%
Personality	3	8%
Priorities	3	8%
Others	3	8%

The majority of relatives (42%) quote the fact, that at this point in the patient's career the patient is alive and they see a future for the patient.

A number of relatives refer to positive changes in the patient and the patient's attitude to life leading to an improved relationship between relative and patient.

CHAPTER Eight: DISCUSSION

8. 1 Difficulties Experienced During This Study

8.1.1 Overview

The purpose of this study has been to follow a group of successive patients in the Royal Marsden Hospital from the time of their decision to go ahead with Bone Marrow Transplantation (BMT) until a year post-transplant. It was decided to take in 75 patients at baseline and it was hoped to recruit this number within a time period of 18 months from the above hospital only. However, the time scale proved to be impossible to maintain. It was therefore decided to approach an additional transplant centre. The Royal Free Hospital agreed to have a number of patients added into this study. The inclusion of another hospital in this study enabled comparisons to be made in the treatment of patients between the hospitals.

The recruitment of patients was one of the difficulties experienced during this study. Others were the high rate of attrition due to illness and death among this patient group; the emotional strain on the author with regards to patient's medical situation and subsequent death; the ward structure; working alone with no help on the wards and changes in the protocol of patients' treatment.

8.1.2. Recruitment

The number of patients to be recruited was estimated on the basis of transplantations performed in the Royal Marsden Hospital during the year 1987 (personal communications with R. Powles). This estimated number should have allowed one new patient per week to be taken into the study. However, at the end of the first 12 months only 20 patients had been entered into the study instead of the estimated 52. This was due to several factors. The number of transplants for the year 1988 was lower than during the previous year and thus the number of eligible patients reduced. Reasons for fewer transplants were multiple.

(i) Availability of isolation facilities.

Patients stayed longer in isolation than in the previous year and the number of beds available was thus reduced. There was a lack of isolation facilities due to medical problems with previous transplant patients who still occupied the limited number of isolation rooms.

Technical problems in isolation facilities (i.e. heating problems).

Prospective patients developed medical problems and their transplant needed to be postponed (i.e. patients relapsed prior to transplant).

Patients transplanted did not fulfil the inclusion criteria for this study. (e.g. non-English speaking patients.)

There was an increase in patients judged to be "too nervous" and/or too "fragile" by the then BMT co-ordinator who reserved the right to "select" patients for this study. (Initially patients were approached through the then BMT co-ordinator).

(ii) Technical reasons:

The radiation machine needed repair during March and April of 1988 and no transplants were performed during these two months.

8.1.3 Rate Of Attrition

Fluctuation of numbers occurring throughout the procedure was mainly due to illness and death. In addition, seven patients refused to continue at various stages during the treatment. The majority of these patients voiced their disappointment with the course their treatment had taken and felt angry with the team. It may not be unjustifiable to assume that the psychological researcher was perceived as the member of the team who was least essential for their physical well-being and survival. These feelings came to the fore at times of unexpected medical complications. At these times patients voiced their surprise and anger. Statements made by patients were to the effect that they had not expected particular medical complications, that they had been misinformed and misled. A similar concern was voiced over the severity of expected side effects of the treatment. This led to disenchantment with the transplant team. Patients explained that they had kept their side of the bargain, taken the medicine, followed instruction and gone through unpleasant and painful procedures, but were deprived of their promised progress. Some refused any cooperation and would 'most certainly not answer any more of the researcher's questions', as one relapsed patient phrased it. However, after a moment's thought he added : 'Sorry love, it has nothing to do with you'. A similar phenomenon was reported by Kuechler et al. (1992), who stated that patients opted out of psychological research at times of dissatisfaction with the medical procedure.

8.1.4 Contextual Problems In Pursuance Of The Research

The research produced practical and intellectual problems for the researcher. Doctoral research is generally a solitary experience, pursued alone even though one's supervisor is present as a mentor and advisor. Such solitariness is particularly taxing while investigating this kind of treatment. As I continued the study, moving between 2 hospitals at different ends of London, I began to experience the need for the support of a team and I was fortunate to find this support in the team of Psychological Medicine at the Royal Marsden and in the individual support of my supervisor Dr. Margaret Wood. Despite this support , research work with this particular patient group proved to be emotionally highly taxing.

8.1.5 Sample Bias

A sample bias towards psychologically more resilient patients was due to two factors.

1. The bone-marrow coordinator on the ward in the Royal Marsden Hospital tended to 'select' patients for this study according to their perceived emotional strength. Patients who appeared 'nervous' were excluded. After some discussion with the BMT coordinator it was clear that I had no option but to accept her choice of patients for my research.

2. Patients with previous psychiatric histories were excluded.

8.2 Hypotheses

The stated hypotheses were looked at and are discussed in the following sections. In these sections I discuss the hypotheses in relation to all stages except stage 'Relapse' (stage III). This for the following reasons: this stage included a very small number (n=8); these patients needed immediate further chemotherapy and in several cases died very soon after relapse. However, this stage is discussed separately later.

In the following discussion significant data for the whole population and the groups are discussed and references are made to pages showing relevant graphs.

8.2.1. Hypothesis No. 1

It was hypothesised that:

1. The degree of Anxiety and Depression does not remain constant during the treatment. It is influenced by the changes in the medical treatment during the different stages.

This has been confirmed by the findings of the present study.

(Anxiety and Depression were measured on the Hospital Anxiety and Depression (HAD) Scale).

The literature about Bone Marrow Transplantation (BMT) stated repeatedly that psychological morbidity throughout transplant occurred mainly in the form of anxiety and depression and the implication was that these two tended to occur together. (Gordon, 1975; Gardner et al., 1977; Powazek et al. 1978; Gluckmann et al., 1979; Foester, 1984; Pot-Mees 1987; Lesko 1993).

However, data of the present study suggest that the occurrence and degree of anxiety and depression do not necessarily overlap, but each runs a distinct course throughout the BMT procedure. In this study both anxiety and depression were the main cause of emotional morbidity, but the course taken by anxiety and depression respectively followed an individual pattern. They did not increase necessarily during the same stages of treatment. At only one stage did both increase simultaneously. This was at the end of 'Conditioning' (stage 2). For the above reasons they will be looked at individually and not together as a single cause for emotional morbidity.

Anxiety

Anxiety was highest at stages 'Baseline' (stage 1) and 'Conditioning' (stage 2), thereafter anxiety tended to decrease steadily. At the 'Three Months' (stage 6) anxiety had significantly decreased from baseline assessment. This is reflected in the number of patients scoring above the cut-off point (scoring 8 and above) on the subscale Anxiety of the HADS and qualifying as 'cases' .

A comparison of anxiety scores between males and females showed a difference at 'Baseline' (stage 1) and 'Somnolence' (stage 5). At both stages females are significantly more anxious than males (p=0.03 at both stages) and this is reflected in the number of patients qualifying as 'cases'. (Baseline: M=19%; F= 30%; Somnolence: M=5%, F= 32%).

Epidemiological data presented by Weissmann (1985) from a large scale United States Community Survey reports for generalised anxiety that the rate for women is twice that for men. [1]

Other group differences in the level of anxiety occurred between patients in the two hospitals during three isolation stages: 'First 7 Days' (stage 3, p=0.09), 'Week 3' (stage 3b, p=0.01)) and 'End of Isolation' (stage 4, p=0.04). Patients at the Royal Marsden Hospitals scored significantly higher on the subscale 'anxiety' than those at the Royal Free Hospital at stage 'End of Isolation' (stage 4). Patients at the Royal Marsden Hospital increased their anxiety score on the HADS while those at the Royal Free Hospital had decreased scales.

Depression

For the whole sample 'depression' increased significantly at the end of the 'Conditioning' (stage 2) and continued to show significant increases from 'Baseline' (stage 1) throughout isolation until discharge. The number of patients scoring above the cut-off point (score of 8 and above) on this subscale and qualifying as 'cases' increased during isolation, rising to a peak during 'Week 3' (stage 3b) when 40% of all patients scored above the cut-off point. The first decline in depression from the 'Baseline' (stage 1) occurred at stage 'Twelve Months' (stage 7).

Comparing the groups Males and Females the differences in the scores relating to the percentages of 'cases' in depression between the two genders are significant at stage 'Somnolence' (stage 5) 26% for Males and 67% for Females (p=0.09) and stage 'Rehospitalisation' (stage II) 25% for Males and 80% for Females, (p=0.007).

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[1] Generalized Anxiety Rates/100 - Males: 4.3 / Females: 8.0

The difference cannot solely be explained by differences in Physical Symptoms (as measured on the Rotterdam Symptom Checklist (RSCL), which although higher for Females at stage 'Somnolence' (stage 5), were not significantly so. Other possible explanations arise from discussions with women during the recuperation phase. It appeared to the author that males were better supported and looked after by their families than females during these early weeks after discharge. Females implied in discussion that there was an expectation from their families that they should now be functioning at pre-treatment level and so should be able to look after the family rather than be in need of support and help from the family.

A comparison between the two hospitals showed no significant difference at 'Baseline' (stage 1) but significant differences throughout isolation until the 'End of Isolation' (stage 4). Patients at the Royal Marsden Hospital were significantly more depressed and showed a higher percentage of patients qualifying as cases 'cases'. (Stage 3 -p=0.04; 3a-p= 0.01; 3b: p=0.09; 3c: p=0.05; 4: p=0.01).

Possible explanations for these differences in depression are the differences in isolation procedures within the two hospitals. Isolation in the Royal Marsden is more exclusive of the patients' contact with visitors than is the case in the Royal Free Hospital as explained earlier. There are no comparative data showing the effect of the degree of isolation on patients' emotional morbidity . However, social support has been recognised to ease the time in isolation. It is far easier for the patient in the Royal Free to draw on this support than at the Royal Marsden, where visitors are clearly discouraged by the strict rules concerning access to the patient.

Other possible explanations for these findings are differences in physical symptoms between patients at the two centres throughout the isolation stages. Patients in the Royal Marsden Hospital score higher on physical symptoms, but the difference is only significant at stage 'End of Isolation' (stage 4).

A comparison between the two different types of transplant (i.e. Autologous and Allogeneic) showed that Allografts were more depressed at 'Baseline' (stage 1). (p=0.08) than Autografts. During isolation at 'Week 3' (stage 3b) the difference is significant (p=0.01), 'Week 2' (stage 3a) and 'Week 4' (stage 3c) the differences are not significant, but there is a trend. The Allograft group experienced more physical symptoms.

One explanation for the differences in the level of symptoms and ultimately in depression could be that Allografts need higher doses of chemotherapy during conditioning prior to transplant than Autografts (Lesko, 1993).

8.2.2. Hypothesis No. 2

It was hypothesised that:

2. The quality of life does not remain constant during the treatment. It is influenced by the changes in the treatment during the different stages.

This has been confirmed by the data of the present study.

Quality of Life was assessed on the Rotterdam Symptom Checklist (RSCL).

The two subscales 'Psychological Symptoms' and 'Physical Symptoms' are discussed separately. The two subscales follow differing courses.

Subscale 'Psychological Symptoms'

Data obtained in the subscale 'Psychological Symptoms' for the whole sample showed a comparable pattern to those obtained on the HAD subscale 'Anxiety', with a temporary increase at stages 'Conditioning' (stage 2), 'First 7 Days' (stage 3) and 'Week 4' (stage 3c). There were significant decreases at stages 'End of Isolation' (stage 4, $p=0.04$), 'Somnolence' (stage 5,$p=0.05$) and 'Three Months' (stage 6,$p=0.01$).

The similarity in the course of these two subscales may have arisen from the similarities of the items on the questionnaires. Five out of the eight items on the subscale 'Psychological Symptoms' are symptoms of anxiety. These are Nos: 2: 'Irritability'; 4: 'Worrying'; 9: 'Nervousness';18: 'Feel Tense'; 19: 'Anxious'.

Subscale 'Physical Symptoms'

The level of 'Physical Symptoms' for the whole sample increased significantly from 'Baseline' (stage 1) at the end of 'Conditioning' (stage 2), and these increases remained significant throughout Isolation (stages 3, 3a-c, 4), 'Discharge' (stage I), 'Somnolence' (stage 5) and until 'Rehospitalisation' (stage II). The highest level of physical symptoms was experienced within the first 2 weeks after transplant when the first wave of side-effects to the conditioning,

such as nausea, vomiting and muscositis occurred. Surprisingly, at 'Three Months' (stage 6) the level of side effects is still raised from baseline, although not significantly, and only at 'Twelve Months' (stage 7) post-transplant did it fall below baseline levels. Patients themselves have named the slowness for physical symptoms to lessen as discouraging throughout the period following discharge.

8.2.3. Hypothesis No. 3

It was hypothesised that:

3. The patient's attitude towards cancer does not remain constant during treatment. It is influenced by changes in the treatment during the different stages.

This has been confirmed by the data of the present study.

The attitude towards cancer was assessed on the Mental Adjustment to Cancer (MAC) Scale.

Data for the whole population from this present study suggest that scores on the MAC remained relatively stable throughout transplant. The notable exceptions are scores on the subscales Fighting Spirit and Helplessness. At stage 'Conditioning' (stage 2) scores on the subscale Helplessness showed a significant increase from 'Baseline' (stage 1) ($p=0.02$) and a decrease on the subscale Fighting Spirit ($p=0.08$). These changes from Baseline are reflected in a significant increase in the combined FSH-T scores which rise above the cut-off level (score 50 and above) at this stage ($p=0.02$). The T scores for FSH remain elevated and above the cut-off for 'cases' throughout Isolation (stages 3,3a-c,4), 'Discharge' (stage I), 'Somnolence' (stage 5) and until 'Rehospitalisation' (stage II) ($p=0.06$). At 'Discharge' (stage I) Helplessness was significantly increased from 'Baseline' (stage 1) ($p=0.05$) and the raise for FSH-T scores at this stage from 'Baseline' (stage 1) shows a trend ($p=0.06$). The T-scores for FSH only fall below cut-off at stage 'Three Months' (stage 6). Both Fighting Spirit as well as Helplessness show an improvement at stage 'Twelve Months' (stage 7); Fighting Spirit an increase and Helplessness a decrease.

Scores on the subscale Fatalism for the whole population were also significantly raised at Discharge (stage I, $p=0.04$) from Baseline.

Comparison between groups Autografts and Allografts show a significant difference between Fighting Spirit for at stage 'First 7 Days' (stage 3), Allografts showed a lower Fighting Spirit than Autografts. The difference could be explained by the higher doses of chemotherapy used in conditioning for ALLOGRAFT transplants and the observed higher levels of physical symptoms.

Patients at the Royal Marsden Hospital compared to patients at the Royal Free Hospital scored significantly higher on the subscale Helplessness at stages 2 and 'Conditioning' and 'First 7 Days' (stages 2 and 3).

A similar pattern to Anxiety (measured on the HAD) emerged for the MAC subscale Anxious Preoccupation for the whole population. The levels of Anxious Preoccupation rose from Baseline to stage 'Conditioning' (stage 2) and fell thereafter. However the APT scores remained elevated throughout the transplant procedure.

The group females scored significantly higher than males on Anxious Preoccupation at 'Baseline' (stage 1), 'Conditioning' (stage 2) and 'Rehospitalisation' (stage II) than Males. ($p=0.03$ for both stages).

Allografts scored higher on Anxious Preoccupation at Conditioning (stage 2, $p=0.09$) and First Seven Days (stage 3, $p= 0.04$), but Autografts scored higher at 'Rehospitalisation' (stage II, $p=0.06$). The elevated scores at stage 2 and 3 for the group Allograft can be accounted for by the difference in doses during treatment. The reversal at stage 'Rehospitalisation' (stage II) may reflect the pervasive fear of relapse patients with AUTOGRAFT continued to have, since they were reinfused with their own treated marrow. There was always a possibility that leukaemic cells did survive the treatment and had started to multiply and that rehospitalisation indicated a relapse of the original disease.

8.2.4. Hypothesis No. 4

It was hypothesised that:

4. Perception of control does not remain constant during the treatment. It is influenced by the changes in the treatment during different stages.

This has not been confirmed by the data of the present study.

8.2.5. Hypothesis No. 5

It was hypothesised that:

5. Emotional problems and emotional morbidity are expected to be higher in some stages than in others.

This has been confirmed by the data of the present study.

Emotional morbidity is looked at in the subsequent paragraphs in relation to the enunciated stages.

(i) The Pre-Transplant Period

This period includes the stages: Baseline (stage 1) and Conditioning (stage 2).

Decision For Transplant - 'Baseline' (Stage 1)

The decision for transplant has been considered a major stressor by Popkin & Moldow (1973) and Haberman (1988) insofar as patients are confronted with the uncertainty of treatment outcome. However, the evidence from the present study only partly support this: e. g. evidence from the questionnaire does support the notion that the decision for transplant is a potential stressor causing emotional morbidity. Twenty-four percent of the sample scored above the cut-off point and qualified as 'cases' on the HAD subscale 'Anxiety'. This high level of anxiety was only superseded at the end of the conditioning treatment, (Stage 2), when 26% scored above the cut-off for anxiety. At all later stages, with the exception of 'Relapse' (Stage III), levels of anxiety decreased.

However, evidence from interviews with patients indicated that patients did not experience the decision as a difficult or stressful process. In this study 64 % of the patients interviewed found the decision for transplant an easy one and only 11 % a difficult one. The remaining 25% reported that there was no decision to be made. This is not surprising since BMT was introduced to half of this group (50%) at the time of their diagnosis almost as the next step in their outlined treatment plan. This made an active consideration of possible alternative

treatments redundant. The majority of patients (73 %) did not perceive an active choice.

These conflicting data may have arisen from different time perspectives. Questionnaire data collected during the first assessment at Baseline did not coincide with the decision for transplant but were collected after the decision had been made and reflected the patient's psychological status at the time of assessment rather at the time of their decision. The interview data recorded patients' retrospective assessment of the decision making process and their perception of it. It may well be that patients recalled this decision to be an easy one once it had been made. The high level of anxiety, on the other hand, may reflect anticipatory anxiety with regards to the transplant ahead.

Haberman (1988) and Lesko (1989) argued that hope for 'cure' is a decisive factor in making the decision for transplant. Hopes for this treatment are high in this sample of patients. Seventy-three percent expected to be cured and to lead a normal life thereafter, while the other third expected a prolonged life of better quality. Other authors argued that without this hope patients would not agree to the transplant procedure. The latter was not confirmed by this study where patients did not have considered alternative treatment options but considered BMT as part of their total treatment for their disease. Very few patients (12%) based their expectations on their beliefs, most (56%) explained that they arrived at these expectations from discussions with their doctor either at the specialist unit or their own hospital where they were diagnosed. Certainly, considering the number of long-term survivors in this study, patients' expectations of their chances of survival are very inflated. However, these high expectation were, at least in part, based on medical influence. BMT was not introduced as a final rescue procedure at the end of a patient's treatment career but at the beginning as part of the treatment plan. It confirms Philips' (1988) cautioning when he advised his colleagues that;

> " Although it is very unlikely that a member of the transplant team would deliberately mislead a patient, the mere fact of his or her enthusiasm for marrow transplantation might subtly influence a patient to accept marrow transplantation rather than more conventional therapy". p.26.

Conditioning For Transplant - 'Conditioning' (Stage 2)

This stage commences with preparing the patient for transplant. At the beginning of the stage this includes familiarisation with the transplant unit and meeting with the Bone Marrow Coordinator. Later on this stage includes the conditioning of the patient for transplant, that is, administration of high doses of Chemotherapy, or Chemotherapy +Total Body Irradiation (TBI). During this stage patients were admitted to hospital and entered isolation.

Psychological assessment took place at the end of this stage after completion of the conditioning procedure a day after transplant.

The stage 'Conditioning' (stage 2) has received very little attention by researchers in Bone Marrow Transplantation. Despite the considerable number of papers based on observations of patients, very few refer to the psychological side-effects of this period. (Cohen et al., 1977; Gardner et al., 1977; Farkas-Patenaude et al., 1979; McGahan Hutchinson & Hubbard King, 1983; Lesko, 1986, 1989).

Popkin & Moldow (1977) condensed it into an "interval and ordeal to be bridged in order to reach hope", but did not consider it a major stressor.

Data from this study, however, strongly indicate otherwise. The evidence emerged from these data suggest that this is a major stressor and far from being an interval to be bridged it leaves the patients psychologically very vulnerable for the succeeding period in isolation.

Data of all the measures given to patients at this stage indicate an increase in psychological vulnerability and morbidity. Patients scored worse on all psychological and physical measures at this stage. Patients scored their highest levels of anxiety throughout transplant; showed significant increases in depression (HAD); scored significantly higher on 'Physical Symptoms' and higher on 'Psychological Symptoms' on the Rotterdam Symptom Checklist; showed less 'Fighting Spirit'; significant more 'Helplessness'; increased 'Anxious Preoccupation' and increased 'Fatalism' (MAC) compared to 'Baseline' (stage 1).

Morbidity in the whole sample population in the form of 'cases' as measured on the HAD subscales Anxiety and Depression increased. (Anxiety to 26%, and Depression to 34%). Morbidity in the form of combined Fighting Spirit/Helplessness (FSH) T-scores on the MAC-Scale increased significantly from baseline. ($p=0.02$)

The stage 'Conditioning' (stage 2) is a critical period during the BMT procedure which causes high levels of psychological vulnerability and morbidity. At no other stage do patients show a deterioration on all measures combined.

(ii) The Immediate Post-Transplant Period

The immediate post transplant period includes the time spent in isolation and the period after discharge until 'Three Months' (stage 6). It includes the stages in isolation, that is: 'First 7 Days' (stage 3) and the weekly assessments (stages 3a, 3b and 3c) until 'End of Isolation' (stage 4). The immediate post-transplant period also includes the stages 'Somnolence' (stage 5) and 'Three Months' (stage 6), Discharge (I) and Rehospitalisation (II). During this post-transplant period patients are usually discharged and very often re hospitalised.

Protective Isolation -Stages 3, 3a., 3b, 3c, and 'End of Isolation' (Stage 4)

Popkin and Moldow (1977) and Haberman (1988) named isolation and adjustment to isolation as an important environmental stressor over a prolonged period of time and subsequent emotional morbidity has been frequently observed. However, during isolation only a minority quoted isolation-related problems as upsetting. At the 'End of Isolation' (stage 4) only 20% of all cases named isolation as the most upsetting event. (Stages: Conditioning 14%; First 7 Days: 17%, End of Isolation: 20%). It may be that it was easier for patients to admit retrospectively to the difficulties experienced during isolation than during isolation itself.

Anxiety was highest at stage 'Conditioning' (stage 2) at the beginning of isolation, and thereafter it decreased. This corresponded with Gordon's (1975) findings that patients were more anxious at the beginning of isolation, but anxiety decreased and tolerance of isolation increased with increasing time spent in isolation.

However, Gordon (1975) also reported that in his observations anxiety tended to return at times of physical deterioration. The present data did not confirm this. At times of increased physical symptoms there was no increase in anxiety. However, this applies only to patients who were well enough to be assessed; a considerable number were not and by the end of isolation 18 patients had died.

Emotional morbidity in the form of depression, however, emerged as the biggest problem during isolation and is highest ' Week 3' (stage 3b) after transplant with

40% of all assessed patients scoring above the cut-off point (8 and above) on the subscale 'depression' and qualifying as 'cases'. However, at the 'End of Isolation' (stage 4) 25% of all assessed patients still scored above the cut-off point qualifying as 'cases.'

Helplessness was quoted and attributed to the loss of ability of self-government , i.e. dependency and not being able to do things for oneself, by Koehle et al., (1971); Cohen et al., (1977); Rooyman et al., (1979) and Foester, (1984).

This was confirmed by data collected on the Mental Adjustment to Cancer (MAC) Scale. Helplessness significantly increased from 'Baseline' (stage 1) at 'Conditioning' (stage 2) and remained high throughout isolation in combination with a decrease in patients' Fighting Spirit. The Combined FSH-T scores during isolation were above the cut-off point (50 and above) for emotional morbidity.

Other severe psychological problems mentioned in the literature are: hallucinations (Popkin & Moldow,1977); cognitive impairment and paranoid ideas about being poisoned, (Koehle et al., 1971). The latter were not observed among patients who were assessed. However, cognitive impairment in the form of confusion was observed by the author of the present study in patients severely ill, but these were not documented.

The above findings relating to emotional morbidity during isolation are in contrast to those reported by Holland et al. (1977). These researchers had found no depression nor anxiety in a group of 52 adult patients in isolation, who managed to maintain emotional stability throughout. (See introduction, page 30).

The majority of researchers in this field see psychological disorders as consequences of medical complications such as high temperatures and not of isolation per se; and argue that psychological and psychiatric conditions are most strongly influenced by patients' somatic conditions. (Fine et al., 1974; Koehle et al., 1971; Holland et al., 1977; Gluckman et al., 1979; Gordon 1975).

Discharge

Lesko (1993) reported that during convalescence, anxiety and depression are by far the most common psychiatric sequelae of the transplantation procedure. Data from this study only partially support this statement. Depression remained a problem for the population in this study during this period, but not anxiety.

Discharge is the gate to convalescence and according to the published literature this time is viewed with fears of leaving the security of the transplant unit and a resulting rise of anxiety has been reported among discharged patients. (Popkin et al., 1977; Freund et al., 1985; Freund & Siegel, 1986; Lesko, 1986; Hengelveld et al., 1988).

The present data do not support these previous findings. Emotional morbidity does not increase at 'Discharge' (stage I). On the contrary, the levels of anxiety and depression fell further when patients were discharged. Anxiety showed a significant decrease (2-tailed p=0.04) at 'Discharge' (stage I) from 'Baseline' (stage 1), and the percentages of cases fell to 8% at 'Discharge' (stage I) compared to 19% at the 'End of Isolation' (stage 4). Anxious preoccupation, too, showed a decrease from 'Baseline' (stage 1).

Patients' quality of life on the Rotterdam Symptom Checklist showed also improvement at this stage. Psychological symptoms are significantly lower than at Baseline. Although physical symptoms at this stage are still higher than at Baseline they are starting to decrease.

Mental Adjustment to Cancer showed different results at this stage for Anxious Preoccupation and Helplessness. The APT-scores are still above cut-off for morbidity. Helplessness is significantly raised from 'Baseline' (stage 1) (p=0.05) and so are the FSHT-scores but not significantly. There is, however, a trend. (2-tailed p=0.06)

One could speculate that patients although not anxious about leaving hospital feel helpless in relation to how to deal with possible emergencies away from the security of the transplant centre where medical help and expertise was always readily available.

Nonetheless, patients were not afraid, only 6% voiced fear of leaving Hospital.

Somnolence Stage 5

This stage was added to assess the effects of Total Body Irradiation on patients. The consultant in charge at the Royal Marsden Hospital had observed that patients tended to be very 'depressed' during this period.

Results did not support this notion. Although depression was still raised from 'Baseline' (stage 1) for the first time since 'Conditioning' (stage 2) it was not significantly ($p=0.12$) raised from 'Baseline' (stage 1) and Anxiety was significantly decreased ($p=0.02$) from 'Baseline' (stage 1). However, there is a slight increase in the level of Physical Symptoms compared to stages 'Discharge' (I) and 'Rehospitalisation' (II), indicating that somnolence is above all a physically trying time for patients. Patients during this period tend to be sleepy and inactive and this state may have been interpreted as depression rather than as a delayed physical side effect to TBI.
Data do not support the need for this stage.

Rehospitalisation Stage II

Sixty percent of patients rehospitalised named this event as the most upsetting and 22% experienced it as discouraging. This was reflected less in their levels of anxiety than in their levels of depression. Thirty-four percent scored above the cut-off for 'cases' on the subscale' depression' of the HAD. The combined T-score for Fighting Spirit and Helplessness on the MAC-Scale was highest at this point[2], indicating that this group of patients experienced increased helplessness and decreased fighting spirit to face this challenge. However, from the interviews it seems that this group did not experience fear. Eighty percent did not report any fear of the consequences of being rehospitalised at this stage.

Although Hengelveld et al. (1988) reported that patients were aware that infections may lead to rehospitalisation when rehospitalisation was necessary 12 out of 17 patients in their sample felt not sufficiently prepared for complications and rehospitalisation. Stream (1983) found that patients attending the out-patient clinic after BMT viewed readmission as a major set-back.

[2] There were not enough cases to allow statitical analysis at this point.

At Three Months (Stage 6)

At 'Three Months' (stage 6) patients are significantly less anxious than at Baseline ($p=0.02$) but they are still very vulnerable and 10% still scored above the cut-off point for 'cases' on the HAD subscale Anxiety and twenty-one percent still score above the cut-off for cases on the HAD subscale Depression. However, patients at 'Three Months' (stage 6) show less Helplessness and greater Fighting Spirit on the combined FSH T-score, falling for the first time below the cut-off for emotional morbidity.

Quality of Life has further improved, psychological symptoms are significantly less than at 'Baseline' (stage 1) ($p=0.01$) but physical symptoms remain higher than at 'Baseline'.

Nonetheless, 48% named disease and treatment related problems as the most upsetting events at this time;whereas for 10% is was rehospitalisation and for 10% relapse.

(iii) The Late Post-Transplant Period

It is difficult to draw valid conclusions from the existing literature about emotional problems occurring during the three to twelve month period, although there is a considerable body of published work about the long term survivor. (Wolcott et al., 1986; Hengelveld et al., 1988; Andrykowski et al., 1989; Andrykowski et al., in print). Included in this period fall the stages 'Twelve Months' (stage 7) and 'Relapse' (stage III).

'Twelve Months' -(Stage 7)

The Post-transplant period of convalescence lasts according to Lesko (1986) up to one year. Data from patients who survived until this time showed a great improvement in their psychological well-being on all dimensions assessed. At this stage Anxiety and Depression were less than at 'Baseline' (stage 1), Anxiety significantly so ($p=0.03$). However, a surprising 20% of all surviving patients still scored above the cut-off point for cases on the subscale' depression'.

Quality of Life as measured by the RSCL had improved and physical symptoms had significantly decreased from Baseline ($p=0.02$). Despite the improvements in quality of life 29% found the disease and treatment related problems experienced at this stage discouraging. Fourteen percent reported that they felt scared when going for an appointment at the hospital. This is in agreement with reports from the literature indicating that for the-long term survivor fear of medical complications requiring rehospitalisation and of relapse was ever present.

The present data confirmed Andrykowski et al.'s (1989) finding that there is a period until a year post- transplant characterised by significant improvement in functioning. Their study suggests that patients may reach a ceiling within approximately two years post-transplant. In this study patients were not followed beyond the 'Twelve Months' (stage 7) assessment.

Relapse

At stage 'Relapse' (III) numbers were very small and were treated with caution.

Alby et al. (unpublished paper) found that the fear of relapse was ever present in long-term survivors and relapse did occur for 14% of the sample of the present study. Although the fear of relapse experienced by long-term survivors has been mentioned (by Andrykowski et al., 1989 and Alby et al., unpublished paper) there exists no literature which looks at the psychological and social impact that relapse may have on the lives of the long-term survivors.

Relapse of cancer has been identified in other cancers as an extremely stressful event. Silberfarb et al. (1980). Relapse of the original disease led to an increase in psychological distress, particularly in the form of anxiety and depression. Psychological distress was paired with a negative attitude towards the primary physician.

In the present study adverse reactions were observed on all measures used. 'Relapse' is no doubt a very trying event for patients. The number in the present study was too small to allow greater interpretation of the presented data. However, this event at the end of all the physical and emotional distress caused during transplant was a very sad event for the patient, the family and the staff. It was not always handled well by the staff. On more than one occasion the author of the present study observed the helplessness of the consultant dealing with relapsed patients. It was apparent in discussions between patient and consultant. There was a reluctance to acknowledge, that a patient had reached the end of the road.

8.2.6 Hypothesis No. 6

It was hypothesised that:

6. Patient's expectation of treatment outcome does not remain constant. It changes over time and stages.

This hypothesis was only partially confirmed by the data from the interviews conducted with patients. Usually expectations remained stable throughout the transplant procedure, but did change in response to dramatic events, such as relapse, which alter medical realities for the patient.

The majority of patients remained stable and unchanging in their expectations. At 'Baseline' (stage 1) 73% expected to be cured and to lead a normal life thereafter, and this expectation remained the same throughout almost all stages of the transplant procedure. However, there were two exceptions to this: these were expectations at stages 'Rehospitalisation' and 'Relapse' (II and III). At 'Rehospitalization' (stage II) 12% reported that their expectations had changed slightly for the worse. At 'Relapse' (stage III), however, this number rose to 67%, and patients reported that their expectations had changed considerably for the worse. Nonetheless 33% did not perceive a change, even at this stage. At 'Relapse' (stage III) patients hoped merely for an improvement in their health status. They no longer talked about cure or the possibility of living a normal life normal life.

At 'Relapse' (III) numbers were very small and should be treated with caution.

8.3 Other Factors Influencing The Transplant Experience

In the following sections other factors influencing the experience of the transplant procedure are discussed.

8.3.1 Mediating Factors

These factors were found to be support, information, available coping strategies and religious beliefs.

(i) support

Popkin & Moldow (1977) argued patients require substantial support from both family and staff and that this support can ease the isolation experience and Lesko (1986) reported that families were asked to visit the patient daily for support.

The present data confirmed the important role of the family in supplying support for the patient. The main source of support was provided by patients' families; this included siblings and parents as well as the partner. Friends, too, played a considerable role in supporting the patient. Data suggest that the source of support did not remain static but changed over time. Throughout isolation, during stages 'Conditioning' (stage 2), 'First 7 Days' (stage 3) and 'End of Isolation' (stage 4) a large number of patients (at stage 3- 36%) drew support from the staff, mainly nursing staff. This source of support became less and less important as patients entered the late post-transplant period when the family became again the main source support.

The importance of the family throughout the transplant procedure is confirmed by data obtained from interviews with the Significant Other in the Study of the Relatives. Eighty-seven percent of this group visited the patient daily while in isolation. They could often be seen sitting in patients rooms keeping the patient company, reassuring, helping and supporting.

However, at the very time when the patient is most in need for support from the family and friends this support is least encouraged and facilitated due to the strict isolation procedures on the wards. In the Royal Marsden Hospital visitors are actively discouraged. They are not allowed into the room; except for one

previously selected relative, they have to stand in the corridor conversing with the patient through a plastic window. The author feels that part of the significant difference in depression found between transplant patients in the two hospitals during the isolation period is due to the different attitude between the two hospitals towards relatives and friends in their restriction of support for the patient.

In the BMT literature social support, or lack of social support, was found to be a factor in the severity of depression in a stage related study by Baile et al. (1992)

(ii) Information

Information provided by the medical team to patients in this study was on the whole perceived as sufficiently informative by patients. However, there are two stages in this study when a number of patients expressed that they did not have enough inforrmation. These are the stages 'Conditioning' (2) and during 'Rehospitalization' (stage I).

At 'Rehospitalization' (stage II) a variety of causes lead to rehospitalisation These ranged from infections to complications caused by the GvHD syndrome. It is impossible to predict for any individual whether rehospitalisation is necessary and if so what kind of complication might arise to lead to rehospitalisation. In view of these two factors it is not surprising that information provided could not cover all possible eventualities and was by its very nature perceived as inadequate.

However, the perceived lack of information voiced by 17% at stage 'Conditioning' (stage 2) is less explicable. Conditioning is routinely administered in these two centres and patients are provided with information packages regarding the procedure and its short and long term side effects.

It is not within the scope of this study to provide an answer whether these shortcomings of information at 'Conditioning' (stage 2) were due to a lack of information provided in the first place, or due to the way information was presented to patients which made it ill understood and easily forgotten. The issue, however, needs to be addressed by the staff involved with providing information leading to the transplant procedure.

(iii) Coping Strategies

Coping strategies do not remain static but tend to change over time and stages. No one coping strategy emerged as the answer to how a patient might cope best during the transplant procedure. It appears that patients were flexible in the coping strategies they employed and these strategies appear on the whole appropriate.

During 'Conditioning (stage 2) and at 'Twelve Months' (stage 7) a quarter of patients quoted a 'positive attitude' as the most frequently employed coping strategies.

However throughout isolation the strategy 'trying to keep busy' was employed by a third of patients. While 22% of patients at 'Discharge' (stage II) said that they take the difficulties of readjustment to life outside the hospital on a 'day to day' basis.

At 'Relapse' (stage II) 'trust in doctors' was a strategy employed by 25% of those who relapsed.

(iv)) Religious Beliefs

In conclusion approximately half of the patients felt at times supported by their religious beliefs, the other half did not. Data do not allow a firm conclusion.

8.3.2 Factors Contributing To Distress

3. Are stressful events common to all patients or are they experienced by more vulnerable patients? (i.e. patients showing high levels of anxiety and depression).

On the whole their appeared to be an agreement among patients interviewed that treatment related events and procedures such as TBI , infections and very often at a later stage the time it took for these problems to resolve caused most distress. However, the death of a fellow patient was an event causing surviving patients to feel upset. (See section below).

8.3.3 Fellow Patients

Factors contributing to easing isolation included the support provided by fellow patients in isolation. (Holland et al., 1977; Rooymans et al., 1979; Farkas Patenaude & Rappeport , 1982). Patients were usually away of other patients undergoing transplant and kept in tough with them. They had met them prior to transplant either on the ward or in the out-patient waiting areas. When the patient in the other bed died patients are very upset. The death of a fellow patient was quoted by patients as the most difficult time during isolation. (Patenaude & Rappeport, 1982). This was confirmed by the data from this study but not at the time when it was most likely to occur, that is during isolation.

At Twelve Months post transplant (stage 7) the most upsetting event quoted by 40 % of patients was the death of a fellow patient. Patenaude and Rappeport (1982) reported that the death of a fellow patient is the most difficult time and patients coped by denying the significance of the death of another transplant patient for them. Although denial was not looked at, it was only from the 'safe' distance of a year post-transplant that patients could admit the impact of the death of a fellow patient.

8.4 Data From Interviews With The Relatives

Alby (1991) pointed out how easy it is for families to feel like outsiders and helpless spectators. From the observations of the author of this study the ward structures are certainly organised to increase these feelings.

The Significant Other was interviewed at three months post-transplant. How did this important group experience the time of transplant? Data from these interviews indicate that their supportive function was already evident at the time of the initial discussion of BMT as a treatment option and 88% of the relatives interviewed had attended this discussion.

Although on the whole satisfied with the information provided during this discussion, a quarter (26%) would have liked to spend some more time on discussing side effects, management and emotional problems, and 46% did not feel themselves able easily to ask questions. Fifty-four percent reported unexpected side effects experienced by the patient; among these side-effects were those occasioned by GvHD and also the psychological effects such as depression.

Information gathered by the relatives fulfilled an important function. Rait & Lederberg (89) report that support for the patient in isolation takes the form of collecting information at times of decision making when the patient is unable to manage to do this for him/herself. During these times the family takes over the decision making process.

From the above answers outlining the problems with collecting information this sample was unable to fulfil the described functions in case of need. These were the relatives of surviving patients. They may not have been confronted with the task to make decisions for the patient. However, when patients are too ill, information gathering and decision making falls onto the relatives and they did not find it easy to collect information.

From the answers given by the relatives it was not clear whether the difficulties experienced by the relatives in asking the staff questions was due to staff reluctance in answering these questions or whether these busy wards did not encourage exchange of information.

The three most frequently quoted sources of distress experienced by the relatives came from the patient feeling low, in pain and vomiting. This has been observed by other researchers in this field. Popkin et al. (1977) reported a relationship between the medical state of the patient and the stress experienced by the family.

During this first three months period relatives were mainly supported by their own family (36%) and by friends (28%), but 36% found support from organisations and professionals.

From these interviews it emerges that 74% would make use of professional help if the hospitals were to offer it.

Andrykowski et al. (1993) found that 68 % of an interviewed cancer population sample found love for and relationship with the partner improved due to the experience with cancer in more than half of their sample. In the present study 18% of the interviewed relatives reported positive changes in their relationship with the patient after transplant and 8% positive changes in the personality of the patient.

In conclusion the relatives of patients are expected by others -' medical staff especially - and by themselves to be able to contain their feelings and function supportively toward the patient'. (Rait & Lederberg, 1989). The need for the family's support is acknowledged (Tebbi et al. 1985; Rait & Lederberg, 89), although the form and content of this support have rarely been elaborated, nor how these relatives should be supported themselves.

8.5 Conclusion

The published literature in BMT has tended to repeat observations until they appeared to become established findings, which are no longer challenged e.g. when talking about emotional morbidity Anxiety and Depression were always quoted together. But data from this research suggest that they take a very diverse course throughout the treatment. Anxiety peaks at the end of 'Conditioning' (stage 2) and then diminishes while depression becomes the main psychological problem from this stage onwards throughout BMT.

It is depression which needs to be observed and treated. However, the staff, though highly trained in oncology, was not necessarily trained to assess depression correctly. The author of the present study repeatedly experienced that anxious patients were readily identified by the nursing staff and subsequently referred to professionals in the hospitals, but depressed patients were only identified through the questionnaires administered in the course of this study. Symptoms of depression were interpreted as treatment side effects.

8.5.1 What I Would Have Done Differently

What should have been looked at:
Patients felt ill prepared particularly for emotional and sexual problems. Sexual problems were not investigated but should have been. Future research has to take the impact BMT has on this important aspects of patients' life into account. This area cetainly needs more research.

8.5.2 Critical Aspects /Stages

Although a theory of stages offers itself as extremely useful to the psychological researcher in the field of BMT, we must remember that with leukaemic patients the stages are imposed from the outside, by the medical procedure they have elected to undergo. Formulated stages in this study of research do not represent the process of healthy development. Indeed, they could even be construed as the opposite of, e. g. Piaget's continuum, as more and more is taken away from the patient (hair, appetite, human company, libido) during the attempt to cure.

Stages during this study have been a valid and useful framework for assessing emotional problems throughout the transplant procedure. They will be useful frameworks for future approaches allowing prediction of psychological responses which can be expected at given stages.

Not all stages found useful for this research need to be maintained for support and treatment planning. The division of stage 'Isolation' (stage 3) into weekly assessments was necessary and helpful to establish whether a relationship exists between length of isolation and responses in the form of Anxiety and Depression and Physical Symptoms. However, as a basis for treatment and support guidelines this division is not strictly necessary. Isolation, commencing at the end of the stage 'Conditioning' (stage 2) and concluding with the lifting of isolation requirements is the most distressing period for the majority patients. The period after 'Isolation' (stage 3) contained stages 'Discharge' (stage (I), 'Somnolence' (stage 5), 'Rehospitalisation' (sage II) and 'Three Months' (stage 6) , the late post-transplant period contains stages 'Twelve Months' (stage 7) and stage 'Relapse' (sage III).

The concept of stages is necessary to this particular treatment, it has been shown to be helpful, however experience now indicates, that the stages seemingly most helpful for patients' psychological support and management should be as follows:

Stage 1 DECISION FOR TRANSPLANT

This stage covers the period leading up to the patient's decision for transplant.

Stage 2 CONDITIONING

This stage covers the period from the decision for transplant until the conclusion of conditioning for transplant including transplant itself.

Stage 3 ISOLATION

This stage covers the period in isolation.

Stage 4 THREE MONTHS

This stage covers the period from the end of isolation until three months. During this period particular attention has to be paid to patients' first rehospitalisation after discharge.

Stage 5 TWELVE MONTHS

This stage covers the first year after transplant. During this period particular attention has to be paid to the relapsed patient.

These are the six stages proposed as a framework for the management of patients undergoing Bone Marrow Transplantation.

8.6 Recommendations

From the data of the presented research it emerged that patients and their relatives need more support, better support and more specific support.

This support should be in the form of more information during the time preceding transplant and leading up to transplant. Support should be in the form of easier access to families and friends willing to support the patient with their visits and presence. This view is shared by Alby (1991). She expresses her view by saying " patients and families need to be carefully prepared for hospitalisation". They should be allowed to express their anxieties, their anger and their ambivalent emotions. They should also be allowed to question.
Finally, support has to be provided by professionals for patient, relatives and the staff.

Alby (1991) stresses that psychological and social support for these families should be an integral part of the patient's care and should be provided throughout transplant. She stresses that support 'must begin before transplantation and last until a total physical and psychological recovery is achieved'.

Providing psychological care- requires extensive knowledge and familiarity with psychological stages of this procedure, (confirmed by Lesko, 1993). The professional providing support must be familiar with coping strategies available and primarily used by this group during different stages and with aspects of the treatment which increase distress and those which mediate stress.

Guidelines for staff need to be provided to strike a balance between isolation procedures protecting the patient on the one hand but allowing access to relatives and friends on the other. This is particularly important considering the evidence from this study which strongly suggest that strict isolation can increase patients psychological distress. Furthermore, there is evidence from a prospective study by the Seattle Transplant team reported by Peterson et al. (1987) that patients survive when nursed in a conventional hospital room without special isolation procedure. Patients were followed for 100 days and the differences in isolation did not effect survival during this period.

The role of the liaison psychologist and/or psychiatrist needs to be defined. This professional needs to be a full member of the team involved in the patient's care from the very beginning of the treatment.

Support needs to be extended to patients' relatives and the staff. Patients, relatives and staff are particularly in need of support when a patient on the ward dies. Partenaude & Rappeport (1982) recommend that this support should include discussions of the circumstances of the death and the similarities and differences in the patient's courses. It should include encouragement for the staff, and information to the staff about the meaning of a fellow patient deaths to other patients. Staff should be given the opportunity to discuss the implications of a death for patient care.

This study has above all shown that Bone-Marrow-Transplantation is psychologically a very demanding treatment on all individuals involved with it.

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X APPENDICES I

1. The Hospital Anxiety and Depression (HAD) Scale (Zigmond & Snaith, 1982)
2. The Rotterdam Symptom Check List (RSCL) (de Haes et al ,1990)
3. The Mental Adjustment to Cancer (MAC) Scale (Watson et al., 1988)
4. The Cancer Locus of Control (CLOC) Scale (Watson, Pruyn, Greer & Van Den Borne, 1990)
5. Interview Questions for Patients

HAD Scale

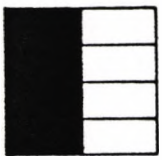
ame: Date:

octors are aware that emotions play an important part in most illnesses. If your doctor knows about these feelings he will be able to elp you more.
his questionnaire is designed to help your doctor to know how you feel. Read each item and place a firm tick in the box opposite the ply which comes closest to how you have been feeling in the past week. or if less since I last saw you
on't take too long over your replies: your immediate reaction to each item will probably be more accurate than a long thought-out sponse.

Tick only one box in each section

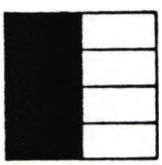
feel tense or 'wound up':
- Most of the time .....
- A lot of the time .....
- Time to time, Occasionally .....
- Not at all .....

still enjoy the things I used to enjoy:
- Definitely as much .....
- Not quite so much .....
- Only a little .....
- Hardly at all .....



get a sort of frightened feeling as if omething awful is about to happen:
- Very definitely and quite badly .....
- Yes, but not too badly .....
- A little, but it doesn't worry me .....
- Not at all .....

can laugh and see the funny side of hings:
- As much as I always could .....
- Not quite so much now .....
- Definitely not so much now .....
- Not at all .....



Worrying thoughts go through my nind:
- A great deal of the time .....
- A lot of the time .....
- From time to time but not too often ...
- Only occasionally .....

feel cheerful:
- Not at all .....
- Not often .....
- Sometimes .....
- Most of the time .....

can sit at ease and feel relaxed:
- Definitely .....
- Usually .....
- Not often .....
- Not at all .....

I feel as if I am slowed down:
- Nearly all the time .....
- Very often .....
- Sometimes .....
- Not at all .....

I get a sort of frightened feeling like 'butterflies' in the stomach:
- Not at all .....
- Occasionally .....
- Quite often .....
- Very often .....

I have lost interest in my appearance:
- Definitely .....
- I don't take so much care as I should.....
- I may not take quite as much care .....
- I take just as much care as ever .....

I feel restless as if I have to be on the move:
- Very much indeed .....
- Quite a lot .....
- Not very much .....
- Not at all .....

I look forward with enjoyment to things:
- As much as ever I did .....
- Rather less than I used to .....
- Definitely less than I used to .....
- Hardly at all .....

I get sudden feelings of panic:
- Very often indeed .....
- Quite often .....
- Not very often .....
- Not at all .....

I can enjoy a good book or radio or TV programme:
- Often .....
- Sometimes .....
- Not often .....
- Very seldom .....

Do not write below this line

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These questions ask about your symptoms. Read each item and place a firm tick in the box opposite the reply which comes closest to how you have been feeling during the last week or if less since I saw you last.

1 Lack of appetite

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

2 Irritability

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

3 Tiredness

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

4 Worrying

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

5 Sore muscles

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

6 Depressed

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

7 Lack of energy

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

8 Pain

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

9 Nervousness

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

10 Nausea

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

11 Feel desperate about the future

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

12 Difficulty in falling asleep

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

13 Headache

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

14 Vomiting

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

15 Dizziness

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

16 Lack of sexual interest

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

17 Feel lonely

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

18 Feel tense

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

19 Anxious

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

20 Constipation

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

21 Diarrhoea

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

22 Heartburn, belching

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

23 Shivering

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

24 Tingling hands/ feet

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

25 Awaking with a start

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

26 Pain in mouth when swallowing

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

27 Loss of hair

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

28 Burning eyes

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

29 Short of breath

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

30 Dry mouth

- Not at all ☐
- A little ☐
- Somewhat ☐
- Very much ☐

MAC SCALE

Name: _____ **Date:** _____

A number of statements are given below which describe people's reactions to having cancer. Please circle the appropriate number to the right of each statement, indicating how far it applies to you at present For example, if the statement definitely does not apply to you then you should circle 1 in the first column.

		Definitely does not apply to me	Does not apply to me	Applies to me	Definitely applies to me
1.	I have been doing things that I believe will improve my health e.g. changed my diet	1	2	3	4
2.	I feel I can't do anything to cheer myself up	1	2	3	4
3.	I feel that problems with my health prevent me from planning ahead	1	2	3	4
4.	I believe that my positive attitude will benefit my health	1	2	3	4
5.	I don't dwell on my illness	1	2	3	4
6.	I firmly believe that I will get better	1	2	3	4
7.	I feel that nothing I can do will make any difference	1	2	3	4
8.	I've left it all to my doctors	1	2	3	4
9.	I feel that life is hopeless	1	2	3	4
10.	I have been doing things that I believe will improve my health, e.g. exercised	1	2	3	4
11.	Since my cancer diagnosis I now realise how precious life is and I'm making the most of it	1	2	3	4
12.	I've put myself in the hands of God	1	2	3	4

	Definitely does not apply to me	Does not apply to me	Applies to me	Definitel applies to me
13. I have plans for the future, e.g. holiday, jobs, housing	1	2	3	4
14. I worry about the cancer returning or getting worse	1	2	3	4
15. I've had a good life what's left is a bonus	1	2	3	4
16. I think my state of mind can make a lot of difference to my health ...	1	2	3	4
17. I feel that there is nothing I can do to help myself ...	1	2	3	4
18. I try to carry on my life as I've always done	1	2	3	4
19. I would like to make contact with others in the same boat	1	2	3	4
20. I am determined to put it all behind me	1	2	3	4
21. I have difficulty in believing that this happened to me	1	2	3	4
22. I suffer great anxiety about it	1	2	3	4
23. I am not very hopeful about the future	1	2	3	4
24. At the moment I take one day at a time	1	2	3	4
25. I feel like giving up	1	2	3	4
26. I try to keep a sense of humour about it	1	2	3	4
27. Other people worry about me more than I do	1	2	3	4

	Definitely does not apply to me	Does not apply to me	Applies to me	Definitely applies to me
28. I think of other people who are worse off	1	2	3	4
29. I am trying to get as much information as I can about cancer	1	2	3	4
30. I feel that I can't control what is happening	1	2	3	4
31. I try to have a very positive attitude	1	2	3	4
32. I keep quite busy, so I don't have time to think about it	1	2	3	4
33. I avoid finding out more about it	1	2	3	4
34. I see my illness as a challenge	1	2	3	4
35. I feel fatalistic about it	1	2	3	4
36. I feel completely at a loss about what to do	1	2	3	4
37. I feel very angry about what has happened to me ...	1	2	3	4
38. I don't really believe I had cancer	1	2	3	4
39. I count my blessings	1	2	3	4
40. I try to fight the illness	1	2	3	4

Below are a number of statements relating to your illness.

Please indicate to what extent you agree or disagree with each statement by circling one of the numbers as follows:-

1 if you completely disagree' with the statement
2 if you slightly disagree' with the statement
3 if you slightly agree' with the statement
4 if you completely agree' with the statement

Please give an answer for every statement

		Completely Disagree	Slightly Disagree	Slightly Agree	Completely Agree
1.	I can definitely influence the course of my illness	1	2	3	4
2.	My doctor can definitely influence the course of my illness	1	2	3	4
3.	My spouse/partner/ family can definitely influence the course of my illness	1	2	3	4
4.	By taking care of myself (i.e through exercise & diet) I can influence the course of my illness	1	2	3	4
5.	By living healthily I can influence the course of my illness	1	2	3	4
6.	If I follow the advice of my doctor I can definitely influence the course of my illness	1	2	3	4
7.	I can influence the course of my illness by fighting against it	1	2	3	4

Questions For Stage One (Baseline) Only

1. When was Bone Marrow Transplantation offered to you as a treatment option?

2. Did you have a choice between BMT and other treatment options?

3. Why did you go ahead with BMT?

4. Did you discuss BMT with somebody outside the hospital? If so, with whom?

5. Did anybody influence your decision?

6. You have decided to go ahead with BMT. What are your expectations regarding the outcome of this treatment?

Questions for Stages 2 (Conditioning), 3 (First 7 Days), 4 (Isolation Ends), I (Discharge), II (Rehospitalization), 6 (Three Months), 7 (Twelve Months), III (Relapse).

1. From the time I saw you last to the present what events caused you to feel upset?

2. What was the most upsetting event?

3. How long did you feel upset?

4. Since I saw you last have you experienced an incident, a period of time or a treatment procedure as discouraging?

5. Was there a time when you felt scared?

6. What kind of support helped you most to manage difficult times?

7. Have you developed a method to cope at these times?

8. Did you religious beliefs help you to cope better?

9. What are your expectations regarding the outcome of the BMT treatment?

10. Have your expectations changed?

11. Have you had enough information?

X APPENDICES II

1. Letter and Leaflet to Patients
2. Consent Form
3. Assessment Protocol for Stage 1 (Baseline)
4. Assessment Protocol for all Stages except Stage 1

PATRON: HER MAJESTY THE QUEEN

CHAIRMAN:
M. J. HUSSEY
GENERAL MANAGER:
MISS P. M. CUNNINGHAM

THE ROYAL MARSDEN HOSPITAL
LONDON & SURREY

DOWNS ROAD
SUTTON
SURREY SM2 5PT
TELEPHONE: 01-642 6011

EXT. .....

Explanatory Notes for the Psychological Study

When patients receive a Bone Marrow Transplant this is often a very challenging time for the patient and the family. There are periods which are more difficult and others which are easier.

We still don,t know enough to predict which events and treatment procedures upset patients most, when most patients feel lonely, depressed and would welcome extra support, and who should provide this support.

The study we are starting now at the Royal Marsden Hospital is trying to answer these questions. We will assess you at different stages during the Bone Marrow Transplant, starting after you made the decision for transplant and ending a year post-transplant.

To help us to assess your physical and mental state we use a number of well established questionnaires and some questions. We want to see whether your well- being changes during the transplant, and if so when. We want to find out the difficulties for you and identify stressful events, difficult periods and stressful treatment procedures.

The more patients participate, the more we can learn. Please answer each question as accurately as you can. Your answers will help us to understand and help other patients in the future.

Thank you very much for your time and your attention.

Hilde Funaki

Hilde Funaki
Psychologist

ASSESSMENT POINTS
(Explanation For The Patient)

1. First Assessment

After the decision for BMT has been made.

2. Second Assessment

At the conclusion of preparation for transplant.

3. Third Assessment

Day seven after transplant, during isolation.

4. Fourth Assessment

After leaving isolation.

5. Fifth Assessment

For patients who received TBI; 6-10 weeks after transplant.

6. Sixth Assessment

Three months post-transplant.

7. Seventh Assessment

Twelve months post-transplant.

8. Eighth Assessment

Within seven days after discharge.

9. Ninth Assessment

In the event of rehospitalization; as soon as possible.

CONSENT FORM

The nature and the extent of the psychological study has been explained to the patient and the patient has agreed to participate.

Hilde Funaki
Psychologist Signature:.....

Member of the nursing staff who
witnessed the explanation. Signature:.....

Date:.....

Initial Protocol

Research No: | | | | | | |

HOSPITAL STICKER

Hospital No: | | | | | | |

D D M M Y Y

Date of interview: | | | | | | |

Marital Status

Single ☐

Married/Cohabiting (State M or C) ☐

Separated/Divorced ☐

Widowed ☐

Age ☐☐

Sex

Male ☐

Female ☐

Type of Leukaemia

AML ☐

ALL ☐

Myelodysplasia ☐

CGL ☐

Others ☐

(Specify) .....

Date of first Diagnosis:

D D M M Y Y

Did patient obtain remission: YES/NO

Date of first Remission:

D D M M Y Y

Did patient relapse: YES/NO

Date of 1st Relapse:

D D M M Y Y

Did patient obtain remission: YES/NO

Date of second Remission:

D D M M Y Y

Did patient relapse: YES/NO

If YES date of 2nd relapse:

D D M M Y Y

Not applicable ☐

Transplant Sheet

[1] Date of Transplant

D	D	M	M	Y	Y

[2] Type of Transplant

autologous ☐

allogeneic ☐

syngeneic ☐

[3] If allogeneic was the donor:

related ☐

unrelated ☐

If related was the donor:

sibling ☐

father ☐

mother ☐

other/specify ☐

.....

Assessment Protocol

[redacted]

[1] Hospital No: ☐☐☐☐☐☐

Research No: ☐☐☐☐☐☐

Date of interview: ☐☐☐☐☐☐

[2] Stage of Assessment

Assessment point

1 Decision for transplant ☐

2 Admission ☐

3 End of preparation ☐

4 Day 6-10 ☐

5 Day 14-28 ☐

6 6 weeks ☐

7 3 months post-transplant ☐

8 12 months post-transplant ☐

I 7 days after discharge ☐

II 1st rehospitalisation ☐

III leukaemic relapse ☐

[3] Assessment continuing

Yes: ☐ [4]

No: ☐

Unable to contact (details) ☐

Patient too ill ☐

Patient has died ☐ → REFER TO DEATH FORM

Patient refuses ☐

Other (specify) ☐

---

[4] Assessment Place

Isolation ward: ☐

Hospital ward: ☐

Psychological Medicine Unit: ☐

Out-patient ward: ☐

Home: ☐

Other (specify) ..... ☐

.....

Details of Death

Research No: ☐☐☐☐

Hospital No: ☐☐☐☐☐☐

Enter date of death: ☐☐☐☐☐☐

Cause:

- Cancer ☐
- Other (Specify) ..... ☐

  .....

Notified by:

- R.M.H. ☐
- G.P. ☐
- Other ☐

Place of death:

- Hospital ☐
- Home ☐
- Hospice ☐
- Other (specify) ☐

  .....

X APPENDIX III

1. Questionnaire for Relatives

QUESTIONNAIRE FOR THE SUPPORTING RELATIVE OF THE PATIENT IN BONE MARROW TRANSPLANTATION

The following questionnaire is confidential and there will be no need for you to identify yourself, except to provide some general infrmation regarding your background.

Your Sex: Male
Female

Age Group:

20-30	31-40	4-50	51-60	61-70

Relationship to patient:

wife/husband partner	sister/brother	daughter/son	parent

1. Were you able to be present at the time of the discussion about Bone-Marrow -Transplantation?

Yes	No

IF NO. Was this because:

a) You did not want to

b) You were discouraged

c) You were prevented for practival reasons

IF YES, were You satisfied with the way your questions were answered during the discussion?

a) completely satisfied

b) satisfied

c) not really satisfied

d) left with unanswered questions

2. Would you have liked more time spent discussing the treatment and the effect it had upon your relative?

Yes	No

3. When Bone-Marrow-Transplantation was explained to you, could you understand it:

a) fully understood

b) not enough understanding

c) no clear idea

d) no understanding

4. Were the possible side effects of the treatment explained to you?

Yes	No

4b. Can you state what side effects you expected?

_____

_____

_____

5. Were there any unexpected side-effects?

Yes	No

If Yes:
Can you name some?

_____

_____

_____

6. Did you feel free to ask questions when problems arose during the transplant period until now?

a) Most of the time

b) Frequently

c) Sometimes

d) Not at all

7. Did you feel that you yourself needed emotional support during your relative's, the patient, Bone-Marrow-Transplantation?

Yes	No

8. Did you find such support?

Yes	No

9. Who gave you emotional support?

Family Doctor
Social Worker
Psychologist
A Friend
Family
Church
Counsellor
Other

10. If qualified counsellors were available for you to consult regarding any problems, would you use this service?

Yes	No

11. Can you name the most stressful events during your relative's Bone-Marrow Transplantation?

Diagnosis
Decision for BMT
Discussion about BMT
Waiting for transplant
Chemotherapy
Total Body Irradiation
Serious Infections
Waiting for the count
Leaving isolation
Returning home
Rehospitalization
Leukaemic relapse
Others: (specify)

Cam you now go back over your list and indicate the most stressful event you have experienced by numbering it No: 1, and proceed to the next most stressful event numbering it No: 2, until you have rated all the events on this list that you have found stressful.

13. Were you pleasantly surprised by any aspect of the patient's care and if so, by what?

---

14 What positive benefits have you observed at this stage for the patient?

Hilde Funaki 1988