The Efficacy of Massage with and without the Use of Essential Oils to Reduce Stress in Patients on a High-Dose Therapy Isolation Unit

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Author's declaration

All the data contained in the main body of this thesis is a result of my own work. Analysis of anti-microbial action of the essential oils used in this trial was commissioned by the author as independent but parallel work to explore one aspect of the safety and efficacy of the oils. This required the contribution of an experienced scientist. Consequently a team at the Faculty of Medicine, University of Manchester, provided this data. Whilst conclusions to come from the in-vitro work which relate to the clinical use of the oils have been included in the text, the main body of results associated with Dr Warn's work can be found in appendix XV. A development of this parallel in-vitro work commissioned by the author on the essential oils used in this study is now the subject of an international patent application. Consequently **the data presented in the journal paper submitted here in appendix XV is subject to confidentiality agreements.**

Data obtained during the pre-pilot audit was published in 2000, in the peer reviewed journal Complementary Therapies in Nursing and Midwifery. Papers linked to this project were presented in March 2000 at the European Bone Marrow Transplant conference in Austria and in April 2003 at the British Society of Haematologists conference at Glasgow. Some of the data obtained from the main study was presented in March 2004 at the European Bone Marrow Transplant conference in Barcelona.

Glossary

ACTH..... Adrenocorticotrophic Hormone

ALU..... Adult Leukaemia Unit

ANOVA..... Analysis of Variance

BMT..... Bone Marrow Transplant

BP..... Blood Pressure

BPI..... Brief Pain Inventory

CML..... Chronic Myeloid Leukaemia

CRF..... Corticotrophin Releasing Factor

DHEA..... Dehydroepiandosterone

EORTC..... European Organisation for Research and Treatment of Cancer

FACT..... Functional Assessment of Cancer Therapy

GCSF..... Granulocyte Colony Stimulating Factor

g/dl..... Grams per Decilitre

HADS..... Hospital Anxiety and Depression Scale

HMI..... Humorally Mediated Immunity

HPA..... Hypothalamic-Pituitary-Adrenal Axis

HIV..... Human Immunodeficiency Virus

HR..... Heart Rate

K-S..... Kolmogorov Smirnov Test

KPS..... Karnofsky Performance Scale

K-W..... Kruskal-Wallis 1-Way Analysis of Variance

MAP..... Mean Arterial Pressure

mmHg..... Millimetres of Mercury

MOD..... Multi-Organ Dysfunction

MRSA..... Methicillin Resistant *Staphylococcus Aureus*

MSA..... Magnetic Separation Assay

MUD..... Matched Unrelated Donor

mU/L..... Milliunits per Litre

µg/dl..... Micrograms per Decilitre

ng/ml..... Nanograms per Millilitre

NHS..... National Health Service

NK-cells..... Natural Killer-Cells

nmol/L..... Nanomols per Litre

PMN..... Polymorphonuclear Granulocytes

PNI..... Psychoneuroimmunology

PSN..... Parasympathetic Nervous System

QLQ C-30..... Quality of Life Questionnaire C-30

QoL..... Quality of Life

RCT..... Randomised Controlled Trial

RSCL..... Rotterdam Symptom Checklist

SI units..... International Units

SNS..... Sympathetic Nervous System

SSI..... Semi-Structured Interview

TBI..... Total Body Irradiation

Th_1..... T-Helper Cells - associated with cell mediated immunity

Th_2..... T-Helper Cells - associated with cell mediated immunity

TIDHA..... Tisserand Institute Diploma of Holistic Aromatherapy

VRE..... Vancomycin Resistant Enterococcus

Abstract

Massage, as a complementary therapy is no longer controversial in many settings, such as palliative care. Within the field of haematological oncology however, there is still major concern regarding its safety. The aims of this study were firstly to show that massage with and without essential oils can be given to isolated haematology patients safely and that physiological and psychological benefits are evident following such therapy. Secondly to demonstrate that such benefits are manifest following single sessions of massage. This is the first time work of this nature has been undertaken in such an environment.

The efficacy of this treatment was fully evaluated in a clinically relevant way by employing a mixed methods approach to the design of the study. The study took the format of a randomised controlled trial. The primary outcome measure was reduction in cortisol and prolactin levels; these hormones were chosen as physiological indicators of stress. Change in hormone levels in patients who had received a 20-minute massage either with or without the use of essential oils were compared to change over the same time period for patients in a control arm.

The results showed a statistically significant drop in hormone levels in the first 30-minutes following therapy thus suggesting a decrease in physiological levels of stress. This was accompanied by a universal feeling of relaxation for patients in the experimental arms of the study – suggesting a reduction in subjective appraisal of stress. The physiological and psychological elements of the results were combined in case study format for a sample of three patients in order to illustrate some of the relevant issues identified.

This work has major implications for the supportive care of the isolated patient undergoing active treatment for haematological malignancies. The potential consequences for care are examined in detail within the discussion chapter

Chapter 1:

Introduction

1.1 Introduction

This thesis describes the evaluation of a dream. The dream was to enhance patient care by establishing a service offering massage and aromatherapy to all inpatients on the Adult Leukaemia Unit (ALU) at the Christie Hospital NHS Trust in Manchester. The ALU is an 18-bedded isolation unit where high dose chemotherapy and stem cell transplants are used to treat patients suffering from various types of haematological malignancies. The vision was prompted because patients in this environment are vulnerable and often lonely in their isolation. Although pharmacological support is vital to get them through their treatment, for example antimicrobial agents are crucial to combat infection, these people also need holistic care to enhance feelings of security and wellbeing in the midst of an atmosphere more conducive to anxiety and stress. This study was performed to show the power and importance of touch.

The dream was achieved in 1997. Offering touch therapies like massage and incorporating the use of essential oils, in this environment, went against the opinion of most of the senior haematologists in the country at that time, the majority of who refused to let such services be set up in their own departments. Having shown it to be realistic clinically to offer a safe, effective massage service to such a vulnerable set of people (Stringer, 2000), it was felt important to review the service formally in order that the benefits could be confirmed, the service could be further developed and potentially other units could be persuaded to develop similar initiatives. The benefits of massage using essential oils have not previously been evaluated in such an at risk patient group. This thesis is an account of that evaluation process and the introductory chapter will familiarize the reader with:

1. The background to the work.
2. The contribution the work will make to the current knowledge base - including the aims of the study.
3. A brief overview of the thesis.

In order to fully evaluate the efficacy of massage as a therapy in a clinically relevant way, it was imperative to employ a mixed methods approach for the design of the

study. Using mixed methods allowed me to apportion equal status to both the quantitative and the qualitative elements of the data. This work is currently unique in its approach to evaluating the use of massage and essential oils in the clinical setting.

As the researcher, therapist and author of this thesis I was integral to the evaluation process. Consequently, regarding writing style for the thesis it was appropriate to write in the first person and in certain sections use reflection. There is a section in the background part of this chapter (section 1.2.3) for example and a reflective section of the qualitative results (section 4.6.2.d) where it would have been inappropriate to write in any other style.

1.2 Background to Study

1.2.1 Technical Aspects of Treatment

Patients hoping to be cured of haematological malignancies such as leukaemia, lymphoma or myeloma have to be prepared to undertake very intensive forms of treatment including high dose chemotherapy and often total body irradiation (TBI) (Gratwohl, 2004). The aim of treatment is to remove all trace of the malignancy from the patient's body, particularly the bone marrow. The patient's bone marrow is then replaced by marrow clear of diseased cells (Dunleavy, 2001), either their own or preferably - especially in the case of leukaemia patients, that of a matched donor. Whilst undergoing treatment the patient is very vulnerable to infection as their immune system is severely compromised (Forman, 2004). Frighteningly, the patients may well be almost ready for discharge home one day and dying of septic shock the next. To try and protect the patient from infection therefore, he or she is nursed in isolation, for a prolonged period, which may extend to several months.

A large number of newly diagnosed patients feel, up to the day before admission (the same morning in some cases) well, their only symptom being a little fatigue. They have no real warning of the gravity of their situation, yet if they are not treated within days their chances of an early death escalate rapidly. Paradoxically, before it is possible to treat these people, it is necessary to assault their bodies by tunnelling a central line catheter close to the heart, through which to infuse their extremely toxic chemotherapy (Buchsel, 1998). In certain cases, if the patient's white cell count is very high at presentation - raised to abnormal heights with non-functioning and / or immature white cells, there is a possibility of death through leukostasis. Leukostasis occurs when a patient's circulatory system becomes blocked by non-functioning cells causing amongst other things, impaired levels of consciousness and cardiac dysfunction (Wiernik, 2001). In cases where the white count is over 150 x 10^9/l, the bemused patient will have their blood filtered using an apheresis machine to remove some of the abnormal cells prior to starting treatment (Wiernik, 2001).

It can be appreciated from the text above that people with haematological malignancies undergoing active treatment are subject to many of the standard contra-indications to massage. To re-iterate, they have massively reduced platelet counts

(O'Donnell, 2004) (see chapter 2, section 2.2.3 for normative data) so bruise very easily. They often have few or no mature, functioning white cells in their blood so are at high risk of infection (Cordonnnier, 2004). They may have to endure septic episodes, which are associated with pyrexia or hyperpyrexia, rigors and low blood pressure. Equally they may be covered in extensive purpura (although these are frequently drug induced). It is for these reasons that there are few centres treating patients with haematological malignancies using curative protocols, in which work involving massage has been undertaken.

1.2.2 Practical Issues

It is hard to imagine patients enduring procedures such as those described above and the many months of treatment required to eradicate the malignant cells without becoming overwhelmed by the situation, yet that is what is expected of them. Additionally, they can choose only two people of those closest to them to be allowed into their room during their stay - assuming of course that the family and friends live near enough and/or have transport to visit. As a centre of excellence for the North West of England, patients come from many miles away, abroad sometimes.

It is impossible to paint the full picture of what it is like to be nursed on a unit, which is as technology based as the ALU. It is easy for the staff to get swamped by the requirements of the myriad of equipment necessary to deliver drugs and monitor the patients, leaving them little opportunity to spend time with the patients themselves. The nurses are besieged by the demands of the apparatus used to dispense the many drugs prescribed for the patients; these machines seem relentlessly to be sounding an alarm due to, for example completion of an infusion, air in the tubing or a low battery. The doctors continually need to update the regimens of drugs prescribed and the patients themselves find their lives ruled by the necessity of being near an electrical socket for their mechanical appendage. All these factors add to the patients' disorientation and frustration.

One issue it is vital for the reader to understand is the speed with which a patient's clinical condition can change – particularly through sepsis or haemorrhage. It is important to understand this because it means that by definition, the speed at which the staff must respond to any change in the patient must also be rapid. Such speed in

the midst of so much technology is frightening, even when the person rushing is someone who is trusted. Imagine the small child who falls and has hurt himself more than he realises - he may well be frightened by the amount of attention he is receiving. So it is with these patients, they often don't understand what is happening and like the small child, they have no control over the situation; they have to trust in others and so feel very vulnerable.

Fundamental to this research was the desire to try and redress the balance of care and control for these patients. It is not possible, and in most cases inappropriate, for nurses to respond physically to a patient's vulnerabilities by hugging them. Yet that is often what is needed and there is no more legitimate way of doing that than in the form of a massage from someone they trust and who understands both their condition and treatment.

1.2.3 Personal Perspective

Why was providing this service important to me? Because for five years I had worked on the ALU as a research sister and had come to realise that whilst as a nurse I was there because I wanted to care for and nurture people undergoing a terrifying experience, the reality was, that as explained above, most of my time was spent looking after machines. Most patients suffering from malignant haematological conditions (especially leukaemias and lymphomas) do not conform to the norm expected for people potentially close to death. They do not require bed baths, their hair washing or anyone to help feed them. In short they are usually self-caring. They even have the mindless distraction of a television to keep them entertained in their splendid isolation. As nurses we are very grateful for the televisions because, as previously suggested, administering drugs (such as chemotherapy, antimicrobials and analgesia) takes up the majority of the working day of a nurse on a high dose therapy unit. My concern with this state of affairs was simple; what if patients need more but don't know what to ask for? What if they need human touch, someone to talk to, a friend? The only way they have of accessing a nurse is to press the call buzzer, what excuse can they use so they won't be labelled a 'problem patient' or feel as if they are wasting the nurses time - even though they desperately need reassurance because they're terrified of what is going to happen to them and their family? As such, my reason for going against general medical consensus and setting

up this service was straightforward, to offer patients a legitimate way of asking for a physical nurturing - through massage. With a career spanning 20 years in haematology / oncology and post graduate training in both specialities, I felt I had the necessary appreciation of the doctors concerns, which centred principally around the risk of bleeding and cross-infection and a knowledge of how to prevent such complications through gentle massage technique and scrupulous hygiene, to provide a safe service to the patients. Because the Medical Director, with whom I had worked for five years, trusted and supported me, my vision evolved into reality.

However, to stop at this point would have been inappropriate. Despite my intuitive understanding that massage would be beneficial, evidence was required to demonstrate the value of the service. To gain such evidence would help ensure its continuation and development as well as providing an evidence base showing the effects of massage on isolated patients for other nurse practitioners hoping to start similar initiatives. The thesis presented here describes the quest for such evidence.

1.3 Contribution to knowledge base

Massage, as a complementary therapy is no longer controversial within many settings such as palliative care, as its benefits are well recognised and documented (Wilkinson 1995 and 1999; Field, 2000; Smith et al, 2002). However, as explained in section 1.2, there are still major concerns regarding the safety of massaging patients within the field of haematological oncology because of the risk of haemorrhage through low platelet counts and the potential complication of cross infection caused by massaging patients who have no functioning immune system.

Various researchers have documented therapeutic effects from using essential oils as part of massage therapy (aromatherapy massage), through for example enhancement of the feelings of relaxation brought about by the massage (Corner et al, 1995; Wilkinson, 1999). However, within the arena of haematology there is a very genuine concern about the possibility of patients suffering sensitivity reactions to the oils. Equally, as the majority of substances, which are introduced into the body, undergo 'biotransformation' with the aim of 'detoxifying' them (Battaglia, 1997), the use of oils will require the liver to perform the extra work of metabolising or biotransforming, the chemical constituents of the oils when it is already dealing with the by-products of the chemotherapy and various support drugs. It is therefore realistic for doctors to feel that the potential risk of using oils negates any possible benefit such as enhancement of relaxation to the patient.

The first aim of this work was therefore to evaluate the safety and efficacy of massage with and without the use of essential oils through documentation of the physiological and psychological effects of the therapy on patients in an isolation unit. Because of data already available from a previous audit of the clinical work performed on the ALU (see appendix I, page 272), it was anticipated that the results provided here would demonstrate that massage can be offered safely to patients undergoing high dose therapy whilst in isolation, as an integral element of care and that it will benefit them both physically and psychologically. Such evidence is currently unavailable.

There is an ever expanding research base showing that a *series* of massage sessions can, through reduction of psychological stress, reduce levels of cortisol and the down grading of certain aspects of immune function (Field, 2000; Hernandez-Reif et al, 2003; Ironson et al, 1996). However, there were no studies identified looking specifically at the benefits of individual massage sessions. In relation to haematology patients, because of the nature of chemotherapy protocols, they often have to endure weeks or months as inpatients on the unit. However, they may equally be admitted for a relatively short period of time – frequently under one week, to receive part of their chemotherapy regimen. Patients undergoing more prolonged parts of their treatment such as a stem cell transplant will go through periods of being too unwell for massage to be appropriate. Accordingly, for massage to be of consistent benefit to all patients in such surroundings each session has to evoke a positive response; relying on the cumulative effects of a series of sessions is both impractical and inappropriate. In order to evaluate the service in a clinically relevant way therefore, it was important to show that every individual massage session was of benefit to the recipient, as the patient often does not have the luxury of completing an uninterrupted course of treatments. This approach is also the most appropriate in relation to the discussion in section 1.2.3; if a person is asking for massage because they feel in need of nurturing, it is of no help if the nurturing only becomes beneficial after six weeks of therapy.

Consequently, the second main aim of this work was to confirm that single sessions of therapy can induce a clinically relevant reduction in cortisol and prolactin levels as markers of stress in patients undergoing active treatment for haematological malignancies. Once again, such data is currently unavailable.

One of the intentions of this thesis was to evaluate the use of essential oils within the field of haematological oncology. To date research into the benefits of aromatherapy using scientific endpoints is minimal (Diego et al, 1998), the goal was to help change that situation. It was recognised however, that essential oils have many properties, not all of which could be usefully evaluated within the current setting. Consequently I independently commissioned parallel in-vitro work to look at the anti-microbial properties of the oils. Because the in-vitro work was a discrete project and given that I did not carry out the study myself, it will not be included in full within the

main body of the thesis. However, because the work had been instigated to inform the evaluation of the benefits of essential oils, it was felt necessary to include it within the thesis as the results helped expand the conclusions relating to clinical practice.

To summarise, whilst there is a growing body of evidence confirming the various benefits of massage as a therapy in several fields (Ironson et al, 1996; Hernandez-Reif et al, 2000; Cassileth and Vickers, 2004) there are still large gaps in our knowledge. It is the focus of this study to provide data to fill two of those gaps; firstly to show that massage both with and without essential oils can be given to isolated haematology patients safely and that physiological and psychological benefits are evident following such therapy. Secondly that such benefits are manifest following single sessions of massage. This information is seen as important in identifying changes in clinical practice that can be made in order to improve the supportive care of the isolated haematology patient undergoing intensive chemotherapy. The data from this study is also seen as an important first step to exploring potential physiological benefits to the recovering immune system massage may have, primarily through the reduction of stress levels (see section 2.4.4).

Due to the combination of its distinctive subject population; identification and assimilation of the physiological and psychological benefits of massage; evaluation of single sessions of massage and the use of essential oils blended individually for the needs of each patient (see chapter 2, section 2.7), this work is unique in the assessment of touch therapies.

1.4 Study Aims and Hypotheses

The massage service on the ALU has been ongoing for 8 years (started March 1997) and was monitored by an ongoing audit for the first 18 months of that time (see appendix I, page 272). What that audit showed was that the patients appeared to benefit from the therapy with no reports of adverse effects from either the massage or the essential oils. Many of the patients commented for example on the feeling of relaxation and calm they experienced during and after the therapy and several specifically mentioned relief of physical pain. Considering their situation, anything which shows signs of making their time in hospital more bearable requires further investigation, in terms of improving the quality of patient care.

Evidence to date suggests massage is beneficial for patients with life threatening conditions, Naylor (2001) for example highlighted the use of massage to improve pain tolerance in patients with fungating wounds – primarily through breaking the anxiety / pain cycle. However there is little in the literature relating to work with patients suffering from leukaemia. Indeed as has been highlighted in section 1.2.1, there are many contraindications for the use of massage in this particular patient group. Nevertheless it has been shown on the ALU that it is possible to use touch therapies with this client group without causing any harm, in fact evidence from the audit would suggest that they profit greatly from it. It was proposed therefore that research was necessary to highlight the benefits patients in this setting may gain and to document that such benefits are possible without any detriment to the patient.

One of the major challenges for this work was the fact that because patients are nursed in isolation they are not allowed out of their rooms, as such they are exposed to all the noise and chaos of the unit during their massage. As a consequence it was anticipated that benefits seen from the intervention were likely to be short lived.

The primary focus of the research was to evaluate the massage service provided on the ALU through observation of outcomes, with a view to possible development of the facility. A secondary directive was to stimulate similar work in other isolation units. Aims of the study were therefore:

- To show physiological and psychological benefits of massage, with and without essential oils, could be achieved through reduction in the stress hormones cortisol and prolactin, without adverse side effects of therapy. This involved a comparative assessment of whether massage with essential oils was more effective than massage with base oil or time for peace and calm at reducing physiological and psychological symptoms of stress.

- To confirm that single sessions of massage either with or without the additional use of essential oils could induce a clinically relevant reduction in cortisol and prolactin levels in patients undergoing active treatment for haematological malignancies.

- To look for any relationship between physiological and psychological changes in stress levels following massage in case study format.

The experimental hypotheses being that:

- Massage using essential oils and those using base oil only will both be shown to be safe and effective in reducing physiological and psychological signs and symptoms of stress after only a single session of massage.

- Aromatherapy massage will be more effective than massage using purely base oils in reducing above signs and symptoms.

- Because of the impact of the disturbances on the ALU the effectiveness of both interventions will be relatively short lived.

The basis for the aims of this thesis come from the field of research known as Psychoneuroimmunology (PNI). PNI is itself based on a philosophy, which proposes an integral link between the immune system, the neuroendocrine system and the responses of these systems to stress and stressors (Caudell, 1996). This relatively new field of research owes its existence to our developing comprehension of the complex links identified as connecting the immune system with the neuroendocrine system, and how stressors influence such interactions. There is a

growing body of evidence showing the benefits of massage (see chapter 2), particularly in relation to the reduction of stress and improvement of certain aspects of immune function. This study is a platform for assessing whether massage is powerful enough as a therapy to induce similar effects in the highly stressful environment of a high-dose therapy isolation unit. It is essential to show that massage in this setting can successfully reduce physiological measures of stress before attempting to look at the potential effects of massage on immune function.

1.5 Organisation of the Thesis

1.5.1 Chapter 2: Literature Review

In order for the reader to understand both how the immune system works and how leukaemia can disrupt this, chapter 2 will begin by giving an overview of the normal physiology of the bone marrow and how that is affected by various haematological malignancies. It is equally important to understand the basic physiology of the neuroendocrine system and how it interacts with the immune system, consequently this will be reflected on in the subsequent section when the relevant literature will be examined. As stated above the connections and regulatory processes linking these systems are extremely complex, therefore only the most relevant parts will be discussed in detail. Following on from these sections there will be a review of the relevant literature discussing the influence of stress on the immune system and the neuroendocrine system including an in depth appraisal of work carried out in the field of PNI. To facilitate tying the literature into this study, a synopsis will be given of research showing the influence of massage on stress levels. Some researchers have looked at the additive effects of essential oils in their work with massage (Wilkinson et al, 1999) and have shown that they appear to enhance the benefits of massage as a supportive therapy. This work will be examined as a basis for the decision to use essential oils in this study.

1.5.2 Chapter 3: Methodology

This chapter will begin by re-iterating the aims of the thesis and describing the theoretical framework of the work presented. The reality is that there is no one framework in which to place work of this kind. However, an explanation of why this is the case will be put forward and philosophical theories, which helped to underpin the study will be reflected upon. Equally, as a complex intervention, it was not simple to decide on a methodology for the study. The potential benefits of massage to be explored were both physiological and psychological. Physiological change is most effectively monitored through comparison of patients who did and did not receive a massage as in the format of a randomised controlled trial. Open-ended questioning was thought to be the best way of exploring psychological effects as seen in qualitative research. Therefore a mixed methods approach was used and

qualification of the rationale behind this decision can be found in the introduction to the methodology chapter.

The chapter goes on to include a comprehensive description of the methodology of the various stages of the study; this includes a précis of the parallel laboratory investigations, carried out by a collaborator, in order to better understand the overall benefits of essential oils. Within the methodology chapter there will be subsections describing: the subjects, the design of the study, the protocols used, the proposed outcome measures and analyses. Prior to the start of the study a lot of background work was necessary to ensure the safety and efficacy of the work. Consequently following the descriptive subsections outlined above, there will be a piece dedicated to outlining all the pre-pilot work. In this subsection is included information on how the original service was set up, a clear description of the environment in which the study takes place and results obtained from an earlier audit of the service. It also clarifies some quality control issues such as how research assistants were chosen and trained, how the questionnaires were selected and an account of how and when ethical approval was gained. In order to ensure all parts of the study design were practical and workable, a short pilot study was undertaken. The next subsection of the methodology chapter explains the reasons for the pilot study in greater depth and gives a brief synopsis of the results obtained. The main study is examined in greater detail tying together all strands of the methodology as reviewed individually above and finally there is a brief explanation of why the laboratory testing of the essential oils was included.

1.5.3 Chapter 4: Results

Chapter 4 contains all the results from the various aspects of the work. Initially it describes the demographic information relating to the subject population. Findings relating to the analyses of the physiological data, focusing mainly on the changes in serum cortisol and prolactin levels are then described. At the first post-session assessment point (30 minutes after the commencement of the session), statistically significant reductions were identified compared to baseline, in both cortisol and prolactin levels, for patients in the experimental arms compared to those in the control arm, using logarithmically transformed data (cortisol, $P = 0.007$; prolactin, $P = 0.048$). The section describing the quantitative results is followed by an overview

of the results from the two questionnaires. Results from the qualitative aspects of the study will then be presented. This sub-section of the chapter will include mainly the patients' responses to the semi-structured interview (SSI), which will be integrated with the reflections of myself as the therapist as laid out in my sessional diary entries. This section is followed by three case studies. Subjects were chosen arbitrarily (one from each arm of the study) for an in depth review of their individual physiological and psychological data in order to give a meaningful reflection of what patients appeared to gain from their session. Finally there will be a brief review of the in-vitro essential oil data.

1.5.4 Chapter 5: Discussion

Chapter 5 centres on discussion pertaining to the results presented in chapter 4. It includes a more generalised integration of the physiological and psychological findings. This chapter also highlights specific issues, which may have had a bearing on the impact each session had on the participant, for example their coping strategies; do they use passive or active approaches to coping? Within this section there will also be emphasis on my reflections as the therapist, observations and potential bearing such therapies can bring to the supportive care of the isolated patient. Chapter 5 will develop to consider the problems encountered whilst carrying out the research including, the triple role of me as the researcher and the support I had for that; recruitment, including the issues around closing the trial early and the influence of external disturbances. Also included will be general problems around managing a research project within a clinical area. Crucially, implications of the results presented here for clinical practice are reflected on. Finally proposals for future research will be offered including recommendations for work correlating cortisol levels with immune function, the aim being to enhance both current understanding and the clinical care of the patient.

1.5.5 Chapter 6: Conclusion

In chapter 6 conclusions will be drawn from the results in relation to the original aims of the study, directions for future work will be re-iterated and the key points within the thesis summarised.

1.6 Summary

To summarise, the rationale behind this work is to enhance the qualitative or holistic elements of clinical care in a very vulnerable patient group by providing an evidence base for the use of massage. The focus of this work is to examine the safety and efficacy of single sessions of massage performed within the setting of a high-dose therapy isolation unit where acutely ill patients with haematological malignancies are treated with chemotherapy and stem cell transplantation. Any additional benefits from the incorporation of essential oils into the massage oil will be documented and the implications discussed in the light of the results from this study and the additional in-vitro work.

This thesis has been set out in order to firstly inform the reader of the relevant literature, then take them along the journey that is the research – from the development of the massage service to the identification of future paths for the service and research to take. In doing so the work provides evidence for the benefits of massage for a vulnerable cohort of patients and enhances the intelligence of the field.

Chapter 2:

Literature Review

2.1 Introduction

This thesis was centred on evaluating whether massage with or without essential oils was both safe for and beneficial to, isolated patients undergoing high dose chemotherapy for haematological malignancies. It was anticipated that many benefits would be seen as a result of reduction in the patients' level of stress. Consequently this chapter of the thesis has been set out to guide readers through and inform them on the aspects of literature most pertinent to the philosophy underpinning the study, namely that of psychoneuroimmunology. For that reason most of the literature reviewed focuses on stress, its impact on the physiology of the body – including the immune system and available evidence showing massage to be beneficial in reducing the adverse effect of stress. However, before expanding any further on the study it is also helpful for the reader to have a basic understanding of haematological malignancies and what effect they have on the normal functioning of the body. Accordingly, the section below offers a very brief overview of the impact on normal physiology of haematological malignancies.

2.2 Physiology of Haematological Malignancies

2.2.1 Introduction

Although there are a variety of haematological malignancies (such as the various forms of leukaemia and myeloma) it is suggested that in each case they originate from a single cell: 'the haemopoietic malignancies are clonal diseases which are thought to derive from a single cell in the marrow or peripheral lymphoid tissue which has undergone a genetic alteration' (Hoffbrand et al, 2001). Through mutation of the genes responsible for either cell proliferation and/or suppression of proliferation, the mutated cell proliferates uncontrollably until eventually the normal cells of the bone marrow become replaced by malignant cells (Hoffbrand et al, 2001). It is recognised that some genetic syndromes such as Down syndrome lead to a higher incidence of leukaemia (O'Donnell, 2004). Equally secondary events, for instance chronic infection may put sufficient stress onto the vulnerable immune system to trigger the onset of leukaemia or lymphoma (Wiernik, 2001).

2.2.2 Physiology of Haematological Malignancies

The leukaemias are malignancies whereby the normal bone marrow and blood cells are replaced by rapidly proliferating malignant cells, which are immature and therefore do not function appropriately (Hoffbrand et al, 2001). The consequence of such a disorder is bone marrow failure leading to reduction in all the major blood cell lines – red cells, white cells and platelets (pancytopenia) (Hoffbrand et al, 2001). In other words the person will show signs and symptoms of chronic fatigue because of anaemia, chronic infection through failure of the immune system and unexplained bruising due to lack of platelets (O'Donnell, 2004). In some cases leukaemic deposits also infiltrate organs such as the liver, spleen, brain and skin (Wiernik, 2001). Lymphomas are characterised by malignant lymphocytes accumulating in lymph nodes, which give the patient the classical feature of lymphadenopathy (hypertrophy of lymphoid tissue) (Provan et al, 2003). Multiple Myeloma is another haematological condition in which there is an abnormal proliferation of one of the blood cells called the plasma cell (Desikan et al, 2004). Characteristic of this condition are the lytic bone lesions; the patient is often diagnosed following a pathological fracture due to minor trauma (Provan et al, 2003).

Although the pathological progression of each of these conditions is different, what is characteristic of all of these malignancies, unlike most forms of cancer, is that isolated lesions do not cause them; they are the result of diffuse proliferation in either the bone marrow or the lymphoid tissue, of cells with genetic mutations (Hoffbrand et al, 2001). Because both bone marrow and lymph glands are found throughout the body, any treatment also has to be disseminated throughout the body – which is why chemotherapy is used. Chemotherapy involves drugs being given either orally or by injection to destroy cells as they are dividing (Page and Takimoto, 2003). Unfortunately, these drugs are not specific to the malignant cells; because normal cells also proliferate they are also damaged by the chemotherapy (Dougherty and Bailey, 2001). Cells in some tissues (for example, the gastrointestinal tract) proliferate faster than others (Dougherty and Bailey, 2001), which is why patients undergoing high dose chemotherapy often suffer from debilitating side effects such as intractable nausea and vomiting. The use of high-dose chemotherapy is supported by either auto or allogeneic haemopoietic stem cell transplant (Frassoni, 2004).

2.2.3 Change to Normal Physiology of the Blood

To understand the impact of these conditions on the body it is useful to know the normal blood count for a healthy individual. As such these are presented below together with some examples of the complications encountered by patients with haematological malignancies – through both the disease process and the treatment, how these complications are dealt with clinically is also described:

Normal Blood Count for a Healthy Adult

Haemoglobin	- (male) 13.5 – 17.5g/dl (female) 11.5 – 15.5g/dl
Leucocytes (white cells)	- (male and female) 4.0 – 11.0 x 10^9/l
Neutrophils	- (male and female) 2.5 – 7.5 x 10^9/l
Lymphocytes	- (male and female) 1.5 – 3.5 x 10^9/l
Platelets	- (male and female) 150 – 400 x 10^9/l

(Adapted from Hoffbrand et al 2001) Figure 2.1.

Red Blood Cells (Erythrocytes): The main function of the red cells is to deliver oxygen to the tissues from arterial blood and in the venous blood to collect carbon dioxide from the tissues and deliver it to the lungs (Hoffbrand et al, 2001). To

perform this task effectively the erythrocytes comprise a specialised iron containing protein called haemoglobin, which combines with the oxygen. When the effects of leukaemia and its treatment lead to bone marrow failure a patient's haemoglobin level can reach levels as low as 6g/dl. However, well before this they will become symptomatic of anaemia, showing signs and symptoms such as excessive fatigue and breathlessness due to the impaired oxygen carrying capacity to the tissues. To support a low haemoglobin level, transfusions of whole blood or packed red cells are administered (Dunleavy, 2001).

White Blood Cells (Leucocytes): The leucocyte or total white cell count is a broad term to encompass the different type of cells within the immune system, which can be divided into the granulocytes, monocytes and lymphocytes (Hoffbrand et al 2001). The most important component of the white cell count for protecting the body against opportunistic infections (such as the common cold) that can become potentially life threatening for patients with leukaemia, is the neutrophil or polymorphonuclear neutrophils (PMNs). These innate or non-adaptive cells are one of the body's first line of defence when under attack and account for 60 – 70% of leucocytes in adults (Roitt et al, 2001). When a patient becomes neutropenic (with a neutrophil count under 1.0 x 10 9/l, often as low as 0.0 x 10 9/l, plus or minus a total white cell count) it is very important to protect them from infection. It becomes the role of the medical and nursing staff to support the immune system if a patient has evidence of neutropenia. Support is provided by such measures as isolation nursing, administration of prophylactic antimicrobial drugs and strict hygiene procedures for all involved with the care of the patient (Ito, 2004). If, despite these measures the patient contracts an infection - seen through symptoms such as pyrexia (temperature >38.5°C), sweats, feeling cold (caused by vaso-constriction), shivering (rigors) and sometimes a dramatic drop in blood pressure, then high dose intravenous antibiotics are given following the clinical guidelines provided by individual hospitals.

Lymphocytes form the other main part of the immune system and their function is to provide adaptive or specific immunity, which occurs after a person has been exposed to an antigen. This section of the immune system contains memory cells, which allow for future recognition of the encountered antigen, thus minimising chances of future infections (the basis of inoculations) (Roitt et al, 2001). The T and B-

lymphocytes control this part of the system. It is the lymphocytes, which are most greatly influenced by the effects of long-term stress and therefore will be discussed in greater detail within the thesis.

Platelets: Platelets are central to maintaining haemostasis by preventing leakage of erythrocytes through capillary cell walls. They are also involved in initiating the intrinsic clotting cascade responsible for minimising bleeding following vascular injury (Jassak and Haeuber, 1998). When, as in cases of leukaemia, a patient's platelet count drops (under 20 x 10 9/l) they are vulnerable to bleeding through trauma but much more commonly, by seepage of blood through the capillaries (Dunleavy, 2001). Signs of a low platelet count are excessive bruising after minimal trauma but more commonly; tiny pinprick bruises which look like a rash known as petechiae. A low platelet count also puts a patient at risk of major haemorrhage, which can be fatal. It is therefore imperative that the medical and nursing staff monitor the patient's platelet counts and observe them for signs of active bleeding. When they are seen to be at high risk of haemorrhage (usually with a count below approximately 15 x 10 9/l) prophylactic platelet transfusions are indicated (Forman, 2004).

2.2.4 Summary

The above outline is a brief overview of the physiological effects of leukaemia and the supportive care required by a patient with haematological malignancies. However, it should hopefully give the reader enough of an insight into the dangers of the disease process, to appreciate the vulnerability of a patient being cared for on an isolation unit such as the one in which this study was carried out. Such knowledge will lead to an understanding of why it is important to ensure massage does indeed offer benefits to patients who endure many problems normally classed as contra-indications to massage such as extensive bruising and life-threatening sepses, prior to recommending it for wide acceptance and integration into clinical care.

2.3 Physiology of Stress

In order to put this work into context it is necessary to review some of the literature relating to the primary psychological difficulty facing patients admitted to a leukaemia unit for high dose chemotherapy and one of the fundamental reasons for setting up the massage service, stress. It is assumed that the stress encountered by the patients is primarily due to diagnosis, treatment and possible prognosis and is compounded by periods of isolation. A diagnosis of cancer and the associated stress is known to cause extreme emotional distress and anxiety, as well as generally compromising the patients' quality of life (Jacobsen & Holland, 1991).

Stress is a concept, which is difficult to define, because it means different things to different people. Many however have tried; Leonard (2004) for example, describes stress quite simply as:

'Any event (external or internal to the body), which upsets the biological equilibrium.' (Leonard, 2004)

Stress can be identified as an external stressor such as an examination or excessive workload. Many researchers focus on external stressors such as bereavement, as a measure of the amount of stress a person is under. In their review of stress, Herbert and Cohen in 1993 noted that associated immune alteration was greater in studies where the outcome measures used were objective in the form of negative life events, than in research where self-reported stress was monitored. They also suggest that there is only a problem if the demands of a stressor are perceived as greater than the person's ability to cope. Stress therefore can be proposed as a product of subjective lack of coping with one's external environment; Aldwin & Park (2004) document in their paper that the relationship between stress and coping is complex. Despite this complexity the authors advocate coping will eventually be shown through future research to moderate the effect of stress on health. The proposal that coping in relation to health is a composite issue and one directly linked to the concept of stress is also put forward by Heim (1991) in relation to the specific demands placed on a person by a diagnosis of cancer. He defined coping as follows:

'Coping refers to the attempt to ward off, to reduce or to assimilate an existing or expected demand (or stressor) either by intrapsychic effort (cognition- or emotion related) or by an action (field-related).' (Heim, 1991)

Heim suggests that for several reasons the moderating or adapting effort of coping relating to the impact of illness may or may not be successful and may affect psychosocial adjustment (Heim, 1991).

Stress can also be observed as a continuum, from the relatively low-level of stress everybody encounters, which up to a certain point is helpful – necessary even, to motivate one into action, to the universally accepted major stresses such as bereavement or loss of employment. However it is interpreted, stress always involves an emotional and or psychological response which has been recognised for many years to trigger a sequence of complex physiological events which can, if they continue, bring about long term changes in the body's physiology. It was nearly 70 years ago when Selye described the physiological impact of stress. Possibly the best known part of that model is the "fight or flight" aspect. "Fight or flight" can be seen as the body's acute response to something (or someone) it perceives as threatening. Through a complex system initiated mainly through the sympathetic nervous system, the body is primed to either fight or run away from a threat (Evans et al, 2000). Examples of physiological changes induced by this trigger include; increased heart rate, high levels of adrenaline, and increased levels of cortisol produced on demand by the adrenal glands in order to increase glucose production which is required for aerobic cell respiration (Smyth et al, 1997).

2.3.1 Hypothalamic – Pituitary – Adrenal axis

If the perceived threat continues for more than a few hours then other bodily systems are triggered to assist in an adaptation process. This is necessary to prevent the state of bodily exhaustion, which would occur if such an extreme intensity of response requiring elevated levels of energy, continued for any length of time. The systems involved include the continuing response of the sympathetic nervous system (SNS), the triggering of the hypothalamic – pituitary – adrenal axis (HPA axis) with an associated rise in cortisol levels and the release of endogenous opioids (Shamgar, 2003). These in turn have a powerful impact on the functioning of the immune

system, as shown by Roy & Loh (1996). The process is complex as are the cascade of consequences, particularly in relation to the functioning of the immune system and an in-depth account can be found in a book by Clow and Hucklebridge (2002). McEwen in his 1998 paper reflected on the effects of stress mediators and summarised the perception and effects of stress on health as follows:

'The perception of stress is influenced by one's experiences, genetics and behaviour. When the brain perceives an experience as stressful, physiologic and behavioural responses are initiated, leading to allostasis and adaption. Over time, allostatic load can accumulate, and the overexposure to mediators of neural, endocrine and immune stress can have adverse effects on various organ systems, leading to disease'. (McEwen, 1998)

However, the purpose of this work was not to explore such complexities in their entirety but to use aspects of the response as recognised indicators of reaction to stress. Therefore the system of primary importance here and the one to be focused on within this thesis is the response of the HPA axis to continuing or chronic stress and to centre primarily on the influence of one of the hormones produced, cortisol.

As stated previously, the HPA axis is just part of the intricate bi-directional feedback loop which is activated during periods of stress. It is inappropriate to provide an in-depth description of this process within the thesis, (for those desiring a more in depth description, see Evans et al, 2000), however it is necessary for the reader to have an understanding of the basic functioning of the HPA system in order to understand the rationale for using serum cortisol as an outcome measure. As such the influence the HPA axis has over the body and how that changes differentially in the presence of stress - either acute or chronic, will now be outlined:

A diagrammatic representation of the sequence of events involved in the pituitary-adrenal axis response to stress is illustrated in figure 2.2:

Hypothalamic – Pituitary – Adrenal Axis Response to Stress

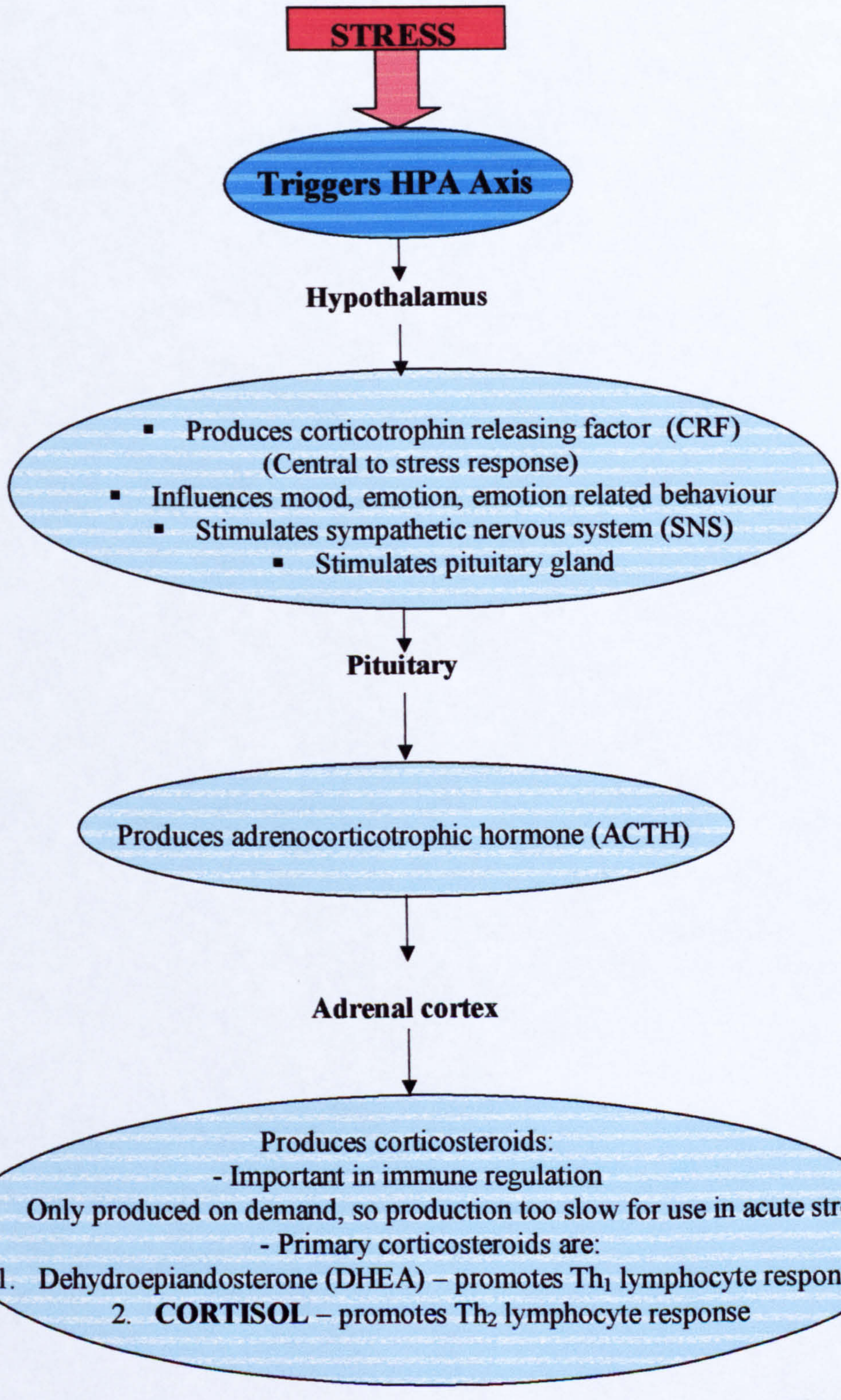


Figure 2.2

Figure 2.2 shows a summary of the influence of stress over the body through the action of the HPA axis.

Figure 2.2 shows that a stress response impacts on a person in several ways. It not only has a bearing on physiological reactions for example, but also psychological, including affect and may influence for example the development of depression. It has been suggested that psychological factors such as depression may themselves influence and alter the progression of some diseases including certain cancers - possibly due to their intimate relationship with the consequences of prolonged stress. Reiche and colleagues, (2004) went as far as to conclude that:

'*Evidence mainly from animal models and human studies suggests that stress and depression result in an impairment of the immune response and might promote the initiation and progression of some types of cancer.*' (Reiche et al, 2004)

As can be seen from figure 2.2, the body's response to stress is intimately connected with the functioning of the immune system. It is important to note however that the situation is complex and not clearly understood, due in part to different workers choosing to measure different indicators of immune function, including rate of lymphocyte apoptosis (programmed cell death) (Dominguez-Gerpe and Rey-Mendez, 2001; Shi et al, 2003) and numbers of various populations of lymphocytes (Van der Pompe et al, 1997). However, there appears to be a general consensus that it is primarily chronic stress which has a detrimental effect on immune function – especially on cellular immune function (Shi et al, 2003) whilst acute stress such as mental tasks including exams or role play can be seen to heighten certain immune responses (Naliboff et al, 1995), although as shown by Evans and colleagues (2000), this is not a simple relationship. What figure 2.2 also suggests is that prolonged episodes of stress and exposure to stressors, leading to chronically disrupted levels of cortisol, would not universally down-regulate the immune system; it is more accurate to say that they cause a shift in the immune response - Rook (1999) gives a very comprehensive account of how stress impacts on the HPA axis mediation of the immune system, causing the number and level of functioning for various immune cells to alter. The physiology and impact of that shift will be discussed in greater detail within section 2.4.

Because of the apparently central role of cortisol in the relationship between stress and the immune system (Elenkov, 2002) and because it is a hormone which can be

easily measured, many workers have used it as a marker for a subject's level of stress. Heinrichs et al (2003) for example used salivary cortisol to show how social support could protect against the effects of acute stress. Whilst Smyth et al, (1998) documented in their subjects a rise in salivary cortisol levels, both in response to and in anticipation of, naturally occurring daily stressors. Workers in the field have tried to clearly identify the role of cortisol in the stress response (Smyth et al 1997; Smyth et al, 1998), and how different parameters influence its effect. Both Huizenga and colleagues (1998) and Ice et al (2004) for example have looked at the influence of age on cortisol secretion. Van Cauter et al, (2000) observed changes in sleep pattern and cortisol production in relation to age, whilst Bergendahl et al (2000) indicated an effect of fasting on cortisol concentration in different age groups and Zhao et al (2003) looked for cultural differences in cortisol secretion. A review of some of the most pertinent work can be seen in section 2.3.2.

2.3.2 Cortisol

In their comprehensive paper exploring the role of adrenocorticoids (of which cortisol & DHEA are the most important in humans), McEwen et al (1997) describe adrenocorticoids as being:

'*Subtle and complex modulators of immune function...both enhancing and inhibiting host immune responses and thereby influencing disease susceptibility and progression.*' McEwen et al (1997).

They also recognise that cortisol has two modes of production. Firstly there is the cyclical manufacture of cortisol, which constitutes its regular diurnal cycle with high levels of cortisol secretion around 08:00 and a gradual decrease in bursts throughout the day. This circadian rhythm of cortisol production has been recognised for over forty years (Yates and Urquhart, 1962) and has an essential role in certain vital functions such as maintaining glucose production from protein and facilitating fat metabolism (Smyth et al, 1997). Secondly, there occurs phasic secretion of cortisol, which is seen frequently as a response to stress (Reiche et al, 2004). It is suggested by McEwen et al (1997) that these two modes of action occur independently because

the timing of the circadian rhythm is not under normal circumstances affected by the stress response.

It has been recognised for over thirty years that the circadian rhythm of cortisol secretion occurs not in a smooth curve as it is often portrayed, but in pulsatile or episodic bursts throughout the day. Weitzman, et al (1971), were some of the first researchers to show this when they conducted an intensive study measuring the serum cortisol levels of six healthy male volunteers every 20 minutes for a total of seven 24 hours periods. Jusko et al (1975) corroborated this finding when they documented the secretory pattern of cortisol in a group of seven normal children (age not stated), in their attempt to develop a pharmacodynamic model of cortisol, characterising through mathematical formulae, the production and metabolic time-course of plasma cortisol concentrations. Both teams identified that the highest rate of secretion consistently occurred in the hour after waking and the lowest rate was around midnight. Hucklebridge and co-workers (2005), showed in a recent study on 24 healthy adults that the circadian rhythm of secretory activity seen in cortisol over two sampling days, correlated with the diurnal pattern of DHEA production (see Table 2.1):

Correlations Between Cortisol and Dehydroepiandosterone (DHEA) Secretion as Shown by Hucklebridge et al (2005)

Period	Pearson r	Spearman rho
Awakening secretory activity (Day 1)	0.308^{+}	0.548^{**}
Awakening secretory activity (Day 2)	0.164	0.292^{+}
Day secretory activity (Day 1)	0.217	0.575^{**}
Day secretory activity (Day 2)	0.375^{*}	0.390^{*}
$^{**}p<0.01$; $^{*}p<0.05$; $^{+}p<0.10$		

(Table 2.1 Reproduced from Hucklebridge et al. 2005)

Hucklebridge et al (2005) were specifically wishing to evaluate secretory activity of both hormones in relation to awakening. In order to do this they instructed the subjects to take salivary samples for hormone levels immediately on awakening, at fifteen-minute intervals for forty-five minutes then a further four samples at three hourly intervals synchronised with their waking times. This procedure was repeated on two consecutive days. This methodology was unlike that of many other workers

in the field who have measured cortisol at specific times during the day (Huizenga et al, 1998; Ice et al, 2004). Interestingly, whilst their results showed a statistically significant correlation between the two hormones they were also able to demonstrate that DHEA levels were the more stable over days which suggested differential regulation over the activity of the two enzymes with cortisol being the more sensitive to day-to-day variability. I suggest that the variability seen in cortisol secretion identified by Hucklebridge and colleagues may be explained by the superimposed influence of the phasic production of cortisol seen in response to stress. In contrast to the results of Hucklebridge et al (2005), a recent study by Selmaoui & Touitou (2003), showed the cortisol profiles of 31 healthy young men to remain stable over a number of weeks with very little intra-individual variability. However, these authors measured serum cortisol levels in a laboratory with a closely controlled environment including standardised sleeping and waking times and minimal influence from stimulants such as caffeine or external stressors. Ice et al (2004) collected salivary cortisol from 48 healthy but elderly volunteers with a mean age of 76 years over a period of 2 days. They concluded that the cortisol circadian rhythm is constant and that the consistency can be maintained in the elderly. In their study Ice and colleagues attempted to expand on the work of Smyth et al (1997) who collected salivary cortisol from 109 *young* healthy adults with a mean age of 36.7 years over the same time period. Smyth et al proposed that cortisol diurnal cycles could be categorised into one of three types: typical (with an early morning rise), flat or no cycle and inconsistent cycle. The results produced by Ice and co-workers suggested two of the same three patterns of secretion as Smyth and team, and in both studies there appeared to be a high correlation of cortisol slopes over the two collection days – particularly for the subjects showing a typical cycle. Table 2.2 shows the correlations between the variations in cortisol slopes for the subjects in the two studies:

Correlation of Patterns of Variation in Cortisol Slopes for Collection Days 1 & 2 in 48 (Ice et al, 2004) and 109 (Smyth et al, 1997) Healthy Volunteers

Study	Typical cycle			Inconsistent cycle			No cycle		
	N	P*	P-value	N	P*	P-value	N	P*	P-value
Ice et al, 2004	24	0.817	<0.0001	23	0.150	NS	1	NC	NC
Smyth et al, 1997	56	0.66	0.01	34	-0.17	NS	19	0.58	<0.01

P* = Mean correlation between the slopes on day 1 & 2

NS; not significant, NC; not calculable because number too small

Table 2.2 Adapted from Ice et al (2004)

When examined together the results of the studies seem to suggest that the cortisol slope of an individual categorised with a typical diurnal rhythm is most likely to remain constant over time, although Ice et al (2004) proposed this maybe influenced by sleep patterns.

One study, which has provided powerful evidence for the importance of circadian cortisol rhythms in relation to health, was the work done by Sephton et al (2000). Sephton and her colleagues (2000) examined the prognostic value of documenting abnormal circadian rhythms in patients with cancer, that is cycles at variance with the normal steep early morning rise in cortisol secretion followed by gradual decline throughout the day. To do this the team took samples of salivary cortisol from 104 women with metastatic breast cancer at 4 time points on three consecutive days. They also took two serum samples one week apart from 95 consenting subjects, to identify numbers and activity of natural killer (NK) cells as indicators of immune function. They found that patients with flatter cortisol slopes (i.e. without the early morning rise) were linked with earlier mortality (Cox proportional hazards 2-tailed P = 0.0036) and suppressed immune function. Remarkably, Sephton et al (2000), identified that the shape of a patient's cortisol slope can predict survival up to 7 years later.

Unfortunately, what was not identified in the study by Sephton and her team (2000) was the cause of the flattened slope, although a theory was postulated based on tentative evidence that the chronic stress of marital disruption could have influenced the cortisol slope sufficiently to cause long-term change. Selmaoui & Touitou (2003) also recognised that factors such as endogenous stress could influence the pattern of cortisol secretion. However based on the results of their study they concluded that the circadian rhythm of cortisol (and melatonin) appeared to be highly stable and reproducible; as such it would seem to provide a reliable physiological measure. Certain physiological factors have been shown to alter patterns of cortisol release. Vance & Thorner (1989) for example showed the impact of fasting on cortisol secretory pattern by measuring serum cortisol levels in 10 healthy male volunteers on days 0 and 5 of a 5-day fast, sampling at 20-minute intervals. In summary, the fasting led to a flattening of the normal cycle by increasing cortisol concentrations in 48 of the 56 samples taken during the times 13:20 to 07:00 on day 5 compared to day 0 ($P = 0.05 - 0.0001$), whilst values from 07:20 – 08:00 were similar on both days. Equally, Smyth et al (1998) documented changes in salivary cortisol levels due to naturalistic stressors and found a rise in cortisol, which increased as a function of the number of stressors with an average rise of 11% with a single stressor, two co-occurring stressors causing a 21% rise and three stressors a 24% increase.

Interestingly Smyth et al (1998) also demonstrated an increase in cortisol secretion in response to *anticipation* of daily stressors. It is feasible to assume therefore that the way a situation is perceived by a person (threatening or non-threatening) will impact on cortisol response. Smyth and his team provided evidence to suggest that affect or mood may mediate the HPA axis response to stress; a suggestion backed up by the work of Polk et al (2005). Polk regularly assessed the mood of 334 healthy volunteers over a three-week interval. This assessment was followed by the collection of 14 salivary cortisol samples in a 24-hour period. Their results were complex but appeared to indicate a mediating effect of mood on cortisol levels – especially trait disposition. In line with such reflections Deuschle et al (1997), demonstrated that patients suffering from clinical depression expressed an increased frequency of pulsatile secretion of cortisol during the evening thus flattening the classical circadian rhythm characteristic of cortisol. This is a particularly important

observation as it is in line with the findings of Sephton et al (2000) described above, which suggests that it is not high levels of cortisol per-se, which are detrimental to health but alteration or flattening of the circadian rhythm.

To summarise, the literature would suggest that there are two factors in cortisol secretion. Firstly the regular diurnal pattern of high hormone levels after wakening with a gradual drop throughout the day, which appears to be constant. Secondly the phasic secretion, which is more labile and influenced by, factors such as stress and affect. It is proposed that through the reduction of stress, massage may be able to reduce the negative effects of cortisol through reducing the phasic secretion of cortisol. This would help prevent chronically elevated cortisol levels, which when superimposed on the classic circadian rhythm appear to have the potential to adversely effect health status - primarily through its effect on the immune system.

2.3.3 Prolactin

Whilst the primary focus of this work was the reduction of cortisol through enhancement of the diurnal slope, it was felt important to try and corroborate any reduction of cortisol levels with results showing the additional reduction of levels of another stress related hormone in order to enhance internal validity of the results. Prolactin is a hormone produced primarily by the anterior lobe of the pituitary gland and has an essential role in mammalian lactation and early pregnancy as well as playing a part in the regulation of metabolism (Hell and Wernze, 1988). It is recognised that prolactin secretion is higher at night than during the day, shows seasonal variation *and is enhanced by various kinds of stress* (Hell and Wernze, 1988). That the release of prolactin is at least partially stimulus-dependent, (including stress) has been confirmed by recent research conducted on rats (Torner et al, 2004). There is also evidence to show prolactin as having an immunoregulatory role through its influence on lymphocytes. Wilner et al (1990) for example showed in their work with rats, that drug induced lowering of prolactin levels resulted in immunosuppression and enhanced tolerance of cardiac allografts. There is also recent evidence to suggest that cortisol and prolactin work in complementary ways with cortisol responding primarily to psychological stress relating to shock and intimidation whilst prolactin levels appear to surge in response to rage (Sobrinho et al, 2003).

The greatest disadvantage to using prolactin as a marker for stress levels is that it is influenced by a number of drugs such as metaclopramide (Hell and Wernze, 1988) and cyclosporine-A (Nagai et al, 1992).

The reference ranges used by the study site for the two hormones can be seen in figure 2.3:

Reference Ranges Used in this Study for Serum Cortisol and Prolactin

Hormone	**Reference Range**
Cortisol	200 – 650 nmol/L (07:00 – 09:00) 60 – 250 nmol/L (Midnight)
Prolactin	up to – 350mU/L (normal) 350 – 700mU/L (minimally elevated)

Figure 2.3

2.4 Influence of Stress Over the Immune System

2.4.1 Introduction

As can be seen in figure 2.2 (page 27), it is the lymphocyte population of the immune system, which is directly influenced to the greatest extent by the effects of chronic stress and the subsequent impact of the hormones produced in the adrenal cortex. However, secondary effects such as reduction in natural killer (NK) cell activity are also clearly related to the influence of a chronic rise in cortisol levels (Turner-Cobb, 2002). The influence of cortisol over the immune system has been shown to be great enough to suggest a cyclical variation in lymphocyte function, which corresponds to the diurnal variations in cortisol (Rook, 1999). A review of the relevant literature showing the interactions between glucocorticoids and immune function can be seen in a comprehensive paper by Rook (1999). In view of the major influence stress has on the lymphocyte populations, it is appropriate to take time to explain the roles of the different types of lymphocytes and clarify why alteration in the balance of the various sub-populations can have a potentially detrimental effect on the functioning of the immune system as a whole.

2.4.2 Structure of the Immune System

Firstly it is important to understand the role of the immune system and to appreciate where the lymphocytes fit into this complex structure. The role of the immune system has been defined by Hucklebridge & Clow (2002) as providing 'protection of the cellular integrity of the body.' This description adequately encompasses the fact that whilst the primary role of the immune system is to protect the organism from infection through pathogens, it is also capable of identifying abnormally functioning or damaged cells which may originate from within the organism and eliminating them (Lanier, 2001).

The cells of the immune system are usually described in relation to what information they require about a stimulus before they react to it and are typically identified as relating to either *innate* or *acquired* immunity. Innate cells such as neutrophils, are seen as the first line of defence against pathogens like bacteria, because they do not require prior experience of the organism in order to recognise it as foreign and launch an attack (Evans et al, 2000). Cells relating to acquired immunity however

work in a slightly different way. Rather than the whole cell being recognised as either foreign or abnormal, a select number of the immune cells relating to acquired immunity identify a variation in the molecular structure of the cell from 'self'. Once the small numbers of lymphocytes able to detect that specific abnormality have been alerted to the danger, they have then to proliferate before the cascade of defence mechanisms can come into play (Evans et al, 2000). The newly differentiated immune cells become known as 'memory cells' and on future contact with the same antigen can launch a rapid attack (the reason it is very rare for someone to become infected with chicken pox more than once for example). The cells responsible for acquired immunity are the lymphocytes (Roitt et al, 2001).

There are two populations of lymphocytes: the B-cells and the T-cells. Both originate in the bone marrow but the T-cells migrate to the Thymus gland for maturation (Roitt et al, 2001). The B-cells (with the help of the T-cells) are responsible for humorally mediated immunity (Evans et al, 2000). Humoral immunity includes the production of immunoglobulins (antibodies), which have a key role in immune defence - particularly against pathogens that survive outside of the body's cells and any toxic substances they produce; this includes parasites such as worms. T-cells are split into two sub-populations:

- Cytotoxic T-cells, which are involved in cell mediated immunity, this includes immune surveillance aimed at 'flushing out' and eliminating cells which survive within the host cells and produce foreign or abnormal protein such as cancer or viruses (Hucklebridge and Clow, 2002).
- Helper T-cells. These cells 'read' help signals sent by other parts of the immune defence system and by the production of substances called cytokines the helper cells stimulate the activity of certain parts of the immune system (Hucklebridge and Clow, 2002).

The cascade continues in that there are two types of helper T-cells (see figure 2.4):

- Th_1 cells, which through the cytokines they produce, stimulate cell-mediated immunity (CMI).
- Th_2 cells, which stimulate humorally-mediated immunity (HMI).

Diagram Showing the Function and Balancing Mechanism for the Two Populations of Helper T-Cells

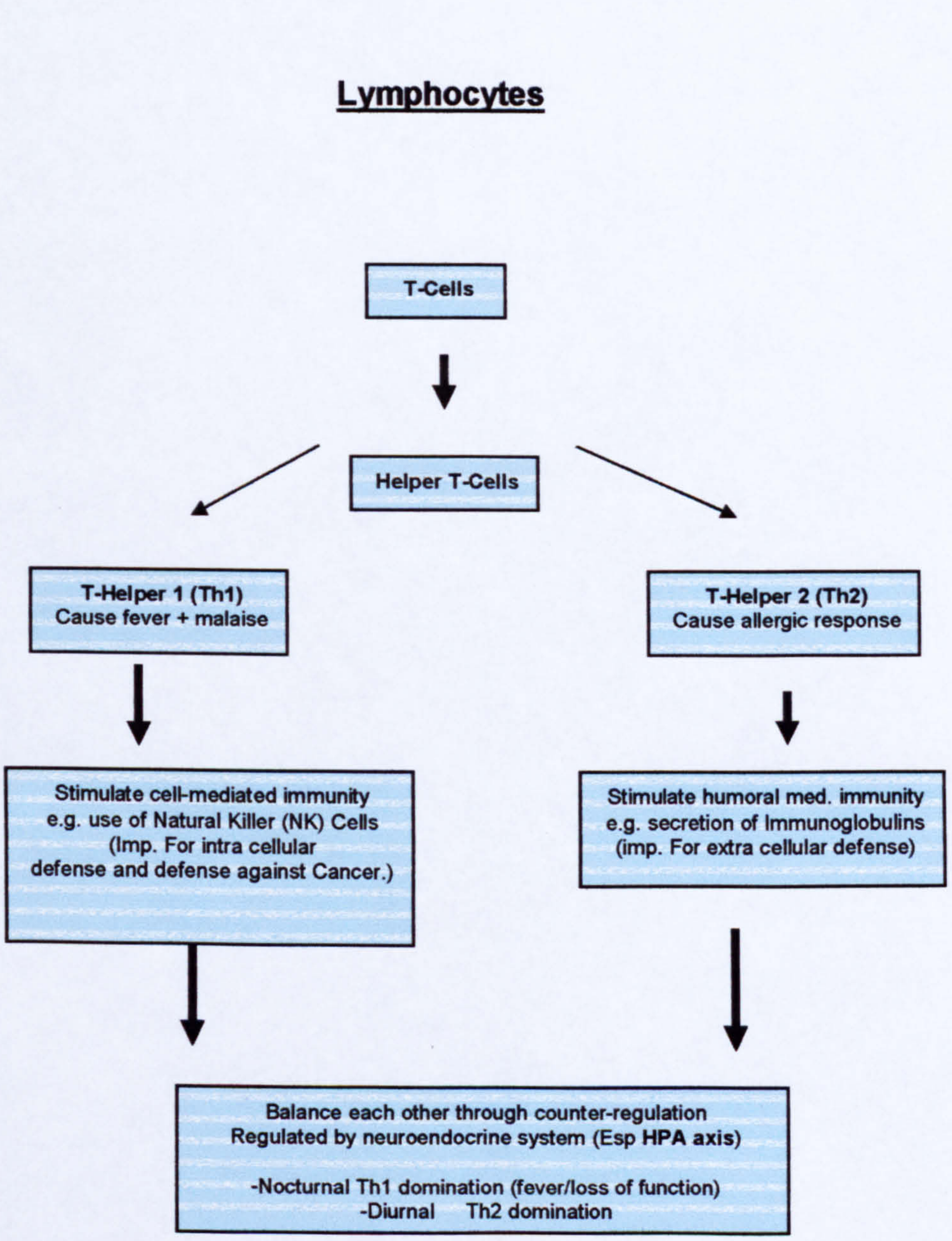


Figure 2.4.

As can be seen in figure 2.4, the T-helper cell populations balance each other through counter-regulation with Th_1 production tending to dominate nocturnally and Th_2 domination occurring during the day (Evans et al, 2000).

2.4.3 Regulation of the T-Helper Cells

The regulation of the different populations of T-helper cells is controlled by the neuroendocrine system. The production of cortisol by the HPA axis causes Th_2 dominance during the day and the production of melatonin via the pineal gland at night-time brings about nocturnal dominance of the Th_1 population (Evans et al, 2000). The evolution of this rhythm is logical and adaptive because when fighting micro-organism invasion, one of the primary functions of the Th_1 cells, takes up a lot of energy – the production of fever, to make conditions less favourable for bacterial replication (Evans et al, 2000). Consequently conservation of energy through sleep aids Th_1 function. This also partly accounts for 'illness behaviour,' when someone is fighting systemic infection they become drowsy and lethargic, which allows energy to be conserved for induction of fever. However this fine balance sometimes becomes skewed leading to inappropriate domination by one of the T-helper cell populations. Simplistically, inflammatory conditions such as rheumatoid arthritis are associated with a move towards Th_1 supremacy whilst allergic conditions such as asthma can be viewed as relating to a skew towards dominance of the Th_2 cells (Hucklebridge & Clow, 2002).

One of the factors known to cause a major threat to the internal balance of the T-helper cell populations is stress both physiological (e.g. trauma) and psychological (e.g. bereavement). Stress induces the secretion of corticotrophin releasing factor (CRF), which then activates the HPA axis thus leading to increased levels of cortisol production and the inappropriate domination of the Th_2 population of T-helper lymphocytes. Understanding this helps us to have a better understanding of the development and disease course of various conditions such as asthma (Elenkov, 2002) and the potential implications of chronic stress.

Figure 2.5 gives a pictorial description of how the two aspects of immunity work when balanced and what typically will happen when one side becomes dominant:

Pictorial Description of the Factors Effecting Functioning and Balance of Cell and Humorally Mediated Immunity

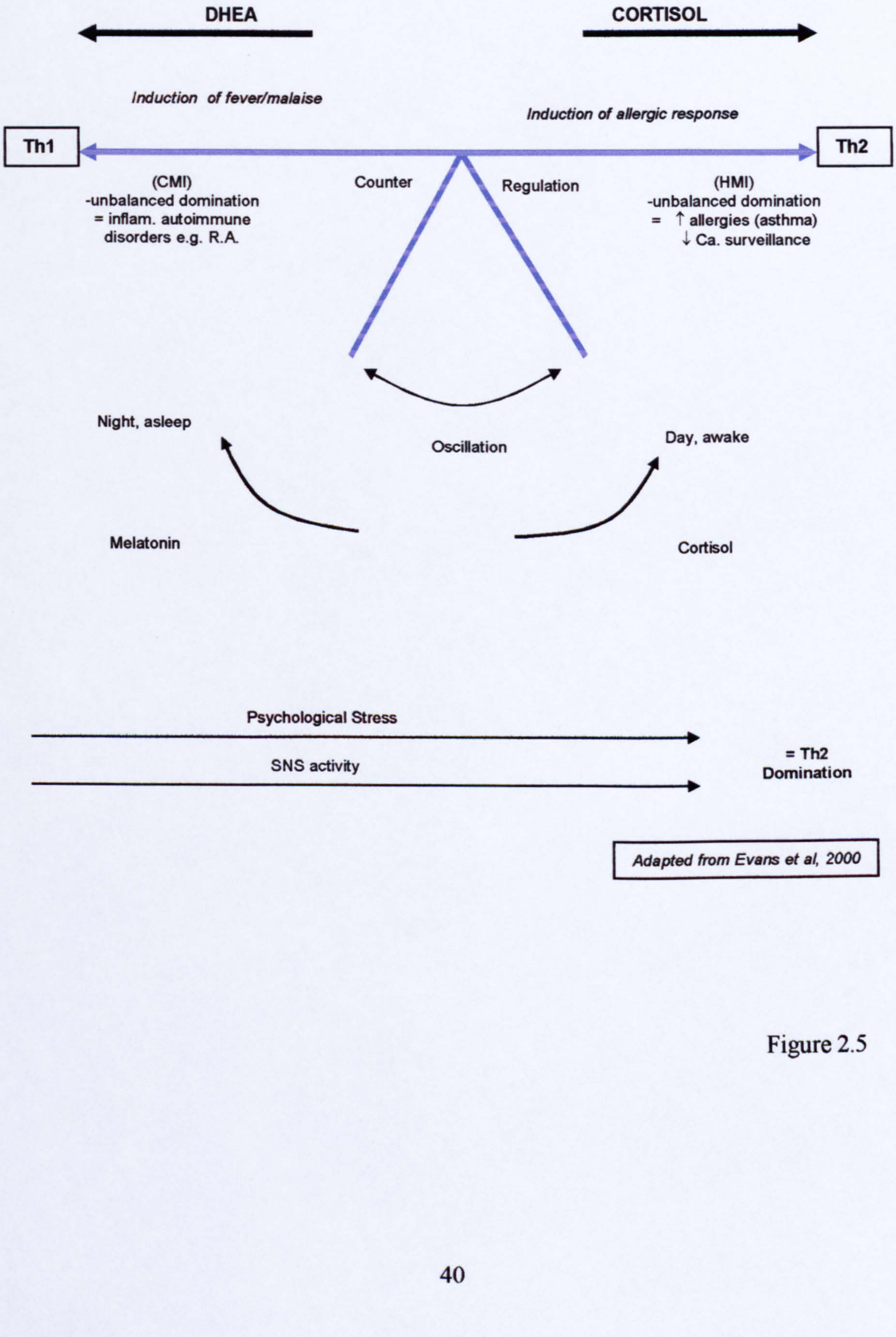


Figure 2.5

2.4.4 The Influence of Stress Over the Immune System

As has been highlighted previously, one of the ways in which stress can cause injury is through the interactive effect it has on the neuroendocrine and immune systems (Miller and Cohen 2001). In situations that evoke high levels of anxiety for example, there is a heightened response from the sympathetic nervous system, which has a primary role in stimulating endocrine responses (Evans et al, 2000). One of the consequences of elevated neuroendocrine activity is the increased production of stress hormones such as cortisol and adrenaline. It has been suggested (McCain and Smith, 1994); that the immunosuppressive effect cortisol has on parts of the immune system is the most important physiological link between stress and illness. This link is confirmed as certain immune cells carry receptors for cortisol thus implying its role in immune modulation (Rabin et al, 1989). Glaser and colleagues (1990) show in their work with medical students that minor factors, which may be seen as predictable and transient such as stress due to examinations, can have a negative effect on immune function through the regulation of interleukin-2 and lymphocytes. Although they did not measure cortisol in their experiments, they used the results of their own work plus existing data relating to the influence of cortisol provided by others, to suggest a mechanism by which stress and cortisol can impact on immune function at the level of gene expression The work of Glaser and others also appears to demonstrate that in some situations of chronic stress, down-regulation of immunological activity continues rather than the body adapting to such stressors (Kiecolt-Glaser and Glaser 1992; Turner-Cobb, 2002). Dominguez-Gerpes & Rey-Mendez (2001) looked at the effect of immobilisation stress on mice over a period of 14 days, and found dramatic reductions in the number of circulating white cells in the experimental animals ($P \leq 0.001$) compared to controls. They also observed changes in the proportions of the different cell populations, in particular they noted a reduction in lymphocytes and of those a high proportion were of an immature phenotype which may show auto reactivity. Their results led Dominguez-Gerpes & Rey-Mendez (2001) to conclude that:

> *'The magnitude of such changes and their physical location most likely reflect the strong and complex influence of stress on the maturation and/or mobility of the lymphoid cells. In general, T-cells are more affected than B-cells.'* (Dominguez-Gerpes and Rey-Mendez, 2001)

Unfortunately the authors did not monitor levels of cortisone therefore it is not possible to identify whether the animals had in any way started to habituate to the stress by the end of the two weeks. McEwen et al (1997) in their paper suggested that chronic stress tends to lead to enhanced immune function, although this was based on the results of only a few studies and more current reviews (Moynihan, 2003) recognise that chronic stress appears to influence immune function in a negative way, as described in the work conducted by Dominguez-Gerpes & Rey-Mendez (2001). These apparently contradictory conclusions may in part be due to individual differences in cortisol response patterns in relation to repeated stress. In a thorough study of 54 pairs of young adult twins (age 16 – 24 years) Wüst et al, (2005) exposed their subjects to 3 discrete periods of moderate psychosocial stress. The team observed that only 52% of subjects expressed signs of habituation to repeated stress (the team's hypothesised response) as shown through decline in their pattern of cortisol response. Whereas 30% of subjects showed no obvious change in response across test days and almost 16% appeared to sensitise to its effects. Herbert and Cohen (1993) suggest that any negative effect of chronic stress on immune function might be partly accounted for by stress 'boosters'- incidents that occur at regular intervals to remind the person of the initial stressor and inhibit habituation. Equally, long-term stressors may be associated with behavioural changes in for example eating, sleeping or smoking which in themselves inhibit habituation or alter hormone levels (Reiche et al, 2004). Finally, pre-morbid individual differences such as sex, age and coping have been suggested to influence immune response to chronic stress (Dominguez-Gerpes and Rey-Mendez, 2001). Therefore, perhaps it is not just the stressor, which causes the harm but also the psychological and behavioural influence it may have over the person experiencing it.

It is important to recognise that there are differential effects of stress on the immune system, which depend on whether the stress is acute or chronic. Based on current knowledge it is generally recognised that whilst acute stress primarily enhances immune function, chronic stress appears to cause marked suppression of certain elements of the immune system (Dominguez-Gerpes and Rey-Mendez, 2001; Moynihan, 2003). Evidence to date appears to indicate that the components of the immune system affected primarily by the immunosuppressive action of stress are those responsible for immune surveillance (cell-mediated immunity). As previously

summarised, Dominguez-Gerpes and Rey-Mendez (2001) observed the effects of immobilization stress on the immune systems of mice and demonstrated a marked effect on the concentrations of the different subtypes of T-cell lymphocytes. This fact denotes it is the cell-mediated immunity which appears to be primarily influenced by stress and may account for findings suggesting that chronically stressed individuals are more prone to viral infections (Moynihan, 2003). Equally Andersen et al (1998) identified that in 116 women who had received a diagnosis of, and surgery for invasive breast cancer, degree of stress predicted reduced natural killer cell and lymphocyte activity to a statistically significant level. Both of these measures are relevant to the cancer prognosis. Cohen and Rabin (1998) consolidated evidence up to date, which pointed to the potential for a correlation between psychological stresses, a compromised immune system and cancer progression. Keicolt-Glaser et al (2002) suggest this may be the case particularly in cancers associated with a viral element such as the Epstein-Barr virus. Bovbjerg and Valdimarsdottir (1998), whilst cautiously confirming that a link is possible between the factors mentioned formerly, emphasise that rigorous research is necessary to establish a definite connection. In line with the need for clear correlational work, Sephton et al (2000) as discussed previously, showed alteration in the normal circadian fluctuations of cortisol levels to be correlated with poor prognosis in patients with breast cancer. To date, there have been minimal amounts of work looking at the influence of chronic stress in relation to the onset or progression of haematological malignancies (Keicolt-Glaser et al, 2002). However logic would suggest that if stress has a role to play in influencing immune function, it may also for example, influence *recovery* of immune function in immunosuppressed patients following chemotherapy by dictating the percentages of the various cell populations within the regenerating marrow. T-helper cells developing in the presence of high levels of cortisol may be influenced to develop a line of Th_2 cells (Rook, 1999). This and other possible connections will be developed further in the discussion chapter.

2.5 Psychoneuroimmunology

Psychoneuroimmunology (PNI) is a field of study, which:

'Investigates the interactions between the neuroendocrine and immune systems in response to environmental circumstances and the psychosocial factors that mediate these interactions' (Caudell 1996).

The theory behind such research lies with the theory that psychological factors such as stress can have a variety of adverse effects on the immune system including suppression of cellular immune mechanisms (Bauer, 1994; Keicolt-Glaser and Glaser, 1999; Lutgendorf, 2003). It is also suggested that psychologically induced changes to the immune system, which are mediated by the central nervous system (CNS) and neuroendocrine system may be partly responsible for changes in susceptibility to immune system mediated disease (Cohen and Herbert, 1996; Fletcher et al, 1998). Lengacher et al (1998) in their review of PNI develop a quote from Solomon (1987) to elucidate the philosophy behind the field:

'PNI adheres to the view that all diseases are multifactoral and biopsychosocial in onset and course, showing the interrelationship between carcinogens, bacteria, viruses, genetic, endocrine, nervous, immune, emotional and behavioural factors'. (Lengacher et al, 1998)

Solomon (1987) in his theoretical paper proposed 31 hypotheses, which have evidence-based support confirming the validity of the postulated links between the psychological and neurological influences on health. Solomon (1987) facilitates the reader to understand that PNI is concerned with observing how stress related behaviour for example, affects the rather complex interactions between the three body systems of the psyche, the immune and the neuroendocrine systems. This obviously involves research into the workings of both the hypothalamic-pituitary-adrenal axis (HPA) and the autonomic nervous system (Glaser and Kiecolt-Glaser, 1998).

The treatment and environment in which the patients on the Adult Leukaemia Unit are nursed is inherently stressful and there is unfortunately very little that can be done to change it. However, what may be possible is the reduction of *perceived* levels of physical and psychological stress in this situation. When patients are admitted to a high dose therapy transplant unit they have many stressful issues to deal with which makes active participation in their recovery difficult for them. Examples identified by Campos de Carvalho et al (2000), include being far from home, long hospitalisation and high morbidity. Campos de Carvalho and colleagues (2000), looked at expressed needs of patients undergoing bone marrow transplant and identified that preservation of patients perceived control, expression of feelings and sensitivity to need for affection by the patient were all-important in making them feel secure. Although health care personnel can do little to reduce the level of stress they are under, as professional carers the aim is to help these patients cope with stressors in a constructive manner. This can be seen as particularly important in light of the fact that there is work showing evidence for the potential role of psychological factors in progression of certain conditions including some types of cancer. In a longitudinal study looking at the effect of prior psychiatric intervention on survival in 68 patients with melanoma, Fawzy et al (1993) documented a statistically higher death rate in control subjects (10/34) than in subjects who had received the intervention (3/34). This longitudinal study constituted a 6 year follow up for a previous randomised controlled trial looking at the effects of psychiatric support on psychological and immune parameters. Fawzy et al (1990 & 1990) reported that patients who received the support showed enhanced coping, reduced psychological distress and enhanced immune function. Butow and her colleagues (2000), argue that the data linking the development of breast cancer to psychosocial factors is not robust, however, Keicolt-Glaser and her colleagues (2002) in their later and more extensive review of evidence conclude that there is now enough data to confirm psychological modulation of immune function in certain pathological conditions including certain types of cancer. Cohen and Herbert (1996) clarify this view in their review of Psychoneuroimmunology studies, which evaluate the influence of psychological factors over immune function:

'Invasion of the body by a disease-causing agent is not sufficient cause for disease. Disease occurs when host defenses are compromised or unable to recognise the

foreign material. This is why psychological variables that influence immunity have the potential to influence the onset and progression of immune system-mediated diseases' (Cohen and Herbert 1996).

If this is so then by definition, there is also the suggestion of a role for psychological support or therapy aimed at reduction of stress in cancer survival. Kiecolt-Glaser and Glaser (1992) examined work linking stress, immune function and health and acknowledged that there is a large body of data which quantifies such a connection, especially in relation to loneliness and/or social isolation as the stressor (Speigel et al, 1998). That social support has the potential to influence immune function can be seen in a study by Baron et al (1990). Baron and colleagues looked at the perceived social support of 23 spouses (2 men and 21 women) of cancer patients and its effect on certain measures of immune function including NK-cell activity, total lymphocyte and total T-cell populations. Baron and his team found that subjects high in social support had an NK-cell activity, which was statistically significantly higher, then those low in social support ($F(1,21 = 7.91, P < 0.01$), but that numbers of cells did not differ between groups. It is suggested by Baron et al (1990), that these findings are consistent with prior studies that appear to indicate it is functional rather than quantitative measures of immunocompetence, which are influenced by psychological variables. These findings have obvious implications for the patients on the ALU who are nursed in isolation. What Kiecolt-Glaser and Glaser (1992) also recognised, was that the work which evaluated the benefits of psychological interventions in these situations, had to date been limited and often flawed in that explanations other than the stress - immune system link were not explored. More recent work however (Van Der Pompe et al, 1997; Cruess et al, 2000; Larson et al, 2000) would seem to confirm psychological interventions to be effective in reducing cortisol levels and/or enhancing the immune function of women being treated for early stage breast cancer. Cruess et al (2000) for example, showed significant reduction in cortisol levels ($P < 0.05$) amongst women with early stage breast cancer ($N = 24$) following a 10-week course in cognitive behavioural stress management (CBSM) compared to a control group of patients who were put onto a waiting list ($N = 10$):

Cortisol levels -

Baseline: (CBSM: mean = 6.14, SD = 3.12; control: mean = 6.68, SD = 3.44)

Postintervention: (CBSM: mean = 4.66, SD = 2.08; control: mean = 6.15, SD = 2.49)

Specific stress-related factors that have been identified as possible contributors to immunosuppression are: sleep deprivation (Krueger et al, 2003; Irwin et al 1994), depression (Herbert and Cohen, 1993; Scheifer et al, 1989; Clow, 2002) and fluctuation of mood (Cohen and Herbert, 1996). Irwin and colleagues (1994) showed that in 24 healthy males volunteers (age range 22 – 61 years), even sleep deprivation of as little as 2.4 hours (average for their study), could lead to statistically significant reduction in immune function. Irwin and his team (1994) measured NK-cell activity as an indicator of immune function. On the night of partial sleep deprivation they documented a reduction in NK-cell activity, which demonstrated only 72% of the baseline activity ($P < 0.01$). There are fewer studies measuring the effect of anxiety (especially chronic) on immune status (Dunn et al, 1995), although it would seem reasonable to assume that due to the high sympathetic nervous system arousal associated with anxiety, it too could be expected to influence the immune system in an adverse way.

One area of work that has major implications for patients treated in isolation units is the wealth of evidence suggesting that interpersonal relationships are influential in the maintenance of health and buffering the effects of stress (Cohen & Herbert, 1996). Using a subject sample of 37 healthy male volunteers (mean age 23.8 years) Heinrichs et al (2003), were able to show the protective effects of social support in times of acute stress. Subjects who were requested to bring a close friend along whilst they took part in the study (completion of the Trier Social Stress Test), showed significantly lower levels of salivary cortisol than those in the control arm (social support x time (1 minute before stress) effect, $F(2.4,80.5) = 8.52$, $P < 0.001$). Loneliness has also been cited as a factor detrimental to immune function (Hawkley and Cacioppo, 2003). Glaser et al, (1985) looked at the fluctuation of Epstein-Barr virus (EBV) titres in 49 medical students (mean age 23 years) before, during and after an examination period. Their results revealed that high-loneliness subjects had significantly higher EBV antibody titres then low-loneliness subjects ($F(1,47) = 3.98$, $P < 0.05$) indicating compromised immune competency. Cacioppo et al, (2000) looked at approximately 130 college students comparing lonely with socially embedded subjects. The authors found the lonely subjects to be at variance with the socially embedded subjects in a number of ways. However, the finding most pertinent to this work was that elevated mean cortisol levels *across the course of the*

day characterised chronically lonely individuals. Unfortunately it is not clear from the paper whether this finding reached statistical significance.

If this is a real effect then logic suggests most patients being treated for haematological malignancies will for at least part of their time on the isolation unit be at risk of decreased immune competency purely through being isolated. As discussed previously, perceived availability of social support, someone to talk to, has been recognised as beneficial to health (Baron et al, 1990; Ernst and Fugh-Berman, 2002). What is not so clear however, is the mode of social and / or psychological support, which is most helpful in alleviating the stress caused by the above-mentioned factors (Cohen and Herbert, 1996). A review of evidence relating to intervention studies by Miller and Cohen (2001) suggest that to date although there appears to be potential for modulation of the immune system through psychological intervention such as stress management or hypnosis, there are important methodological issues which need to be addressed before conclusions can be drawn as to their actual benefit. Equally it may prove inherently difficult to identify one generically superior form of intervention due to the fact that people have different coping strategies to deal with stressful situations (Antoni, 2003) consequently any intervention would need to be tailored appropriately. It has also been recognised that coping strategies themselves may have an influence over immune function. Esterling et al (1994) for example, identified that people who used repression as a coping strategy against for instance threatening information, showed a repression of cellular immune function. It could be argued therefore that one concern with haematology patients nursed in isolation is that they maintain a high stress level by constant repression of emotion through isolation and lack of social support. What is required is research looking at the influence of alteration in 'biobehavioural mechanisms' such as cognitive and behavioural coping strategies (Antoni, 2003). Whilst it may be difficult to find a single psychological support intervention that could deal with all these factors (for example people who cope by repression may not feel comfortable with talking about their problems), it may be possible to reduce stress levels in most patients by relaxation through massage.

2.6 The Influence of Massage on Stress

Based on the literature reviewed in section 2.5 of the thesis, it is accepted that a person under stress is a person in a heightened state of distress and anxiety, with associated disruption in levels of stress hormones such as cortisol. Consequently it can be usefully assumed that if massage reduces perceived anxiety and normalizes levels of cortisol, it is reducing that person's stress levels.

2.6.1 Tiffany Field

One team of researchers stands out in their contribution to understanding the power of touch and that is the team led by Dr Tiffany Field. They are based at the Touch Research Institutes, which is part of the University of Miami, Florida. For almost two decades they have been producing research, which has consistently shown massage to reduce levels of stress as defined above in a variety of settings. They are perhaps best known for their pioneering work looking at the effects of massage on preterm infants. In one of their earliest studies (Field et al, 1986) the team showed in a sample size of 40 pre-term babies, that massaged babies gain up to 47% more weight than non-massaged babies using a very specific massage protocol over a period of 10 days. They also documented that the massaged babies were more alert and responsive and were discharged from hospital an average of 6 days earlier then the non-massaged babies (Field et al, 1986).

Field and her team replicated their earlier work with a study looking at a further 40 babies; 20 neonates in both the experimental and control groups (Scafidi et al, 1990). In this work they addressed the limitations of their previous trial design such as the length of video recording of the babies' sleep/wake behaviour, which rather than being for 45 minutes post stimulation was here recorded for 8 hours. They also stratified randomisation of the infants depending on gestational age, birth weight, entry weight and length of stay in the intensive care unit. Once again they were able to show a statistically significant increase in weight gain for the massaged infants as can be seen by table 2.3, which shows a consolidated overview of their results:

Mean and Standard Deviations for Weight Gain Seen in Neonates During a Massage Study Period of 10 Days

	Treatment		Control	
Measurements	**Mean**	**S.D.**	**Mean**	**S.D.**
Average daily weight gain prior to study (3 days)	19.6	10.5	24.5	11.1
Average daily weight gain during study	33.6	5.4	28.4	5.5
Number of feeds per day	8.6	0.7	8.9	1.4

Table 2.3 (Adapted from Scafidi et al, 1990)

Equally, as previously (Field et al, 1986), they noted a reduction of 5 days in hospital for the neonates who had been in the experimental group. The exact mechanism by which massage helps to bring about these positive effects is as yet unknown and is the subject of current research at the Touch Research Institutes, however it is possible that it includes an element of stress reduction. (For review, see Field 2001 and 2002). Field's team went on to explore the effects of massage in diverse areas and in many cases included measures of immune function. They have shown that massage does improve various parameters of immune function - as was seen to be the case when they provided massage therapy for HIV^+ men (Ironson et al, 1996). In this complex but thorough study, 29 gay men (20 of whom were HIV^+) received daily massage for a month. A subset of 11 HIV^+ subjects acted as within-subject controls and were assessed during the massage month and a control month without massage, half of this control group received their massage first, the other half second. Assessments included psychological parameters such as levels of anxiety, physiological parameters of stress such as urinary and salivary cortisol, and measures of immune function including natural killer cell (NK cell) number and activity - cells which are important to cell mediated immunity. They were able to show a statistically significant reduction in state anxiety over the massage month (Pre: mean, 39.0, SD, 10.5; Post: mean, 31.89, SD, 8.6; $t = 3.28$, $P < 0.01$). Also, a statistically significant interaction was observed in relation to cortisol levels, with a decrease during the massage month and a marginally significant increase during the control month (one-tailed test $P < 0.05$). The immune measures showed several statistically significant results including increase in activity of NK cells during the massage month (Pre: mean, 24.43, SD, 16.4; Post: mean, 33.29, SD, 19.5; $P < 0.01$). Most powerful however were their correlational results:

'Decreases in anxiety were significantly correlated with increases in CD56 lymphocyte number (NK cells) *(r = 0.66, P = 0.001, N = 23) and greater average increases in self-rated relaxation during the massages were also significantly correlated with greater increases in CD 56 lymphocyte number (r = 0.46, P = 0.02, N = 24).'* (Ironson et al, 1996)

Such results show a clear interaction between reduction of stress as measured through reduced levels of anxiety and cortisol and improved immune function. More recently (Diego et al, 2001), the group carried out a similar study on 24 adolescents who were HIV^+ comparing massage with progressive muscle relaxation. Again they showed subjects in the massage arm to experience a greater reduction in anxiety and depression and enhanced immune function as measured by increased numbers of NK-cells ($t(11) = 2.84$, $P < 0.01$ (1-tailed)). Examples of their work specifically looking at the influence of massage over stress include a study of 30 adults in which hypertension and associated symptoms were reduced in subjects who received massage, including salivary cortisol ($P < 0.05$) (Hernandez-Reif et al, 2000). Professor Field and her team have also shown the benefits of massage in reducing signs of stress in patients suffering from psychiatric disorders such as depression and eating disorders, (Field et al, 1998; Field et al, 1992; Hart et al, 2001). In addition they have documented that regular massage for children and adults suffering from chronic conditions such as juvenile rheumatoid arthritis and fibromyalgia not only reduces symptoms of stress but also the perception of pain (Field et al, 1997; Field et al, 2003). Hernandez-Reif and colleagues (2004) have recently completed a study looking at improving mood, immune function and reducing levels of stress through massage, in 34 women with early stage (I and II) breast cancer. Their results suggest massage to be beneficial in a number of ways, including statistically significant reductions in anxiety as measured using the State Trait Anxiety Scale (First day: Pre: mean 37, SD 14; Post: mean 27, SD 13, Last day: Pre: mean 35, SD 10; Post: mean 25, SD 8), ($F(1, 32) = 4.49$, $P < 0.05$) and enhancement of immune function through increase in numbers of NK-cells in the massage group. An analysis of co-variance performed on numbers of NK-cells from first to last day of the 5-week study period disclosed a statistically significant group effect ($F(1,26) = 4.22$, $P < 0.05$), which reflected a significant positive change in NK-cell numbers for the massage arm over

the study period (mean = 27.6, SD = 16.8; t(14) = 1.73, P < .05) and a negative change for the control arm (mean = -17.8, SD = 18.2).

There are many more studies that could be quoted from this prolific team, however, the work described here does illustrate the diversity and thoroughness with which Professor Field and co-workers conduct their studies.

2.6.2 Other Research

One of the methodological concerns with could be directed at some of the otherwise very meticulous studies which have come out of the Touch Research Institutes looking at the effects of massage is that on occasions their sample sizes have tended to be relatively small (Diego et al, 2002). Two recent studies from other workers have gone some way to redress this concern; Cassileth and Vickers (2004) reported effects of massage on over 1,000 cancer patients from the Sloan-Kettering Cancer Centre over a period of 3 years. They concluded that massage had an immediate and substantiative beneficial effect by reducing symptoms of anxiety, depression, pain and nausea. They also reported that in the case of outpatients these benefits were still evident at least 48 hours later. Although these authors did not include physiological measures of stress in their research paradigm, the symptoms they did measure were those commonly associated with stress, therefore it is reasonable to conclude that the massage did reduce levels of subjective stress. In the second study, again with cancer patients, Post-White and colleagues (2003) showed massage to reduce ratings in several measures including anxiety and perception of pain in 230 patients.

Field's work is now being validated by a growing body of additional evidence highlighting benefits of massage (Vickers, 1996; Pan et al, 2000; Smith et al, 2002; Zappa and Cassileth, 2003), including reduction of physiological indicators of stress. Hayes & Cox (2000) in a quasi-experimental study offered 5-minute foot massage sessions to 25 patients (age range of 19 – 81 years) being nursed on critical care units. They documented values for physiological variables including heart rate, blood pressure and respirations before, during and after massage. Results of repeated measures analysis of variance showed a statistically significant effect between the time periods for all three variables.

Mean and SD for Before, During and After a Five - Minute Foot Massage

Time Period	Heart Rate		Mean Arterial BP		Respirations/Minute	
	Mean	SD	Mean	SD	Mean	SD
Before	97.34	20.40	85.53	12.18	23.04	6.22
During	94.68	21.61	83.57	12.26	21.25	5.72
After	96.30	21.04	81.13	12.41	20.97	5.71

Table 2.4 (Adapted from: Hayes & Cox, 2000)

Post hoc tests showed heart rate during massage was significantly lower than either before ($P < 0.005$) or after ($P < 0.02$), blood pressure was significantly lower during foot massage compared with before the intervention ($P < 0.001$) and respirations were significantly lower during ($P < 0.009$) and after ($P < 0.001$) foot massage than before the intervention.

From a slightly different perspective, cancer patients have also been seen to be proactive in using complementary therapies – including massage, to both improve immune function and ameliorate the side effects of cancer treatments. Morris et al (2000), in a postal survey enquiring about use of complementary therapies, received a total of 617 replies from the original 1,935 questionnaires sent to a random selection of cancer patients attending their centre. They discovered that 53% of these patients used massage and that this was one of the top three therapies used (the others being nutrition therapy (63%) and healing herbs (44%)). Interestingly the primary goal stated for use of these therapies was to strengthen their immune system (73%) followed by the alleviation of side effects from pharmacological treatments (39%).

2.6.3 Research in Patients with Haematological Malignancies

Unfortunately, there have been only minimal amounts of work looking at the effect such interventions would have on patients with haematological malignancies such as acute leukaemia. The treatment of choice for patients with acute leukaemias is

potentially curative and involves high dose chemotherapy. As discussed previously such treatment can paradoxically cause rapid deterioration in the patient's physical condition and requires them to be nursed in isolation rooms (Zittoun et al, 1999). Equally such patients are prone to a plethora of contra indications relating to massage (see section 2.2.). Consequently little clinical work has been done with this patient group and even less research. Professor Field and her team (2001) published the results of a small, randomised study (N = 20) in which parents in the experimental arm were trained to massage their children (all female, mean age = 6.9 years) who were suffering from acute lymphoblastic leukaemia (Field et al, 2001). The trial period lasted for 30 days for each child. The team measured immediate and longer-term change in levels of anxiety and depression in parents and children as well as variation in white cell and neutrophil counts across the 30 days; results from children in the massage arm were compared to those in a waiting-list control arm. The results looked promising with for example, a statistically significant reduction in depression scores over the study period for the parents performing the massage (First day mean, 19; Last day mean, 6.0; P = 0.05), which was not evident in the parents in the control arm (First day mean, 13.7; Last day mean, 13.0). The children who had been massaged also had a significantly greater number of white blood cells (WBC's) and neutrophils, which was not evident in children from the control group at the end of the month (WBC's - Massage: First day mean, 2.5; Last day mean, 4.0; P = .05; Control: First day mean, 3.5; Last day mean, 2.9. Neutrophils - Massage: First day mean, 39.8; Last day mean, 52.2; P = .05; Control: First day mean, 40.5; Last day mean, 35.3). Unfortunately the team omitted to say whether the children were being massaged as outpatients at home or whilst they were inpatients, neither did they specify what treatment regimens the children were on. Both these factors had the potential to bias the results if they were not accounted for in the randomisation process. With numbers of subjects as small as those used here, the results could also have been strongly biased due to white counts coming up naturally from a nadir following chemotherapy. Equally, whilst Field et al (2001) state their results show statistically significant changes in levels of anxiety, depression and immune functioning, they do not look for associated change in cortisol levels, nor do they present any power calculations, so it is not possible to identify whether the number of children used were sufficient to show a true effect.

In support of the idea that massage may be beneficial in haematological oncology, a study by Ahles and colleagues (1999) showed that in patients undergoing an autologous bone marrow transplant (though not all subjects were suffering from haematological malignancies), massage led to reduction in diastolic blood pressure, nausea, distress and anxiety - particularly in the period of time directly following the massage. However, in this randomised study of 35 patients, subjects randomised to the massage arm did not all receive the same number of therapy sessions and, as with the Field et al (2001) study, power calculations were not stated therefore it is difficult to assess the validity of the results. Smith et al (2003) looked at specific healing outcomes following three different interventions for patients undergoing bone marrow transplantation. However, only a small minority of patients were suffering from haematological malignancies. Smith et al (2003) showed, using a rating scale developed by the researchers, that there were a number of perceived benefits from massage therapy - including reduced scores in for example, insomnia and anxiety and/or depression. In this study subjects were seen every third day for the duration of their continuation in the study (criteria for discharge not stated) both as in and outpatients, once again the number of sessions received by each subject was not standardised. Smith et al (2003) recruited 88 patients into their study, unfortunately, 27 withdrew (25 of these withdrew following assignment to study arm) – suggesting an element of discomfort with the protocol. Once again the researchers did not provide power calculations to support their choice of patient numbers, and the rating scale used to assess patients' perceptions of the intervention they received was unvalidated.

These three studies suggest a potential benefit to patients undergoing bone marrow transplantation. However they all show serious methodological flaws, including lack of power calculations on which to base the number of subjects required in order to demonstrate true statistically significant change in their chosen outcome measures. None of the studies discussed standardised the number of the interventions each subject received therefore it is possible that a critical number of interventions is required before an effect will be seen. Neither did the researchers in the studies standardise the time of day for the sessions, this is important as a number of physiological variables (including cortisol levels) fluctuate throughout the day and may impact on a persons' response to therapy. Finally it is difficult to assess from

the research papers reviewed whether the patients were isolated for all, some or none of their time in the respective studies. Once again the potential psychological impact of isolation is such that it should be a variable, which is accounted for in the study design.

2.7 Potentially Additive Benefits of Essential Oils

So far only studies looking at the benefits of massage have been reviewed. There are far fewer researchers who have tried to evaluate any additional benefits of using essential oils in massage therapy (Corner, 1995). However, Kite et al (1998) in an evaluation of their service at a cancer support centre confirmed the role of aromatherapy massage in reducing psychological distress. Kite and colleagues used an observational study of practice by working alongside their aromatherapist. The team employed the Hospital Anxiety and Depression scale (HADS) (Zigmond and Snaith, 1983) pre- and post study as part of their patient assessment. In the 58 patients (of an original 89 referred to the service) who completed the 6 sessions of massage required for the study, Kite et al (1998) documented a significant reduction in anxiety, depression and combined scores for the HADS:

Mean and Standard deviation HADS Scores for Oncology Patients Pre and Post Aromatherapy Sessions

	Pre		Post		t-test	P value
	Mean	SD	Mean	SD		
Anxiety	8.9	9.0	6.2	6.5	5.1	<0.001
Depression	6.1	6.0	4.0	4.0	4.3	<0.001
Combined	15.0	14.0	10.2	10.0	5.5	<0.001

Table 2.5 Adapted from Kite et al (1998)

Unfortunately, although this study suggests a benefit to cancer patients of having aromatherapy massage, because there was no comparison group used it is not possible to say whether that benefit is greater then it would have been with massage using base oil only. Buckle (2003) in her paper highlighted several areas of care where aromatherapy massage may be beneficial to children, but acknowledged that a large amount of the evidence specifically relating to essential oils (including that published in texts aimed at professionals such as Price and Price, 1999) is based on historical usage and anecdote (Buckle, 2003). Equally, it is difficult to tease apart the potential benefits of massage from those of essential oils in much of the research

Buckle (2003) quoted. Wilkinson et al (1999), in their work with cancer patients in a hospice setting suggested that the benefits of massage are greater when essential oils are used although not necessarily to the point of statistical significance. Wilkinson and her team (1999) randomised 103 patients to receive a series of 3, hour long weekly massages, either with base oil or with aromatherapy oil. Of the original 103 randomised, a total of 87 patients completed the study. This team used as part of their outcome measures the Rotterdam Symptom Checklist (RSCL) (De Haes et al, 1990) and observed a number of improvements in both physiological and psychological subscales for patients in both intervention arms. Wilkinson et al (1999) noted that improvements appeared to be greater for patients in the aromatherapy arm although suggested this may be partly due to the nurse therapists behaving differently with patients in the aromatherapy arm. The biggest concern with this study by Wilkinson et al (1999), in relation to evaluating the benefits of essential oils is that - possibly for the purposes of standardisation, the team used only one oil (roman chamomile). It is suggested therefore that this study is not an evaluation of the additional benefits of essential oils; rather it is an assessment of the potential benefits of *one* oil. Soden and her team (2004), wanted to identify the more long-term effects of massage and aromatherapy massage on cancer patients. The researchers randomised 42 patients to receive a series of four weekly massages, with either base oil or aromatherapy oil, or no massage (control arm). Soden et al (2004) whilst identifying that weekly massage improved sleep scores, were unable to show any supplementary benefit for the use of lavender essential oil in the carrier oil. It is suggested that as with the study by Wilkinson et al (1999), Soden and her colleagues (2004) did not evaluate the effects of aromatherapy massage in which oils are chosen and blended individually for a specific patient, but the effects of one oil – in this case lavender. One study to have looked at the use of essential oils in an environment similar to that used in this work was a trial by Dunn and colleagues (1995), carried out in an intensive care unit – although it is not stated whether these patients were nursed in isolation. Dunn and colleagues initially randomised 122 (age range 2 – 92 years) into their study, which had 3 arms (massage, aromatherapy massage and undisturbed rest) and required patients to receive 3 sessions of 30-minutes. Unfortunately not all patients were eligible to participate (N = 111) and of those that did, not all received the full three sessions (N = 66). The results of Dunn et al (1995) showed no statistically significant change in physiological measures (blood pressure,

heart rate and respirations) in any of the arms following therapy sessions. However following the first session, a significantly greater percentage of patients in the aromatherapy arm reported a reduction in level of anxiety following treatment when compared to patients in the rest arm (Aromatherapy: N = 36, % of patients with improved assessment, 72; Rest: N = 36, % of patients with improved assessment, 44; P = 0.05) - although this effect was not sustained. Unfortunately, once again the arm described as the aromatherapy arm in the study by Dunn et al (1995) used only lavender oil. Fellowes et al, (2004) in a review of clinical trials looking at the use of massage and aromatherapy for patients with cancer, concluded that evidence was mixed as to whether the use of essential oils enhanced the benefits seen from massage in cancer patients. Unfortunately, as evidenced in this thesis, in the studies identified for the review by Fellowes et al (2004), there was a maximum of two but more commonly one essential oil used in the research. The concern with this approach as previously suggested is that it is not the benefits of aromatherapy, which are being assessed, but rather the benefits of the individual oil.

In an attempt to understand what receiving aromatherapy massage meant to cancer patients, Dunwoody and colleagues (2002), explored the qualitative aspects of receiving massage using an interview technique with 11 oncology outpatients in the setting of a focus group. In this work aromatherapy massage was carried out in a clinically appropriate way with the therapist and patient choosing the oils for the massage together. The results of Dunwoody et al (2002), confirmed the de-stressing effects of massage as well as highlighting other benefits such as empowerment of the patient and aromatherapy as a reward.

In all the studies quoted so far, essential oils were added to massage in order to enhance the relaxation effect of the massage through their suggested sedative effect. However, it is important to recognise that essential oils have in fact been shown to possess many useful qualities and different oils are recognised as being for example antimicrobial agents (Gravett, 2001), anti-inflammatory agents or expectorants (Price and Price, 1999). They have been used for centuries in many different ways for all manner of problems such as relieving minor inflammation caused by sunburn (Price and Price, 1999). In light of the many and varied properties of essential oils it is important to explore their use in a broader sense rather than just focusing on their

potential for enhancing relaxation - although it is obviously recognised how useful such a property is. It was in order to more fully evaluate the potential use of essential oils in the clinical setting that in-vitro testing of the essential oils used in this research had been commissioned. The results of this independent work were anticipated to compliment the results of the clinical trial presented in this thesis.

2.8 Summary

In summary therefore, there is considerable literature looking at the influence of cortisol as an indicator of stress and the impact it has on health, primarily through its influence on the workings of the immune system. Equally there is a growing volume of work indicating the benefits of massage with or without essential oils in reducing stress levels and improving immune function. Rather worryingly however, in none of the studies highlighted in this review was there any mention of documenting negative side effects of the therapy. Also, many studies have serious methodological flaws including lack of power calculations and / or small sample sizes, lack of comparison groups or clinically inappropriate use of essential oils. In each of the studies reviewed here the authors expected the subjects to undertake a series of massage sessions, in seriously ill patients undergoing intensive chemotherapy this is not an appropriate basis on which to assess the benefits of such a therapy as often patients are unable to complete such sessions (Dunn et al, 1995). Also, up until now there has been a dearth of literature looking at whether massage has the capacity to reduce stress levels for patients undergoing high-dose chemotherapy in conditions of isolation.

The work presented in this thesis has begun to address the deficiencies identified in the current literature. The study presented here looked at whether single sessions of massage either with or without the use of essential oils, chosen in a clinically relevant manner, had the potential to safely reduce stress in patients suffering from haematological malignancies. Levels of physiological stress were measured pre and post intervention and reduction or normalisation of cortisol levels, plus reduction in subjective levels of stress, were acknowledged as an indication of the benefits of the therapy. However, during a semi-structured interview patients were specifically asked if there was anything they disliked about the session, thus giving them the opportunity to voice any concerns they might have had regarding the session they received. It was anticipated that this would allow me to highlight any safety issues related to the massage or the use of essential oils.

The main focus when setting up the massage service was to improve the quality of life of the patients on the adult leukaemia unit, fundamentally by reducing their stress

levels and giving them something positive to focus on. As has been stated, the patients are often on their own in their rooms for hours on end with only the television and four walls for company. It is suggested that such an environment would become stressful after only a day or two but these patients have to cope with it for weeks, sometimes months on end. When people are admitted onto the unit they relinquish much of their control over what happens in their lives. They become reliant on others for most things, they have little choice over what or when things occur and they have no choice but to face the fact, day in and day out that if, despite everything, the treatment fails, they will die. It is suggested that massage offers a short retreat from their isolation and the stress of their situation.

Stress is something that is encountered in daily life. In moderate amounts it can be useful in that it stimulates one to act, to maintain motivation. It can be seen as an ongoing interaction between organism and environment, a dynamic relationship (Lazarus and Folkman 1984). However chronic stress is, as has been discussed in the previous sections, detrimental to health (Lengacher et al, 1998), and it is hoped that the use of massage will help to alleviate a portion of the perilously high levels of stress experienced by the patients nursed on the ALU.

Chapter 3:

Methodology

3.1 Introduction

This chapter of the thesis describes the logic behind the choice of methodology, the aims of the work and its philosophical underpinnings. An overview is given of the various protocols used in the work, the outcome measures and methods of analysis. Finally the reader is taken on a chronological journey through the pre-pilot work followed by the pilot and main studies.

3.2 Choice of Methodology

The main challenge for a study aiming to evaluate a complex therapy such as massage, which can be interpreted as providing physiological and psychological support, is the choice of appropriate methodology. The last decade has seen a rapidly developing trend for people to look to complementary therapies instead of, or as an adjunct to, orthodox medicine (Foundation for Integrated Medicine, 1997). Reasons for this include anxiety over ever more powerful drugs and dissatisfaction with the perceived limitations of orthodox medicine. This international move towards public use of a wide variety of therapies has occurred despite the fact that up until recently there has been minimal research showing objective benefits of many of these remedies (Cassileth, 1999). Work done in recent years is beginning to show that aromatherapy and massage may have a useful part to play in the care of patients with life threatening conditions. Dunn et al (1995) provided evidence, which suggested aromatherapy massage might reduce anxiety in patients nursed on an intensive care unit (see section 2.7 for a review of this study). Other researchers have observed effects such as a reduced perception of physiological symptoms, including pain. Nixon et al (1997) used an equivalent groups design to assess the effect of massage on the post-operative pain of 39 patients (19 treatment; 20 control) who had undergone abdominal surgery. Nixon and colleagues (1997), did not standardise the amount of massage received by patients but documented the number of minutes massage a patient received in 24 hours. They also monitored patients' pain scores and self assessed pain tolerance. Using repeated measures analysis of co-variance (within subjects design) they showed that for patients in the treatment arm included in the analysis (those controlling their own analgesia or receiving intravenous medication; N = 16), perceptions of pain were significantly lower following massage ((F (1,139) = 8.73, P = 0.0037). Thy also showed a significant

effect for age (F (1,139) = 20.22, P = 0.0001) with patients between the ages of 41-60 years appearing to benefit more than other age groups. However, this particular cohort of patients received 2.5 times as much massage as patients in other age bands. The use of comparison groups by Nixon et al (1997) was appropriate in order to measure the result of providing massage to patients, unfortunately by not standardising the level of intervention it became difficult to quantify its true level of effect. Weinrich and Weinrich (1990) looked at the consequence of a 10 minute massage treatment on levels of pain in 14 cancer patients using a visual analogue scale, which they compared with a control group of 14 cancer patients who received a visit from the 'therapist' (one of seven senior nursing students). Their results showed a statistically significant drop in levels of pain immediately following massage in males only (Initial score: mean, 4.19; SD, 2.6; Post score: mean, 2.93; SD, 2.93; F(5,13 = 8.24, P = 0.01), however the effect had disappeared one hour later. Whilst Weinrich and Weinrich (1990) used an appropriate randomised trial design for their study, they used nursing students with only one hour of training in massage to carry out the intervention - which only lasted for 10 minutes. These two factors plus inconsistency in massage technique between the seven students may well have been responsible for the low level of response to the massage. As with research carried out on adults, work with preterm babies has shown massage to produce consistent physiological effects such as lowering blood cortisol levels (physiological indicator of stress) (Field et al 1996; Field, 2001). Acolet et al (1993) identified that in 8 pre-term baby boys, gentle massage from an experienced neonatal nurse in the late afternoon resulted in a consistent fall in cortisol levels compared to samples taken from matched controls who showed no evidence of a similar drop in cortisol levels (median difference –35.8 nmol/l, P = 0.035, Wilcoxon matched pairs). Although the numbers in the study by Acolet et al (1993) were small, the study design was appropriate and because of minimal confounding factors (pre-term babies for example cannot get relief from stress or distraction from pain by talking to the therapist in the same way an adult can) the response to massage as seen by the fall in cortisol levels can be accepted as a true effect.

Work has been carried out in the field of oncology to evaluate what part massage and aromatherapy might have to play in the supportive care of patients suffering from cancer. McNamara (1994) used postal questionnaires to review the beliefs of

independent practitioners and massage schools (training institutions for therapists) that were at the time offering massage to clients with cancer. The results showed overwhelmingly that the majority of those interviewed (95.6%) believed the benefits of massage to outweigh any risks. Attempts have been made to quantify the effects of massage on patients with cancer (Corner et al 1995; Sims 1986; Ferrell- Torry and Glick 1993). Wilkinson (1995 and 1999) compared the effects of massage with and without essential oils. All studies have shown a trend for massage to give physiological and psychological benefit to this patient group, and Wilkinson's results suggest that the benefits of massage are non-significantly greater when essential oils are used (1995 and 1999). As discussed in section 2.7, there was no work identified looking at aromatherapy massage, where the essential oils used were tailored to the subjects' needs. For the sake of standardising the trial variables, one or at the most two oils were chosen to work with (Wilkinson, 1999). This is a point which needs bearing in mind, as individually chosen blends appropriate to the needs of the client are important if patients are to gain maximum benefit from the oils. Equally, whilst there is a growing body of evidence highlighting potential benefits of massage there has been very little work done with patients suffering from haematological malignancies. Ahles and colleagues (1999) conducted a randomised study comparing change in several parameters, in 35 patients undergoing an autologous bone marrow transplant following massage compared to controls. However, they did not standardise the number of massages received by each patient nor was there a standard time for collecting physiological data (blood pressure, pulse and respirations).

On reviewing the methodologies available it appeared that the randomised controlled trial (RCT) was still the most appropriate for providing best quality evidence when comparing one type of treatment with another. This was also the case when comparing treatment with placebo, in the arena of orthodox medicine – especially for laboratory based work or large drug trials when extraneous variables can be well controlled. However, as highlighted by Long and Mercer (1999), there are major problems with trying to simplify complex interventions such as massage to fit them into the format of an RCT. The situation becomes more challenging and complicated, as there are no established methodologies in this arena. Kite et al, (1998) for example evaluated their aromatherapy service for patients with cancer, but

highlighted lack of literature giving recommendations for how to set about such an evaluation as being a major problem. An example of one of the issues faced by researchers being that it is extremely difficult to standardise touch therapies (Long and Mercer 1999), and in some cases totally impossible to blind the subject to what therapy they are receiving (such as massage with or without essential oils – essential oils have an aroma), which would be required for strict adherence to an RCT protocol.

Despite these limitations, many elements of the RCT can be usefully adapted and incorporated into less stringent designs in order to enhance their reliability (Walker and Anderson, 1999). It was felt that this approach was the most appropriate way forward for this particular trial. A decision was made to use a mixed methods approach and award equal status to the measurement of psychological and physiological benefits of massage by integrating quantitative and qualitative elements into the design. By using a mixed methods approach and incorporating a large element of qualitative assessments into a study based on the principles of a randomised controlled trial, I was allowed the freedom to design the study in a manner more relevant to service evaluation. As was discussed previously, one criticism of earlier work looking at effects of essential oils, was that they did not use the oils in a clinically appropriate way by choosing them on an individual basis, they were standardised in order to fit with the design of an RCT. Equally, site of massage is often standardised in study protocols, again this is not appropriate clinically as to massage a patient's feet for example when they have tension in their shoulders means the subject will not receive maximum benefit from the therapy. I felt that to have maximum clinical relevance was of greater importance than to have a rigid trial protocol.

3.3 Aims

With regard to the aims of the study therefore, the first aim was to identify psychological and physiological effects of massage primarily through alterations in the levels of stress hormones, both with and without the use of essential oils, and to document any side effects of therapy. The inherently stressful environment of a high-dose therapy isolation unit was the site for the study, and data from massaged (experimental) patients was compared with those from patients experiencing an equivalent amount of time spent in peace and quiet (control). The issue of whether any physiological and psychological changes seen occurred in parallel was addressed through the format of case studies.

The second aim was to look at whether any benefits were achievable after a single session of massage. Moyer et al (2004), in their recent meta-analysis of the benefits of massage call such effects 'single-dose effects' and they appear to date to be focused on psychological effects such as state anxiety (Diego et al, 2001) within a protocol evaluating the effects of a series of massages, rather than within a study designed specifically to evaluate the impact of single sessions of massage.

Because of the additional safety issues surrounding the use of essential oils (see p.8) additional laboratory studies had been commissioned to explore the antimicrobial activity of the oils used in this study. Although this work was independent of the clinical study it was hoped that the results of the work would help me gain a broader view of the effects of the oils before offering suggestions regarding their clinical usage.

3.4 Theoretical Framework

The complex nature of this research means that a number of theoretical frameworks are relevant. It is unusual for example to adopt the mixed methods approach and combine both quantitative and qualitative styles of research in the same study. Philosophical ideas from different theoretical frameworks have been of influence in the design of the work and as such have been described in this section. It is suggested that no one framework is satisfactory in isolation as a basis for the study therefore elements from a variety of approaches such as phenomenology and naturalism have been integrated to provide appropriate context for the data analysis and discussion.

This work is fundamentally clinical in nature, it is a reflection of years of clinical practice and the aim is to develop that practice through expansion based on evidence. There is much literature describing the problems associated with chronic stress, for example sleep disturbance (Bovbjerg, 2003; Backhaus et al, 2004), negative emotions such as anxiety and depression (Keicolt-Glaser et al, 2002) and loneliness (Hawkley and Cacioppo, 2003). These and other relevant issues are discussed in greater detail within the appropriate sections. However, the theory presented here is quite simply that any patient diagnosed with a potentially fatal yet potentially curable disease, who is then isolated from friends and family, subjected to various invasive procedures and treatment which in itself may kill them, is likely to feel under incredible levels of stress. The theory and my own clinical experience is that appropriate supportive care can help to minimise the trauma of going through such an experience. It is important at this juncture to clarify what is meant by 'supportive'. In the clinical setting the term 'supportive care' is used to identify all treatment given to the patients, which is not directly related to the curative aspect of their care, this can range from the delivery of antibiotics to the offering of dietary advice. Within the framework of this thesis the supportive therapy in question is massage. The Oxford dictionary (Swannell, 1986) definition of 'support' reads as follows: 'carry all or part of weight of; keep from falling or sinking or failing...' The implications of such a definition in this situation are both powerful and poignant; it suggests that any care, which is defined as 'supportive,' is also inherently going to enhance the patient's chance of success and therefore, survival. That being the case it is fitting for me to

share my clinical knowledge with others so that greater numbers of patients going through similar experiences can have access to such support.

Although many studies have been published looking at the effects of massage therapy, any theory relating to potential physiological mechanisms through which the benefit occurs tend to be implicit (Moyer et al, 2004). From a physiological point of view there are two theories made explicit by Moyer and colleagues (2004), which are pertinent to this work:

1. That massage shifts the patients' neurological state from the chronic state of heightened SNS activity seen in somebody faced with permanent threat; increased cardiovascular activity and levels of stress hormones (e.g. cortisol) compounded by feelings of anxiety and/or tension. To an increased level of parasympathetic nervous system (PNS) activity indicative of a person at rest i.e. a reduction in cardiovascular activity, lower levels of stress hormones and feelings of calm.
2. Promotion of restorative sleep patterns which lead to better balance of the body's chemistry. The cited authors propose this as a theory for reduced pain perception, it is suggested here however that improved sleep patterns will also redress the balance of hormones in the HPA axis and so lead to reduced feelings of stress and associated physiological and emotional responses.

It is my primary theory however, that regardless of the pathways of bodily change, the way in which massage offers support to each patient centres around the fact that within a massage session the therapist is nurturing or caring for the patient physically and as such showing recognition and acceptance of them and their needs. This in turn sets up a relationship of trust between the therapist and the patient. In a secure environment such as the one described here, the patient is by definition offered a space to deal with their psychological needs. They may use the time to 'switch off' and forget their problems, alternatively they may wish to disclose and reflect on their concerns with the therapist. Either way, from this perspective the patient should always lead the session. It is suggested that the combination of physiological and

psychological care and attention inherent in any massage session is what culminates in the benefits - including any physiological changes, observed following massage. Whilst this is the core philosophy on which the thesis is based, it is acknowledged that there are formal philosophical theories, which will be drawn upon to enhance the design of the study and as such these have been outlined and their influence highlighted below.

3.4.1 Triangulation

In order to perform this study effectively it was important to look at both the individual views / physiological responses of the patients and the generalisable effects such that any results maybe used effectively to develop our service and by other units hoping to set up such a service. Whilst it was important to look for consistent responses to the therapy, without taking into account the individual views of the patients it was possible to miss pertinent issues that may be of great value in any future developments. As such, a process known as 'triangulation' was used. Triangulation is a practice in research whereby combinations of different methods are used in the design to achieve an overall picture (Temple, 1997). Consequently, although the study had the basic layout of a randomised, controlled trial (RCT) in order that any consistent physiological and psychological effects could be monitored, it was actually of mixed methods design, which meant all subjects were also reviewed from a qualitative perspective so that issues specific to individual patients would not be overlooked. This was also important as each patient had their own individual 'cocktail' of drugs and previous history of treatment, the effects of which may have masked the beneficial physiological effects of the massage for a particular patient. This would consequently have reduced the observed effects of the massage on all patients within that arm of the trial as measured through inferential statistics. As such, information from each session (physiological and psychological) was collated into an individual case file for each subject and three of these files have been presented as case studies within the thesis. The process was necessary in order to try and see the massage experience through the eye of each patient, to gain insight into their perspective. To further inform me about an individual's response to therapy, I used discrete sessional diary entries to document issues pertinent to every session such as any conversation that occurred and its general content (was it emotive or general chit-chat), what else was happening on the unit, (was it particularly noisy and

if so did that appear to bother the patient?) and how the patient seemed to be coping with their situation both physically and emotionally. Each diary entry was collated with the appropriate patient file. Such an approach enabled me to put into perspective physiological responses to massage dependant on every patient's sessional experience; did they for example have visitors during the session? Were they due treatment that day? What was their attitude towards what was happening? Did they reveal how they were coping with the experience and was the massage to form part of that coping?

3.4.2 Phenomenology

When working in this way, there are certain philosophies it is important to recognise in order that the work be valid in its interpretation. One such viewpoint is the concept of phenomenology (Bryman, 1992). In its true form as a research paradigm, phenomenology is recognised as a very specific way of working. However, within this thesis the term phenomenology has been used as a broad general concept relating to the idea that people form constructs within which they make sense of their life experiences. This concept has been employed to help create a framework within which to structure the study.

Phenomenology is one of the theoretical principles used to underpin qualitative research and is based on the belief that people create constructs with which to view their world based on their own knowledge, experience and understanding and this helps to give their world structure and meaning. In other words, they use these constructs to interpret their world and what happens within it. As such, it is important when exploring the meaning of something to someone (in this case, massage to a patient) that we look at it from his or her point of view not only the point of view of the researcher. One problem facing the patients on the ALU is that their constructs are likely to have lost their validity; they no longer help the person make sense of their world because their world has changed beyond all recognition. Therefore, do they create new constructs or try and adapt old ones? For a lot of patients, whichever route they elect, the process can take a long time - especially if they are deeply committed to their former views of the world. Consequently a considerable amount of stress may ensue as they come to terms with their reality. A person who experiences life as a leader for example and likes to feel their life has a

high degree of routine and control, relying on timing and appointments to order their lives, will find existing on a unit where timing of procedures and medications can at best be disrupted by unknown influences, at worst random, very disorientating. Accordingly, they are left feeling vulnerable and out of control until they can build up new constructs or adapt old ones to incorporate their new situation. In other words, all participants of life have created their own reality of the world within which they feel comfortable. By putting them into an unknown environment with it's own entrenched traditions, over which the patient has little or no influence, the chances are high that for a short while at least (much longer for some) the patient is put into a situation of discomfort. For some people this is very difficult and can lead to high levels of stress and anxiety, panic attacks or depression, especially when combined with the knowledge that they have a life threatening illness. One of the greatest hardships is that fighting to regain control of a situation that is fundamentally uncontrollable is both stressful and mentally exhausting.

This work recognises and reflects on aspects of phenomenology as being important in order to grasp the fuller picture of the patient experience without embracing the whole philosophy.

3.4.3 Naturalism

Another philosophical theme to be acknowledged in this work is that of naturalism as defined by Matza (1969). Within this view of research methodology, to study any aspect of the social world it must be left in essence unchanged. In other words, not manipulated by the researcher imposing his or her own constructs based on preconceived ideas, which can distort the 'naturalness' of the setting. Whilst it is recognised that the setting under examination in this case is anything but natural, it must be acknowledged to have its own patterns, routines and systems which although alien to the outside world are accepted as normal and unchanging on the unit. For that reason, it was important to know not just whether the massage service had a beneficial effect on the patient *but whether it is beneficial within the environment of the ALU,* if it was not so then any fundamental benefit is irrelevant in this setting. Because one of the broader aims of the work was to encourage other units to develop similar services, unless it can be shown that massage is useful within this environment then any results would be redundant. For this reason the study was set

up to run as the regular service with minimal alteration to the normal care of the subjects; the massage for example, occurred in the patient's room and nurses still came in (if required) to administer drugs to patients. The fact that the patients received the massage on their beds, not in a specially selected quiet room (which would have been inappropriate due to their need for isolation), meant that they were still exposed to all the noise and disturbance of the daily routines. Although this was likely to reduce any observed benefits of the therapy, any benefits noted could be seen as a true reflection of what can be achieved in such a setting. For the same reason, each session was assessed on its own merits. Whilst it is interesting to look for the cumulative effects of regular sessions, in reality many patients are not on the unit long enough to receive a series of massages; as a consequence it is most realistic to look for benefits, which can be achieved after one session. As with phenomenology, this work whilst not based on the philosophy of naturalism, was set up in such a way as to recognise the importance of it.

3.4.4 Summary

To summarise, because of the complex issues being addressed in the study, it was important to try and pull together information from both a quantitative and qualitative perspective within the format of a mixed methods design. The results presented in the work aim to give a numerical assessment of the influence of massage and aromatherapy within an isolation unit. However, that information has been complimented by a report of personal change brought up by patients on interview. In this way it was hoped the work would be seen as assessing the efficacy of the service on a general level as well as taking account of individual reports from service users. Of paramount importance in this study was the *context* within which the work is being performed. Whilst there are studies showing the benefit of massage within other NHS settings (Wilkinson 1995 and 1999), what cannot be ascertained from such works is whether it is feasible to assume such benefits are still achievable within the environment described here.

3.5 Subjects

3.5.1 Recruitment

The nurses working on the unit routinely refer patients for massage therapy, as do the medical staff; equally the patients may request therapy themselves. For the purposes of the trial, all patients newly admitted onto the unit during the study period were told about the trial and given an information sheet to read. At least 24 hours later they were asked if they would be interested in participating. For those wishing to take part a trained research assistant then went through the information sheet with them answering any questions which arose, checking inclusion / exclusion criteria and if appropriate, obtaining informed consent. Those patients already using the massage therapy service continued as before outside of the trial until they were discharged or wished to cease.

3.5.2 Characteristics of study sample

The characteristics common to all subjects taking part in this study were that they had a haematological malignancy (leukaemia, lymphoma or myeloma); were sixteen or more years old and at the time of their entry into the trial they were inpatients on the high dose therapy isolation unit, which was the site of the study.

In order to make the results of this work of clinical relevance, it was imperative that the inclusion criteria be as broad as possible (see inclusion criteria in section 3.5.3). Patients on the ALU can range from newly diagnosed patients with no prior experience of hospitalisation to patients who have received a stem cell transplant for their leukaemia and are back following a relapse in their condition. They maybe 16 years up to 75 years old (note, there is no rigid upper or lower age limit), male or female, unemployed or a hospital professor. They may be physically fit and active or have a life threatening septicaemia; they may be coping well with their condition and their treatment or be suffering from panic attacks, clinical depression or claustrophobia. To try and tease out a homogeneous sample from this group of people would be both impractical and inappropriate. For the massage to be effective it must be effective for all patients, not just a small, carefully selected subgroup – who incidentally could easily move across the boundaries of such an arbitrary grouping system especially if it was based on clinical condition. There were

however, certain factors, which it was important to address when selecting patients for the trial, these are laid out as the inclusion and exclusion criteria and the rationale for selecting these criteria is discussed below. The aim was to deal with the effects of all the above-mentioned variables through the design of the study, through randomisation. The actual demographic details of the subjects are outlined at the beginning of the results chapter (chapter 4).

3.5.3 Inclusion criteria

In accordance with section 3.5.2 above, the inclusion criteria for the study were made as broad as possible. All subjects had to be inpatients on the unit and for consent purposes were of age 16 years or over.

3.5.4 Exclusion criteria

Patients considered unfit for entry by medical staff. The clinical condition of the patients on the unit can vary enormously; consequently it was imperative that each patient had consent to enter the trial from the medical team on order to confirm fitness for entry.

Patients with a history of psychiatric illness. It was recognised that patients with a history of psychiatric illness may have extra problems coping with stress, which could influence their physiological and psychological response to massage considerably. For exclusion to be necessary, the condition had to exist prior to their current condition. It was acknowledged that patients might develop (usually sub-clinical) psychiatric problems such as anxiety or depression because of their current situation, however it was felt that because this was a realistic and common response to what was happening in their lives it would be dealt with through the randomisation process.

Patients who had received aromatherapy massage in the last 6 months. It was accepted that those patients who had recently received an aromatherapy massage were likely to have different expectations to the rest of the subjects and that this might noticeably alter their response to therapy. Consequently an arbitrary cut off point of 6 months was chosen as being the most recent experience of massage allowable, anything more recent then that meant exclusion from entry into the study. Note: anyone who had ever received a massage from me (being as I was the study therapist) before was excluded from the study.

Patients with a history of arthritic problems. It was acknowledged that patients with arthritic problems might require alteration in massage techniques, which were at variance with standardisation of the massage sessions. For this reason it was felt appropriate to exclude them from the trial.

Patients with an aversion to massage therapy. For obvious reasons such patients were not entered into the trial.

Patients with liver function tests and / or urea and electrolytes of greater or equal to 3 times normal limits. The concentration of essential oils used for the study was set at 1%, which was felt to be too high for patients with severely compromised liver and or kidney function as these are the organs responsible for metabolising the essential oils. Accordingly, any patient with severely deranged organ function, as documented through current blood biochemistry showing hepatic or renal function tests raised by a factor of three was excluded from the trial.

Patients requiring certain drugs. There are certain drugs that are recognised as falsely raising, particularly prolactin but also cortisol levels. The drugs of primary concern for this group of patients are high dose steroids and metaclopramide. High dose steroids are used in the treatment protocols of certain leukaemias and can influence cortisol levels. Metaclopramide is an anti-emetic commonly used for intractable nausea and vomiting, which raises prolactin levels. A full list of the drugs leading to exclusion from the trial can be found in appendix IV (page 280). Any patient who had been prescribed and had taken these drugs in the previous week was excluded from the study.

A list of all patients given an information sheet was kept and reasons for non-participation was documented for patients who did not proceed to entry into the study. Any patients who were not eligible for the study were offered massage outside of the trial situation as part of the standard service offered on the unit.

3.5.5 Sample size

One of the intentions of the work was to identify whether comments offered by the patients in the previous audit (see appendix I, page 272) suggesting that massage helped them to relax, might be associated with physiological reduction in stress levels. Therefore it was decided that the primary endpoint of the study needed to be reduction in serum levels of the stress hormones cortisol and prolactin, following

massage. When the initial sample size was determined no directly relevant work and minimal related work was identified on which to base the numbers calculation (Van der Pompe et al, 1997). Consequently the initial sample size was based on standard deviations from the only published data to be found using both cortisol and prolactin as part of the outcome measures. The study was comparing immune and endocrine response to psychological intervention for stress (psychotherapy). The authors were looking at the effects of psychotherapy on several indicators of endocrine and immune function in patients with breast cancer compared with healthy volunteers (Van der Pompe et al, 1997). For the sample size calculation in this study the paired t-test formula of the nQuery Advisor V. 3.0 was used. It was calculated that with 80% power, 63 patients per arm would be required to detect a 0.5 standard deviation shift in the mean values of the parameters measured, independent of the unit of measurement. This calculation assumed normality of data or normality achieved through logarithmic transformation. However, because the methodology of the trials was different, it was decided that an interim assessment was necessary after 16 patients per arm; these numbers were sufficient to detect a 1 standard deviation shift in the mean values with the same assumption of normality. If changes in mean values were seen to be statistically significant at this point then the trial would be stopped. Consequently the final sample size was not fixed and could be changed after the first 48 cases if the estimate of standard deviation was different to that of the published data.

The above calculation proposed that the sample size for the study be a minimum of 48 patients; in practice, the actual sample size for the trial was 39 patients (13 patients per arm). This meant there was 68% power to detect a 1 standard deviation shift in mean values.

In total, 225 patients over the two-year study period were invited to participate. This averaged out at > 2 patients per week. There were a number of reasons for patients' non-participation in the study and a table showing the reasons can be found in section 4.2.1 of chapter 4.

A large amount of data was created during the trial all of which required analysis. There was a set time frame within which these analyses needed to be performed,

therefore, despite not having treated the 48 patients initially set for the interim analysis it was decided following advice from the statistician to close the trial. The statistician's advice was given following a review of the results from the pilot study (see section 3.13 of this chapter), which showed far greater changes in hormone levels following the study sessions then the 1 standard deviation shift originally anticipated and on which the original sample size was based.

For a study of this nature it would have arguably been appropriate to compare results with normative data, to ensure clinical significance of the primary outcome measures (change in levels of cortisol and prolactin). Such a step may also have reduced the number of subjects required per arm. However, whilst there appears to be an inherent constancy to a person's circadian rhythm in relation to their cortisol levels, (see section 2.3.2 in chapter 2) it is also acknowledged that variation in stress levels will cause changes in cortisol levels which overlay the diurnal pattern. Because of this fact and the unpredictability of the environment on the ALU, it was felt that to try and compare results with data from healthy volunteers for example, would have been unrealistic and inappropriate.

3.6 Ethical Issues

In line with government policy of the time, ethical approval was sought from the South Manchester Local Research Ethics Committee in December 1999. Following minor amendments to the study protocol, ethical approval was granted in January 2000 (copy of approval letter attached, see appendix VI, page 285). The hospital research and development unit also passed the study without question. However, there were ethical issues, which were of concern on a practical level:

Issues relating to patients in the control arm: By definition if people consented to the trial they were happy, if not eager to try massage as a therapy. Although it was clearly explained to them from the outset that they may not receive a massage whilst participating in the study, it was anticipated that they would still feel an element of disappointment if they were randomised to the control arm. In an attempt to alleviate their regret as much as possible it was reiterated to them regularly that they would receive a massage as soon as their time in the study was over. That patients in the control arm would receive a massage post-entry into the study was written into the protocol. An associated concern regarding this point was that dissatisfaction relating to their randomisation may falsely raise a patient's baseline cortisol / prolactin levels. Because of this issue, all subjects randomised to the control arm were once again given a formal offer for them to withdraw from the trial, the expectation being that those patients who felt strongly enough would withdraw, thus minimising the risk of any skewing of the results. It is interesting to note however, that this did not occur. A connected ethical issue related to the taking of blood from patients in the control arm who received no massage as recompense for the repeated intrusions whilst the blood was taken. Unfortunately no way around this matter could be found other than to be sure, through explanation, that each patient was clear as to why the control group was necessary and how important their contribution was to the outcome of the study.

Involvement in multiple studies: Although this was not expected to impinge on the current study, the burden of being involved in more than one study needed acknowledgement, especially in such a vulnerable set of patients and as such was a consideration in the recruitment of subjects.

Ethnic background of the subjects: A percentage of patients treated on the unit are of ethnic minorities and some of these do not use English as a first language. Whilst it was not the intention of the study to exclude such people, unfortunately resources were not available to translate the measures into a number of different languages. It was proposed that where suitable, interpreters would be used although this proved not to be necessary.

Use of essential oils: There was a concern around the use of essential oils relating to the risk of sensitivity reactions. However this risk was seen as minimal; careful observation and a past history of allergies were used to highlight potential concerns and close collaboration with medical colleagues meant appropriate medication could be prescribed if required, although it proved not to be necessary.

Interview related anxiety: There is always the possibility that a patient may find the interview process disturbing. However, there were no searching or intimate questions involved and as the researcher, I was well supported in referring patients to appropriate services if the need should have arisen; happily it did not.

Clinical status and age of subjects: Lastly, the majority of the patients who would be recruited for the study would be severely ill, and it was possible that some would be as young as 16 years old. However, the aim of the aromatherapy massage was to ease the stress and anxiety associated with their current position. Equally teenagers admitted to the ALU appear to benefit greatly from massage. In the case of teenagers between 16 – 18 years, the patient's parent / guardian were asked to countersign the consent form. If the patient was too clinically unstable to participate, it was realistic to assume that the doctors would have decided at the point of eligibility that they were too unwell to be entered.

3.7 Study Design

The focus of this study was to see whether massage with or without essential oils could be usefully employed to reduce the impact of stress in all its various guises such as anxiety, depression, sleeplessness and pain for patients being treated on a high dose therapy isolation unit. The reasoning behind this was firstly to ease the suffering of people coping with the daily juxtaposition of life and death whilst isolated from loved ones, through enhancement of the holistic element of their clinical care. Secondly the study was seen as an important first step in exploring the feasibility of using massage as a mediator in the recovery of immune function of immunosuppressed patients.

In chapter two of this thesis attention was drawn to the growing body of literature (Field, 2000) showing the benefits of massage in many different environments, primarily it is assumed, through relaxation and the associated reduction of stress levels. However, the work of Professor Field and her colleagues has not to date explored additional benefits (if any) of essential oils and to date it has not been possible to find any work documenting the impact of massage on patients with leukaemia undergoing high dose chemotherapy. In order to capture what is hoped to be the greatest understanding of each patient's experience, a mixed methods design was used for this study. The expectation in using such methods was that as well as looking at physiological and psychological responses individually, we would be able to look at the relationship between any physiological changes in stress levels for each subject (measured primarily through serum cortisol and prolactin levels) and their psychological experiences – both positive and negative, in case study format. It was also hoped that by using such methods it would prove possible to identify whether any reduction in stress would impact on a physical level such as, reduction in chemotherapy induced nausea, sleeplessness or pain.

It was also important to identify how much of a role the therapist played in the therapeutic process. For logistical and financial reasons I was the sole therapist during the trial as well as the researcher, consequently it was necessary to try and quantify how much any change was down to my presence. Originally, the idea had been to use two therapists throughout the trial to see whether there was any

difference in the way the sessions were perceived by both the subjects and the therapists. This way of running the study would have made it easier to generalize the results, however, such an arrangement did not prove to be a workable option. On reflection, the positive aspect of using one therapist was that it became easier to standardize the sessions.

When the study design was being developed there was discussion about patients in a control arm being visited by a 'caring professional' as a placebo for the therapist's presence, however this may have proved stressful if the patient did not feel like talking to visitors yet felt obliged to converse with the professional 'on demand.' This theory has had recent backing by Smith et al (2003), who accounted for lack of physiological response in patients randomised to the 'friendly visit' arm of a trial assessing the benefit of massage, by suggesting patients may have found the visit 'irritating and annoying.' It was decided after much discussion that the comparison arm for this study should be focused on trying to give patients 'special time' without the false intrusion of someone else, as the therapist does not normally initiate conversation in the standard service, in fact the whole therapy can sometimes be carried out in total silence.

In order to account for all the potential extraneous variables such as: diagnosis, different drug regimens and physical condition of the patients, the study was based on an RCT to ensure random distribution of patients with varying diagnoses and clinical condition in each arm. Although it was recognised that it would be impossible to blind either the patient or myself to the arm they had been allocated, the laboratory staff measuring the serum cortisol and prolactin levels were blinded. The trial was set up with three arms in order to separate the effects of the massage out from any extra effects of the essential oils. Equally it was necessary to include a control arm that received no massage for comparison. As previously discussed, when the protocol was being prepared, the idea of having a trained professional sit with each patient in the control arm was discussed at length, however it was felt that this might be experienced as an imposition with the subject feeling they had to talk. In such cases it was anticipated that cortisol and prolactin levels would rise, as such the idea was rejected and a decision was made to set up the three arms of the study as follows:

- Aromatherapy massage (Experimental 1)
- Massage with base oil only (Experimental 2)
- Rest (control)

It was documented in the protocol that all patients in the control arm were offered massage at the completion of their part in the study. They were made aware that this would be the case on entry to the study.

It was noted in the literature review (section 2.7) that most prior research, looking at the benefits of aromatherapy massage in NHS settings, has only compared the effects of one or two oils with De Valois and Clarke (2001) being the main exception to this as they used seven oils in their work. A decision was made for this study to include all 40 oils normally used in the massage service on the unit (see appendix III, page 279) but to document which oils were used on each occasion (a maximum of three oils were used on any one subject) and why. The carrier oil used for the massage sessions was grapeseed oil. This oil is also used for the regular massage service because it has a low incidence for causing skin reactions (Price and Price, 1999).

Because the primary physiological outcome measure was the reduction of serum cortisol and prolactin levels, it was important to ensure clinically relevant sampling of the hormones. Consequently, following discussions with one of the consultant endocrinologists in the Trust it was decided that a series of blood samples were required with a baseline test taken at 11am in all cases in order to standardise the times of the sessions, and a sequence of 4 serum samples - one taken every ½ hour, following the session for two hours. This decision was based primarily on the knowledge that cortisol and prolactin secretion occurs in pulses throughout the day, leading levels of both hormones to vary - especially in the presence of stress, therefore a simple pre-post sampling would not have given sufficient information.

Finally, the unit in which the study was based is both noisy and busy, therefore it was important to try and identify whether these factors – and other disruptions to the session such as telephone calls, prevented any relaxation from occurring. It was anticipated that such data would be collected through the qualitative results.

3.8 Protocols

3.8.1 Sessional

Informed consent was collected from all patients within the week prior to their expected entry into the study (see copy of consent sheet in appendix V, page 281). They were told when their study session would take place and to expect a visit from the researcher on that day to confirm they were still happy to participate. Because of the possibility of rapidly changing medical conditions and the patient's free choice to change their mind about being involved in the study, it was felt important to incorporate this process into the study design. It also gave me as the researcher the opportunity to introduce myself prior to the study session. At this time I would take the opportunity to confirm the patient's full understanding of what to expect with particular emphasis on the number of blood samples to be taken and why this was necessary. I also reinforced the fact that there was a one-in-three chance they would not receive a massage and why having a control group was important. However, reassurance was also given that if they did fall into the control sub-group they would be offered a massage on completion of their part in the trial. Once it was established that the patient was fully aware of what to expect and that they were still happy to continue they were randomized into an arm of the study through the hospital's computer generated randomisation programme, which is run through the Trust's medical statistics department.

In order to establish baseline measurements for comparison, all patients recruited to the study filled in both the Likert pain scale (BPI) and quality of life questionnaire (EORTC QLQ C-30) with my aid approximately one hour prior to intervention (see appendices XI, page 300 and X, page 297). It was seen as necessary for me to help with these initial questionnaires in order to put some of the questions in context (see section 3.9.2 for discussion relating to EORTC QLQ-C30 and BPI). Because the EORTC QLQ C-30 is not designed for patients being nursed in isolation there are four questions, which could be seen as inappropriate or irrelevant to the patient, such as how difficult they found it to carry heavy shopping bags. However, answers to these questions were anticipated to be useful for assessing the patient's attitudes; did they see themselves as fit enough to carry bags or take long walks? Consequently it was necessary to explain to the patient that these particular questions still required an

answer if only a hypothetical one. From the perspective of the study, change in attitude or perception of overall physical strength was equally important to other aspects of quality of life. With regard to the pain scale not all patients suffered from physical pain so those with no pain were guided to only fill in the initial questions to confirm this.

Following completion of the questionnaires, I assessed those participants in experimental arm one for appropriate essential oils. Oils were chosen after discussion with the patient relating to problems they may have such as sleeplessness, pain or nausea. Because of the common problem of nausea it was also imperative to identify whether the patient had any likes or dislikes relating to aromas. The final choice of oils (a blend of two or three oils) was decided on by the patient and myself depending on the outcome of the discussion; a note was made of which oils were used and the reason for their use. Because of the risk of cross infection, the neat oils are kept in a central clinical area and are blended there with only the final blend being taken into the patient's room as per the unit guidelines (see appendix II, page 276). For this reason all patients were allowed to smell the blend before the session started to check they found it pleasant. If this turned out not to be the case the blend would have been changed at this point. All blends were of a 1% concentration with 4 drops (in total) of essential oil being blended into 20mls of cold pressed grapeseed oil. The company 'Natural Touch' supplied all essential oils and carrier oils used in this study. They were supplied with an expiry date and a batch number, plus each essential oil had a data sheet, which also listed the main components of the oil. Subjects in both experimental arms were asked what part of the body they would like to be massaged. For patients who had no physiological problems that they felt could benefit from massage or appeared unsure of what to expect, I offered advice regarding benefits to be expected from having different areas of the body massaged, before the patient made their choice. In cases of uncertainty it was recommended as standard that a foot massage be tried; it is the least threatening because it does not require the patient to undress.

Once all the documentation had been completed and in order to avoid falsely raised blood hormone levels, the protocol stated that all patients at this point be left to have 20 minutes bed rest prior to the baseline blood sampling and the start of the study

session. Immediately prior to the study session, which had been standardized at 11am, serum samples for baseline levels of the stress hormones cortisol and prolactin were taken. It was important for the timing of the blood sampling to be controlled, as cortisol and prolactin levels are both known to vary throughout the day. All patients have a central venous line and it was from the central line that all serum samples were taken. Because the central line directly accesses the patient's heart it is imperative that a strict aseptic technique is followed when drawing blood. As such the Trust policy for accessing central venous catheters was followed (see section 3.8.2.). Once the blood sampling was completed I took baseline measurements of the patient's blood pressure and pulse using an automated blood pressure machine (A & D Company Ltd, UA-767 Digital BP Machine). Unfortunately, due to issues of cross infection, it was not permissible for the same machine to be taken into the different rooms. Consequently blood pressure and pulse recordings could not be standardized across all patients, but were taken using the machine from the room in which the patient was being nursed. They were standardized however by the fact that all the machines came from the same company and the same machine was used throughout a particular patient's session.

All study sessions lasted for twenty minutes and were timed to commence at 11.15am. For patients in the control arm I took time prior to the start of the session to emphasize its relaxing aspects. Because much of a patient's time on the unit is spent on their own it was important that this time be seen as special. To enhance this it was ensured they were comfortable (either on a chair or the bed); the blinds were drawn and a 'please do not disturb' notice attached to the door. It was explained to the patient that they should see the time as under their control; that unit staff would not come in unannounced, and their privacy was under their command. They were also asked if there was anything they required such as a non-stimulatory drink or a paper to enjoy their time to the maximum. On five occasions patients asked if there was anything they could do to help themselves during their session after they had been randomised to the control arm. I offered them some very simple visualisation techniques, which were quick and easy to teach; they imagined the chemotherapy as a helper in their garden (bone marrow) clearing out the weeds (leukaemic cells). If they were about to have a transplant this was expanded so they then went on to imagine the transplant as fresh seeds being planted in their nice clean soil and

growing into big strong plants of their choice. Although it was possible that allowing such practice would skew the results, I decided that the risk was acceptable - especially since any potential bias was expected to reduce the difference between the groups by relaxing the patients and as such make it harder to prove the benefits of massage.

For those patients in the experimental arms, time was taken to make sure they were positioned comfortably and appropriately in order for them to gain maximum benefit from the massage. It was also reinforced that if at any time they felt uncomfortable or wanted to stop, the session would indeed stop. They were also given permission to talk or be silent in accordance with their wishes and that if they happened to fall asleep that too was fine. I had a routine massage for each part of the body, which consisted mainly of effleurage (stroking) movements (see section 3.8.3).

Repeat blood samples were taken according to the protocol laid out below 10mins after the end of the intervention and half hourly for two hours along with documentation of blood pressure and pulse. At the end of the two hours the semi-structured interview was also conducted. The questionnaires, blood pressure (using the automated blood pressure machine, pulse (also from the automated blood pressure machine) and blood samples were to be repeated after 24 hours. A flow sheet describing the lay out of the protocol can be seen in appendix VII (page 286).

3.8.2 Serum sampling

During the design phase of the study a decision had to be made regarding how to monitor the cortisol and prolactin levels of the subjects. The least invasive method of acquiring samples in clinical trials is through collecting samples of salivary cortisol (Backhaus et al, 2004). Unfortunately, many of the patients on the leukaemia unit suffer from mucositis. Mucositis is caused by break down of the epithelial lining of the oral cavity as a side effect of the chemotherapy, it is very painful with the patient often requiring intravenous analgesia and feeding for several days. Consequently, it was not thought ethical to ask them to try and produce five salivary samples within the space of three hours. It is possible that monitoring cortisol levels using different methods may make results from different trials incomparable; however, there is evidence to show that the reactivity of salivary

cortisol to stressors correlates well with that of serum cortisol (Kirschbaum and Hellhammer, 1994). Because all the patients in this study had a central line in situation it was felt to be more ethical and less stressful to take serum samples from the long lines:

Having washed my hands thoroughly, I would wipe down a dressing trolley with alcohol and open onto it a sterile dressing pack. The pack included sterile gloves for use whilst taking the blood and a sterile field to place underneath the central line catheter. All equipment (e.g. syringes) required for the procedure were opened onto the dressing pack and prepared for use. The end of the line was swabbed with alcohol and the bung removed. 5 – 10mls of waste blood was first drawn from the line to ensure a clean sample. The actual sample was then taken using a clean syringe. The line was flushed using 10mls of saline followed by a maximum of 5mls of a dilute heparin solution to prevent clots forming on the internal end of the line. A fresh bung was applied to the outer end of the catheter to complete the procedure.

3.8.3 Massage

It was important to standardize the massage sessions as much as possible in order that like be compared with like. Despite original plans to have two therapists for the study (see section 3.7), for several reasons there was in the end only one, myself. I am a qualified oncology / haematology nurse with a diploma in holistic aromatherapy (TIDHA). That there was only one therapist made standardizing sessions much easier. Because of the implications for clinical relevance, it was impossible to create a massage routine in which each patient would be worked on in an identical fashion yet patients' individual needs could still be addressed. It was strongly felt that patients' needs took priority over standardization of the sessions, as if these were not addressed, the patient could easily end up feeling irritated rather than relaxed. Full body massages are not appropriate for this group of patients because, far from relaxing the patient, they are likely to exhaust them. Equally, patients undergoing chemotherapy are often hypersensitive to touch; consequently a prolonged massage would become irritating. Therefore each patient chose which part of the body they wanted to be worked on, depending on physiological discomfort. The issues reflected upon, including different individual needs and varying parts of the body massaged, caused obvious problems in regulating the

sessions. However, despite the problems, sessions were standardized through the time spent (20 minutes) on each massage and the type of massage strokes used (mainly light effleurage/stroking movements). However 20 minutes is not arbitrary; it is based on work suggesting that 15 – 20 minutes is sufficient to impact on various aspects of emotional distress. Professor Field and her team have shown massage sessions of 15 – 20 minutes to impact in a positive way on, anxiety during math computations (Field et al, 1996); distress in children during treatment for burns (Hernandez-Reif et al, 2001) and measures of mood, sleep and pain in pregnant women (Field et al, 1999). Equally, short sessions avoid over stimulation of hypersensitive skin and give a reasonable chance of offering all patients on the unit the opportunity of a massage during the standard service. If the subject had specific needs, such as a stiff shoulder, then the routine would be adapted slightly to incorporate such needs otherwise it was possible that the patient would finish the session feeling frustrated and/or disappointed. It must be noted however that in such cases I always explained to the patient before the session began, that deep massage movements (such as deep tissue kneading) were not appropriate to use whilst they were undergoing high dose therapy and could in fact be counter-productive. The part of the body chosen for massage was documented in each case, as were any alterations in routine, which had been incorporated because of physiological problems.

For those patients randomized to the aromatherapy arm, essential oils were chosen on an individual basis from the list of approved oils for this study (see appendix III, page 279), both the oils chosen and the reason for each choice were documented. As has been discussed, although it would be more methologically rigorous to limit the trial to the use of a single essential oil or a standard blend of oils, this would not be compatible with relating the findings back to the clinical service provided, where blends of two or three oils are used, chosen depending on individual needs. However, although there are currently no standards for the production of essential oils, the oils were standardized in terms of supplier (Natural Touch) and concentration used, this was set at 1%.

3.8.4 Semi structured interview

A semi-structured interview was used to give the patient the opportunity to comment directly on their study session. An important aspect of the interview was the prompting of patients to raise any issues, which they felt were negative features of the therapy as these may have had a bearing on the safety element of the massage. Because it was recognised that many of the subjects taking part in the trial would be fatigued due to their medical treatment and side effects thereof, plus they were likely to feel sleepy following the massage, the questions asked were kept to a bare minimum. There were a total of three questions; these can be seen in figure 3.1:

The Three Questions used in the Semi-Structured Interview

1. 'Could you tell me the things you liked and disliked about the session you received?'
   This was followed by three prompts:
   'First the things you liked'
   'And the dislikes'
   'How do you feel now?'
2. 'If offered would you choose to have another rest/massage session again?'
3. 'Is there anything else you would like to add?'

Box 3.1

By keeping the questions general it was hoped that each subject would talk about what was most important to them. The aim was not to guide them to reflect on specific issues such as emotions, their relationship with me as the therapist, or physiological change but to see what was relevant for them. Whilst the questions were standardised and created to elicit most information in a minimal time frame (estimated at approximately 5 minutes per interview), the format was such that if a particular patient wished to greatly expand on their answers that too was possible. The person conducting the interviews was a trained research assistant. It was felt to be important that as the main researcher I was not part of the interview process as I was also the therapist and as such some patients may have felt inhibited in giving their honest opinion to me if anything they wished to say proved detrimental to the service. Each interview was audio taped – after permission had been obtained from the patient, however the research assistant also took notes in case the recording was

inaudible or the patient carried on talking after the cassette recorder was switched off.

3.8.5 Analysis of serum samples

Measurements of both cortisol and prolactin levels were carried out in the department of chemical pathology within the Trust. Because the trial required that a series of samples be taken on the day of the massage, a system was set up with the help of a member of the pathology staff whereby all the blood from a particular patient was analysed in the same batch and the results presented as a series. Both cortisol and prolactin were measured using the *Technicon Immuno 1*® System (Bayer, 1995):

Cortisol: For cortisol measurement using the *Technicon Immuno 1*® *s*ystem the method principle is: Heterogeneous Competitive Magnetic Separation Assay (MSA). Cortisol Antibody Conjugate and label Cortisol Enzyme Conjugate are reacted with the patient's serum sample and incubated on the *Technicon Immuno 1*® *s*ystem at 37°C. The reagent is added and a second incubation occurs during which the antibody /hapten complex is bound. Samples with no cortisol have the maximum label bound, while samples containing high cortisol concentrations have minimum label bound. Consequently the dose/response curve is inversely proportional to the cortisol concentration in the sample. The table below show the expected range of values for cortisol using this method as provided by the company:

Expected Range for Serum Cortisol Values

AM		PM	
Common Units (µg/dl)	SI Units (nmol/L)	Common Units (µg/dl)	SI Units (nmol/L)
6.2 – 29.0	171.1 – 800.4	3.0 – 17.3	82.8 – 477.5

Table 3.1

At the study site in which this trial was conducted, therefore for the purpose of the study also, SI units (nmol/L) are the preferred units of measurement for assessing cortisol levels.

Prolactin: For prolactin measurement using the *Technicon Immuno 1*® system the method principle is: Heterogeneous Competitive Magnetic Separation Assay (MSA). Prolactin Antibody Conjugate 1 and Prolactin Antibody Conjugate 2 are reacted with the patient's serum sample and incubated on the *Technicon Immuno 1*® system at 37°C. The reagent is added and a second incubation occurs during which the antibody complex is bound. Samples with no prolactin have the minimum label bound, while samples containing high prolactin concentrations have maximum label bound. Consequently the dose/response curve is directly proportional to the prolactin concentration in the sample. Table 3.2 shows the expected range of values for prolactin using this method as provided by the company. However, at the Trust in which this trial was conducted, therefore for the purpose of the study also, (mU/L) are the preferred units of measurement for assessing prolactin levels, as such an additional column has been added to table 3.2 showing the equivalent range in expected values expressed as mU/L:

Expected Range for Serum Prolactin Values

GROUP	Common Units (ng/mL)	SI Units (nmol/L)	Christie Units (mU/L)
Male	3.0 – 16.0	0.12 – 0.66	83 – 440
Female	3.0 – 19.0	0.12 – 0.79	83 - 527

Table 3.2

In both cases the results of the assays were correlated with two other assays by the company (Bayer, 1995) using the Pearson's correlations, giving four results in total; in all cases the correlation between the methods were > 0.97:

Table of Correlational Values for Serum Assays Used in the Study

Hormone	Comparative System/Method	r
Cortisol	Abbott TDx	0.988
	DPC Coat-a-Count	0.987
Prolactin	DPC Coat-a-Count RIA method	0.977
	DPC Double Antibody RIA method	0.993

Table 3.3

The coefficients shown in table 3.3 indicate the substantial level of correlation between the two tests.

3.9 Outcome measures

It was suggested in the hypotheses for the study that the effects of the therapies would be short-lived. A transitory response was predicted as the repeated interruptions necessary for blood sampling after the session, together with the intrusion of external disturbances were anticipated to disrupt relaxation. Consequently, each session was assessed as a single session with follow up over 2 hours and again 24 hours later. These two assessment points were chosen in order to give an immediate as well as a more long-term evaluation. The primary endpoint for the study was identified as a statistically significant fall in serum cortisol and prolactin levels as objective, physiological indicators of reduction in stress.

3.9.1 Physiological measures:

The four physiological outcome measures used in this study are described below:

Cortisol and Prolactin: One of the main aims of the study was to identify and link psychological effects of massage with physiological changes. Such changes were identified and measured principally through reduction in stress. Consequently a statistically significant drop in levels of cortisol and prolactin - the stress hormones chosen for this work, following the study session was identified as the primary endpoint for the trial. On the advice of the endocrinologists, cortisol was seen as the principle measure, with prolactin used as a secondary measure in order to corroborate any findings.

Reasons for using cortisol:

- Pivotal in functioning of the HPA system (as described in section 2.3.2)
- Influences immune function (see section 2.4.4)
- Secretion influenced by psychological stress (Sobrinho et al, 2003)
- Easily measured
- Assay relatively cheap.
- Evidence that level can be altered through massage (see section 2.6)

Reasons for using prolactin:

- Secretion influenced by psychological stress (Sobrinho et al, 2003)
- Easily measured
- Assay relatively cheap
- Influences immune function (see section 2.3.3)

Blood pressure and heart rate: Raised blood pressure (BP) and heart rate (HR) are recognised as physiological indicators of stress, with reduction in both measures commonly used in research to show relaxation following intervention (Absi and Petersen, 2003). Therefore in an attempt to validate any change seen in the hormone levels, BP and HR were also documented at baseline and at each of the post therapy assessment points in order to correlate results with cortisol and prolactin levels.

Karnofsky performance status (KPS): The KPS is a one-dimensional physiological assessment scale historically used in clinical trials looking at the impact of chemotherapy on oncology patients. It was employed to give an appraisal of subjects' quality of life (Karnofsky and Burchenal, 1949), however, it is the clinician not the patient who completes it. In the context of this study the KPS was not used as an outcome measure of quality of life, but was included in the patient's baseline assessment in order to give a global evaluation of each person's clinical status on entry to the study (see appendix IX, page 296).

3.9.2 Psychological measures

Although the primary measures were physiological, it was seen as imperative for the validity of the work to ensure that any potential change in physical status be reviewed alongside any change in psychological well-being. For this reason several steps were taken to ensure a comprehensive assessment of psychological state and wellbeing was available for each patient.

Quality of life: Any research aiming to evaluate a complementary therapy service should include some measure of quality of life. However, because quality of life is a complex concept, it is appropriate to dedicate a short section of the thesis to a discussion of how and why the particular quality of life measure selected has been chosen for this work.

Quality of life is in general a rather amorphous structure, that is to say it tends to fluctuate depending on the perception of the researcher who is using the concept. It can be seen as trying to measure the essence of life inclusive of: mind, body and to a certain degree, spirit of the subjects, including their satisfaction with treatment and so on such as the Functional Assessment of Cancer Therapy (FACT)-BMT

(McQuellon et al, 1997). It may alternatively be finely tuned to understand for example, the way patients deal with their illness on an emotional level (Zigmund and Snaith, 1983) Hospital Anxiety and Depression Scale (HADS). Montazeri et al (1996) described some of the controversies within the field of quality of life measurement in relation to cancer medicine. Their work showed very clearly that the definition of quality of life depends fundamentally on what perspective it is being measured from. Montazeri et al (1996) use a quote from Calman (1987) in their paper that is itself from the work of Oliver Wendell Holmes (1860):

'*The longer I live the more satisfied I am of two things. First that the truest lives are those that are cut rose-diamond fashion, with many facets. Second that society is always trying in some way or another to grind us down to a single flat surface'.*
(Oliver Wendell Holmes, 1860)

Quality of life is very much like that diamond and by constantly trying to force it into a shape where we can see it all at once we are in danger of losing some of its most beautiful features. It is suggested to be more appropriate to describe or measure this treasure from the angle at which the researcher is observing it whilst acknowledging that it is almost impossible to capture the radiance of all facets at the same time. In line with this discussion, what one becomes aware of when reading the available literature, is that none of the measures created specifically for use in the hospital environment - some specifically for patients suffering from cancer, correlate sufficiently in what they measure to be used interchangeably (Kopp et al, 2000; Kemmler et al, 1999; Porzsolt et al, 1996). It therefore becomes imperative for the researcher to be clear in their own mind from what perspective they wish to look at their subject's quality of life. It is proposed that for the concept to have any meaning within the framework of a certain trial it must reflect a part of quality of life, which the researcher is able to influence. For the purpose of this study therefore it was important to identify a measure, which could assess the more functional aspects of a patients quality of life as it was expected that these were the areas, which the intervention would be able to effect. Examples of these aspects include:

- Physical functioning (Walking; dressing; looking after oneself independently)
- Symptomatic problems (Pain; nausea; anorexia)
- Emotional response to situation (Anxiety; low mood; insomnia)

It is for this reason that certain well-validated, reliable questionnaires were rejected. The FACT-BMT for example is one of the most thorough quality of life scales aimed specifically at this patient group. However, it is a bit too thorough in that it deals with issues this study could not hope to influence such as the doctor - patient relationship. Another well-respected questionnaire used for looking at aspects of quality of life that would have been relevant, with factors that could have been influenced, is the HADS. Unfortunately this is a bit too focused in that it only deals with emotional issues. Although they are important, it has been suggested that they may be influenced by the patient's sense of physical well-being (Zittoun et al, 1999). Therefore, in order to address this important issue it is imperative that changes in physiological functioning are also monitored within the remit of the study.

A further issue to be addressed is how long any change in quality of life obtained through the intervention is likely to last. It is necessary for any effect seen through the massage to be immediate so that it will influence how the patient feels and ultimately how they cope with being in hospital. However, it has been suggested that quality of life may have a predictive value for survival following bone marrow transplantation (Colon et al, 1991; Andrykowski et al, 1994) therefore it would appear beneficial to be able to monitor any change for consistency over time. As such the scale chosen will need to be valid for use over long and short time periods. It has been suggested (Portzsolt et al, 1996) that the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 has a good balance in assessment over time, in that it focuses on the immediate but encourages the subjects to reflect on how they've been feeling over the last week. This is a manageable time scale in which the patient's perception of events should still be reasonably accurate but it will give the investigators insight into whether any immediate alteration in quality of life may be sustainable.

It is assumed that when answering quality of life questionnaires patients are answering subjectively, that is to say that quality of life measured in this way is an accurate reflection of how the patient feels, of their overall well being. However, it is possible that the subjects are answering questions objectively with no thought for the experiential element of the situation. By use of a 'subjective significance questionnaire' Osoba et al (1998) seemed to show that one scale at least - the

EORTC QLQ-C30, was collecting data that was reflective of subjectively relevant issues in quality of life. This is an important point, because if an intervention performed by a researcher is seen to influence the subjects quality of life but that change is of no personal relevance to the patient's sense of well-being, then it is in many ways an irrelevance, because it is not going to initiate any of the positive effects seen as necessary for influencing survival.

In summary, after reviewing the available literature, certain points became clear. Firstly, that quality of life is a potentially important issue, which if assessed in a meaningful way can give the researcher information that reflects how the patient perceives their situation and how any intervention may influence this. Secondly, it is important for the researcher to take time to find the most appropriate tool for his or her study. That is to say a tool that can capture information regarding the aspects of quality of life, which they are hoping to influence (Haberman and Bush, 2003).

For this study it became clear that the most appropriate tool to use was the EORTC QLQ-C30 (version 3.0). Reasons for this decision include the following:

1. It has been shown on numerous occasions to be effective when needed for cross diagnosis comparisons (Kemmler et al, 1999; Hjermstad et al, 1998; Aaronson et al, 1996). This was important in relation to this particular study, because although all the patients on the unit are there to undergo high dose therapy, they will be suffering from different types of haematological malignancies. The QLQ-C30 was produced as the core questionnaire to be used when necessary, in association with a disease specific module (in this case treatment specific; high dose therapy). Unfortunately the module appropriate for this group of patients was not at a stage where it could be used in a study such as this. Following personal communication with Dr Velikova who was the principle investigator responsible for the development of the module, it was hoped initially that this maybe possible for the later part of the study, which would have made an interesting addition to our findings. Unfortunately the module was not ready for use. However, the core questionnaire has been shown to be reliable in its own right as an appropriate measure of some aspects of quality of life in the field of bone marrow transplantation (Molassiotis and Morris, 1999). Equally, at

the time of planning this work, no other quality of life questionnaire was available that specifically addressed issues relevant to the patient undergoing high dose therapy although work has been done trying to identify the most appropriate measure for patients who have undergone a bone marrow transplantation (Kopp et al, 2000)

2. Although the QLQ-C30 may have various limitations as an all-encompassing quality of life measure, for the purpose of this study it looks at appropriate issues.
3. The core questionnaire has been extremely well validated (Sprangers et al, 1993).
4. An important point from the patient's perspective is that the questionnaire is quick and simple to complete - approximately 11-12 minutes, and the scores do not change regardless of whether the patients complete the questionnaire themselves or with the aid of an assistant (Aaronson et al, 1996).
5. The QLQ-C30 is quite unique in that it has been extremely well validated cross-culturally as well as clinically (Sprangers et al, 1993) which may prove to be important as patients on the unit have different ethnic and cultural backgrounds.
6. The QLQ-C30 has been shown to be responsive to change over time (Faithfull, 1999).
7. Trials have been undertaken using the QLQ-C30, which have shown a tentative link between quality of life and survival time (Coates et al, 1997). The workers suggest a 'significant independent association between aspects of quality of life recorded by patient self-report using the EORTC QLQ-C30 and subsequent survival time'. This does not automatically mean a causative link between these two factors. However, within the remit of this study it should be possible to add knowledge to the growing body of evidence relating to quality of life by influencing the patient's physical and psychological quality of life and observing the results.

Structure of EORTC QLQ C-30: The QLQ C-30 is a questionnaire made up of 30 questions, which either form part of a multi-item scale or form a single measure. There are three broad areas of measurement:

Global scales:	Consist of two single items with scores ranging from 1 – 7 for measurement of health status and quality of life.
Functional scales:	Consist of five multi-item scales measuring: physical, role, emotional, cognitive and social functioning.
Symptomatology:	Consists of three multi-item scales measuring fatigue, nausea & vomiting and pain, plus six single items measuring dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties.

Quality of life was reviewed both at baseline and 24 hours later using a slightly modified version of the EORTC QLQ C-30. Members of the EORTC working group who developed the questionnaire acknowledged these changes as being acceptable and a letter confirming permission to use the questionnaire in its modified state was sent by the EORTC (see appendix X, page 297). As discussed previously, at the time of the study, there was no quality of life questionnaire available looking specifically at issues for patients undergoing high dose chemotherapy and for the reasons reviewed in this section, the EORTC QLQ C-30, whilst not ideal, was seen as the best available quality of life questionnaire for the needs of this trial.

Pain scale: Pain is not a constant problem in patients with haematological malignancies. However, it was documented in an audit carried out prior to this study (see appendix I, page 272), that some patients noted a reduction in perception of pain following massage. I therefore felt it appropriate to include in the evaluation of the massage some measure of pain. On the advice of the Consultant from the Trust's palliative care team a short pain scale was included which took the format of a Likert or visual analogue scale (see appendix XI, page 300). The questionnaire is a short form of the Brief Pain Inventory (BPI) developed by Charles S. Cleeland (Cleeland and Ryan, 1994). It was created to assess the severity of pain and impact of pain on daily activities in patients with cancer and other chronic diseases. This scale was filled out at the same time as the EORTC QLQ C-30; at baseline and 24 hours post intervention.

Semi structured interview: A very important part of the assessment of the psychological impact of the session on the patient was seen as the semi-structured interview (SSI) illustrated in box 3.1 (page 89). This interview was limited to the minimal amount of questions necessary (three) to elicit the relevant information, without the patients being overtaxed. The questions were carefully worded to elicit the maximum amount of information from each patient regarding their session and finished with an open question giving those patients who wanted to, a forum to expand on their thoughts. The first question was simply; part (a) what they liked and disliked about the session they received and part (b) how they felt currently. The aim of this question was to get them to reflect on any changes relative to pre-session. The second question asked them whether they would choose to have another rest/massage session again as an indication of how much they enjoyed / disliked the session. Finally, the open-ended question: 'Is there anything else you would like to add?' was asked, thus giving them the opportunity to add comments about individually relevant issues, which had not been covered by the questions (see box 3.1, page 89). A trained research assistant conducted the interview during the 2hr post therapy session. It was felt to be important for someone other than myself as the therapist / researcher to carry out these interviews to prevent the patients feeling too inhibited to express their true feelings about both the session they received and me as their therapist. The research assistant who performed the interviews was the same person who consented the patients initially, it was hoped that because of this the subjects would feel secure enough with this person to allow her to document their true opinion.

Sessional diary: The final part of the qualitative evaluation was through a sessional diary kept by me as the therapist. The idea of this diary was to document the session from a practical perspective, for example the amount of disturbances, changes to protocol, practical difficulties that were encountered as well as how much conversation went on during the session - and the subject matter of any conversation (general topics or emotive issues). However, it was also a format for looking at each session through the eyes of 'the therapist;' comments that the patients made, whether they appeared to relax / go to sleep during the massage, how I was feeling (rushed, stressed, relaxed and so on). Equally, it was a place for reflection both of the study process as a whole and of individual time spent with each person; whether I felt

comfortable with him or her, whether the massage went well, as well as things I may have wanted to do differently. The idea of this document was to correlate each entry with the answers given during the interview for the relevant patient and changes in their cortisol / prolactin levels to try and get a rounded picture of what happened on each occasion. It was also seen as a tool to be used as an ongoing evaluation of the study process from my perspective as the therapist and the researcher. The diary was part of the qualitative evaluation for each session and the focus was on collecting information relevant to each individual patient. Therefore, because different issues were likely to arise on each occasion the entries were not standardised other than to include the percentage of each session spent in conversation and the topics of conversation taking place.

3.10 Analysis

3.10.1 Quantitative data

The primary endpoint for this study was to look for reduction in serum cortisol and prolactin levels following massage, therefore inferential statistics were used to compare changes in levels between arms. However, other physiological measures of stress were also used to corroborate any findings therefore it was also important to correlate the results from the different measures. Finally the majority of the data produced by the questionnaires required quantitative evaluation. The methodologies for the various analyses have been outlined below:

Inferential Statistics: Initially it was important to establish whether the hormone levels were of normal distribution at baseline using the 1-sample Kolmogorov Smirnov test (K-S), as this gave information as to whether it was acceptable to use parametric tests for the analysis or whether non-parametric tests were necessary. This would be the case if the baseline levels were not normally distributed. The baseline levels turned out not to be normally distributed, therefore non-parametric statistical tests were used for the inferential statistics. However it proved possible to normalise the data through logarithmic transformation (see graphs 4.1 and 4.2 on pages 145 and 146) and the results from the non-parametric tests were corroborated using parametric analyses of variance (ANOVA). The Kruskal-Wallis 1-way ANOVA was the non-parametric test used initially to look for statistical differences in change of hormone levels from pre- to post-session between the arms. Any change noted was investigated further using the Mann-Whitney U-test, the Friedman's 2-way non-parametric ANOVA and the Wilcoxon matched pairs signed rank test. Regression techniques were used to look for any sub-groups within the subjects whose hormone levels may have altered more or less following therapy. The other physiological measures (HR and BP) also proved not to be of a normal distribution, therefore identical tests were used to examine for statistical differences between the groups. For all analyses, SPSSX version 11 was used and differences in all dependent variables were accepted at $P < 0.05$.

Correlation of Physiological Measures: It was decided during the design of the study to correlate the results from the four physiological measures used to indicate change in stress levels (cortisol and prolactin levels, heart rate and mean arterial

pressure), in order to corroborate any findings. The non-parametric Spearman's test was used to perform the correlations as the data had been shown to be not normally distributed. The correlational calculations were carried out for data from patients in each arm separately and for each of the time points separately.

Questionnaires: EORTC QLQ-C30: Firstly the baseline scores for the QLQ-C30 were reviewed and the Chi-square used to look for statistical differences in baseline responses between subjects in the different arms; none were found. Cross tabulation was then used to look at the raw scores, and compare pre- and post session responses for any change. To look for statistical significance in any of the changes by arm, the Kruskal-Wallis test was employed to rank any change documented.

Pain scale: It was anticipated that the results from the pain scale would be analysed using the same methods outlined above for the QLQ C-30.

3.10.2. Qualitative data

Evaluation of themes: Thematic analysis was used to analyse the qualitative data coming from the semi-structured interview and the sessional diary with the relevant themes being discussed in depth and highlighted as appropriate with quotations and segments of text, which are used to clarify and emphasis specific points. For each patient a pseudonym was created, the correlating patient number for each pseudonym can be found in appendix XII (page 302).

The first step of the thematic analysis was to print off hard copies of all the separate patient interviews and all diary entries. A file was then produced for each of the 39 patients in the main study containing a copy of their SSI, the sessional diary entry and a copy of their blood results. Themes were highlighted using different colours as they arose. After completing 6 files they were sent to an academic supervisor for him to review the progress and ensure completeness. No extra themes were identified consequently all the transcribed interviews were reviewed using the same format - although unfortunately in six cases the tape recordings had, for some reason not worked. In these instances the research assistant's written notes were used and in all cases themes from the diary entries were included. At the end of this process there were 12 emerging themes (see box 3.2):

Themes Identified from the Semi-Structured Interviews:

- Physiological change
- Positive emotions
- Comments about therapist
- General comments about session
- Service as a whole
- Prior concerns regarding having a massage / rest
- Disturbances to session
- Attitude of patient (towards life, illness etc.)
- Comments about oils
- Feelings regarding future sessions
- Negative emotions
- Therapist's reflections on the study process

Box 3.2

Before moving on it is important to qualify and expand on the type of comments, which fitted into the various themes:

Physiological change: Remarks categorised under this heading were comments that appeared to intimate a primary effect of the massage on the patient's body rather than mind. Although it was anticipated that such comments would be positive, it was possible that subjects might highlight topics of concern such as bruising or reactions to the essential oils. The most obvious example of comments made which belong in this category relate to reduction of muscular aches and pains such as, 'shoulder feels better' (John). Associated with these remarks were those reflecting on physiological easing of tension; 'My back feels more supple' (Brian) being a classic example. However, there were also more subtle suggestions of physiological improvement and these were more closely related to an improved body image than to reduction of actual discomfort, an example here would be; 'My legs feel nice and smooth' (Paula). Finally, comments were included which suggested that the massage caused a distraction, which in itself minimised physiological distress, 'Took my mind off my nausea, sickness disappeared for a while' (Mike). In total remarks from 50% of all the massage patients were categorised into this theme.

Positive emotions: Under this theme were categorised any comment that indicated the patient had benefited psychologically from the massage. This usually took the form of the patient describing the massage and how it made them feel. The most common description (100% of massage patients) included the word 'relaxing' although other common phrases included; 'gentle', 'soothing' and 'calming'.

Comments about therapist: As discussed previously, it was important to try and quantify how much of any benefit from the massage was due to me as the therapist. It was therefore felt important to have a theme specifically to pick up any comments relating to me personally. In total 12 patients (just under 1/3 of all subjects) did make remarks about me and all those were positive. Interestingly however, they varied in what they reflected on; some talked of massage technique, some of manner whilst others just expressed that they liked me.

General comments about session: This theme mainly picked up patients' remarks about the session they received, which did not fit easily into any of the other themes. Most of the comments in this section consisted of the subject emphasising how much they had enjoyed the experience and extending that to a request for the service to be a regular 'when you want it' offer. Interestingly there were nine comments under this subheading, but two of those came from patients who had been offered visualisation in the rest arm.

Service as a whole: Whilst this was seen as an independent theme initially, on review, most of the comments in this section could also fit into other themes, such as; 'I think it is a very necessary service...' (Ann) slotted into the General Comments about the Session theme. Those that didn't, for example one subject (Cyril) spent a lot of time reflecting on issues tied into the running of the unit, could be seen as peripheral to the aim of the study and were consequently left out of the analysis.

Prior concerns regarding having a massage / rest: It was important to try and identify concerns, which may have potentially prevented patients from taking up an offer of massage. This information was seen as being potentially useful in developing the service rather than evaluating it. Only five concerns were identified, two linked to sexual issues; two relating to issues of vulnerability and one patient had low

expectations of the benefits to be gained from massage. Reassuringly these issues were ones, which could have been anticipated and my initial communications with the patient reassured them sufficiently for them to go ahead.

Disturbances to session: It was recognised from the beginning that it would be impossible to prevent disturbances during the trial sessions (as it is during the normal service sessions) and inappropriate to try. However it was felt important to document the types of disruptions, which occurred and the impact such disturbances had on individual patients; whether they appeared to prevent full relaxation. Consequently having pooled all the comments relating to disturbances, they were then broken down further into categories of disturbance. The categories of disturbances have been laid out in box 3.3:

Types of Disturbance noted During Sessions:

i. Family in Room:	1, 3, 6, 8, 14, 15, 17, 19, 22, 23, 24, 27, 28, 37
ii. External noise:	2, 17, 23, 28, 32
iii. Telephone:	3, 4, 33
iv. Nurses/IV equip:	6, 17, 23, 27, 32
v. Physical upset:	5, 7, 17, 19, 20, 24
Multiple:	3, 6, 17, 19, 20, 23, 24, 27, 28, 32
None:	9, 10, 11, 12, 13, 16, 18, 21, 25, 26, 29, 30. 31. 34. 35. 36. 38. 39

Box 3.3.

Note: The disturbances shown in box 3.3 have been listed indicating the trial number of the patient affected.

Some of the above categories are self-explanatory such as numbers (i) and (iii). To clarify the others: (ii) relates to staff shouting up and down the ward and doors banging, (iv) is anything to do with staff entering the room or disturbance through the IV equipment and (v) includes both physiological problems such as recent vomiting and physical disturbances, for example the subject jumping up off the bed straight after the massage. Patients have also been listed who endured more than one

disturbance (listed under 'multiple') and those for whom no disturbance was reported.

Attitude of patient: The majority of patients (27 in total) made comments or reflected at some point in a manner that expressed their attitudes towards either life in general, or their current situation. Looking at all the relevant data it became obvious that those patients expressing such attitudes either through word or manner often contrasted dramatically with each other. For example, some showed acceptance, either passive giving the appearance of resignation (Roger), or active when they seemed more proactive in helping themselves (Nancy), whilst for others resentment appeared the overwhelming emotion (Cyril). Equally some patients gave the impression of facing their problems head on (Ann), whereas others would ignore issues that they did not want to or could not cope with (Diane). Some were positive (Alan) and others negative (Penny). All these different attitudes were documented and reflected upon in relation to how they may have influenced the subjected response to their study session.

Comments about oils: Just over half (7) of the subjects in the 'aromatherapy massage' arm of the trial mentioned the essential oils. Five of the comments were patients stating that they liked the smells the other two that they couldn't smell them as much as they would have liked, possible reasons for this are discussed in chapter 4.

Feelings regarding future sessions: Whilst it was recognised that patients may have felt obliged to give socially acceptable answers in response to the questions asked in the SSI, a question was included asking them directly if they would like another session of massage or rest as an indication of what they felt about their experience. The hope was that if they had truly enjoyed the experience they would expand their response to emphasis the fact.

Negative emotions: Negative emotions were classified as anything the patient said which expressed dissatisfaction with the session. It was through potential concerns that I expected to highlight latent safety issues such as increased agitation following massage. There was also the implication that if something bothered the subject

enough for them to mention it; it might influence their hormone levels. The most common concerns were around taking the blood samples and the smell of the 'alcowipes' (used in the process of taking blood from a central line), in both cases the remarks came from patients in all three arms. Whilst such comments are a concern in a trial setting, as they are likely to reduce perceived benefits, they are none the less reassuring as they would not be an issue within the normal massage service. Other negative comments included three patients in the control arm understandably intimating that their session was a non-event and two of subjects in the massage arm not wanting their session to finish.

My reflections as the therapist on the study process: Although each session was reflected on individually, there were times when issues arose which had broader implications for the study as a whole and didn't easily fit into one of the other themes and as such are listed separately under this subheading. One example was the impact taking blood samples from patients who had not been massaged had on me as the researcher; another was the issue of informed consent. Some of these reflections have been addressed in chapter 4; however, others sit better in different parts of the thesis and will be discussed where appropriate.

In order to classify the themes for analysis a decision was made to break them down under the subheadings of: 'psychological issues', 'physiological issues', 'environmental issues' and 'therapist's reflections'. It proved possible to categorise each theme under one of these subheadings. The above themes were reviewed and it was decided not to use the comments relating to 'the service as a whole' as they were not directly applicable to the study. However, this theme was replaced by documentation of the amount of time spent in conversation during each of the massage sessions and if there was any conversation, what it related to for example, me and the service I offer; the patient's family; general comments or emotive issues such as their illness.

3.10.3 Case studies

The case studies were seen as the focal part of the results from this study. They were created through assimilation of the physiological and psychological results from individual subjects and formed a powerful and meaningful reflection of the way therapy can affect a patient. Whilst patient files were made up containing all the relevant results for each subject, it was beyond the capacity of this thesis to present all of them, therefore a sample of three case studies, one from each arm of the study have been included.

3.10.4 Essential oil work

As a colleague carried out the laboratory work looking at the anti-microbial properties of the essential oils used in this work, no analysis of results will be described as such. There will be a brief summary of findings at the end of chapter 4 along with a paper written for peer review, which gives details of the methodology and the results in appendix XV (page 326).

3.10.5 Summary

The analysis of the results from the main study will follow a logical order starting with the quantitative analysis of the physiological data and the questionnaire responses. Qualitative analysis of the SSI's and diary entries will then take place using thematic analysis. Finally, for a small sample of patients case studies will be included integrating both qualitative and quantitative aspects of the data. As an addendum, there will be a brief review of the results from the parallel laboratory work looking more closely at the essential oils although this will be tied into the thesis more closely in the discussion chapter.

3.11 Pre pilot work

3.11.1 Study site

The Haematological Division of the Christie Hospital NHS Trust is one of the largest of its kind in the UK. At capacity it deals with over 200 new patients a year with haematological malignancies, predominantly acute leukaemia and myeloma. At the time of writing, the Christie also has one of the largest stem cell transplant programmes in the country undertaking approximately 120 stem cell transplants per year (80 autologous transplants, 25 matched unrelated donor transplants and 15 allogeneic stem cell transplants). At any given time up to 25 inpatients will be treated and most will be neutropenic, suffering the effects of severe immunosuppression. These patients are accommodated in a purpose built Adult Leukaemia Unit (ALU), which has 18 isolation beds, some of which have HEPA-filtered air, this is a positive pressure system which ensures patients are breathing 'clean' air. There are also beds on the Young Oncology Unit and this houses mainly the lower-risk patients between the ages of 15-21 years. Because of their vulnerability to infection none of the patients can leave the protective environment of their isolation room whilst they are neutropenic. The unit is run on multidisciplinary lines with at least 2 multidisciplinary meetings undertaken a week, this highlights the strong ethos of supportive care on a unit that utilises "high technology" medicine.

3.11.2 Development of the service

Soon after starting work on the ALU of the Christie Hospital in Manchester during 1992, I became aware that many of the patients and often their carers needed something in addition to the very dedicated, but by its nature, very high tech ministering of the staff. It was hoped that through a massage service, therapists would be able to nurture the patients' bodies and allow their minds some peace - albeit for a limited time. By the fact that all therapists working on the unit are doubly qualified (para-medical as well therapist; most are nurses) I ensured that all staff would have sufficient knowledge to identify patients that were clinically unfit for massage; to answer pertinent questions if any were asked; the skills to listen to anything the patient may wish to say and the understanding to know when to suggest referral to other professionals.

The feeling that starting this service was the right way forward became stronger and stronger. However, to be able to run such a service safely it was imperative that I complete a diploma in massage and aromatherapy, which would provide as much information as possible on all aspects of the subject. A vital issue as the patients to be treated were such a vulnerable group. The course chosen was the diploma in holistic aromatherapy offered at the Tisserand Institute in London. The massage service was started in a limited capacity as soon as I had it confirmed that I was safe to practise. From the beginning the Medical Director was supportive and prepared to back the initiative as long as it was deemed safe by the senior consultant in microbiology. In order to allay any fears regarding the potential risk of cross infection through the oils, the subject was discussed at great length with the senior scientist from the biochemical sciences department of the Scottish Agricultural College; Professor Stanley Deans. Once the consultants were satisfied that there was no apparent risk to the patients, it was agreed that the service could begin.

It was important before starting the service to have the appropriate paperwork. Therefore the following were created:

1. A consent sheet: Which a member of the medical team signed for each new patient, to confirm they were happy for that person to be treated. This is taken to the patient as reassurance that the doctors are indeed happy for them to be offered massage. The patients also sign to confirm they understand what is being offering and that if they wish the session to stop it will.
2. A simple audit sheet: To audit the service from the outset. The patients answered whether or not they were interested in taking up the offer of a massage. Once they had received a massage they were encouraged to comment on the treatment they received.
3. Treatment sheets: These were adapted from general treatment sheets and used to take down the patients' history, monitor blood counts, blood biochemistry and microbiology results and to make notes on their treatment sessions.

Guidelines and policies for treating patients suffering from haematological malignancies with massage were not created at this point. It was felt appropriate to liase with the rest of the complementary therapies committee to help create standard

documents for the Trust. This occurred soon afterwards.

Time was taken to network with people who had already set up massage services in other hospitals. This helped to ensure nothing had been overlooked. Unfortunately it proved impossible at that time to find another high dose therapy unit where such an facility had been initiated, the closest equivalents being intensive care units and general haematology wards.

The intended outcome of the service was simply to improve the quality of life of the patients on the ALU and that of their carers. Realistically, it would be impossible to completely alleviate the stress and anxiety of being nursed on a leukaemia unit. However, some of the problems associated with such stress may be open to reduction, for example; loneliness, insomnia, anorexia, depression and anger. As a consequence the need for psychiatric referrals, sleeping tablets, anti-depressants had the potential to be reduced.

3.11.3 Audit

The massage project started in spring 1997. Because I could only work one day per week at this time it took longer to develop than would be expected. Between the months of April 1997 - December 1998, 92 patients requested massage and were then treated. This was equivalent to 26% of all patients admitted during that time (data from Trust Business Information Officer). The service was audited from the outset. It was inappropriate to have anything but the simplest form of audit as the patients had to be motivated to comply. At the beginning, it was hoped to assess the percentage of patients who would be interested in aromatherapy massage by requesting that the nurses ask as many as possible to answer a simple question to that effect. Unfortunately, it soon became apparent that this was not a practical venture - the patients had too many other things to think about. What it did do however was to highlight awareness as far as spreading the word that the service was available.

The audit form merely entailed the patient saying (anonymously if they so wished) whether they were happy with the service and whether it was appropriate to their needs. An area was available on the form for them to make further comments if they wished to do so; this was actively encouraged. The questionnaires were collected

over the 18- month period and the results shown here summarise the patients' responses (a copy of the audit in full can be found in appendix I, page 272):

- 37 questionnaires were returned up to October 1998 when the results were evaluated. All of them responded that they found the treatment beneficial.
- Some of the different comments made by the patients to describe the therapy included; 'relaxing,' 'therapeutic,' 'eased pain,' 'reduced stress,' 'escape,' 'tailored to needs' and 'slept well afterwards.'
- There were in fact only two comments made which showed possible dissatisfaction: 'more frequent sessions please' and 'a longer session would be nice.'

Judging by the returned forms, it appeared that the massage service had made a positive contribution to the services offered on the ALU. Twenty-six patients for example commented that the therapy was relaxing and/or soothing. In a time of high stress and anxiety, to be able to relax somebody is an important contribution to their treatment and will improve their sense of wellbeing. 2 patients noted specifically that massage eased their physical pain - without the aid of drugs, again a positive step. It is interesting that 4 people commented on being able to talk to the therapist and how that also helped, suggesting that it is the therapy as a whole which is beneficial.

It must be noted that there is the possibility some patients may not have enjoyed the therapy but did not feel inclined to return the form. However, it was never the case that a patient declined to be seen by me on subsequent occasions having once received a massage. Therefore one can only assume that the therapy was generally appreciated.

3.11.4 Research staff

An important part of the pre pilot work was to ensure all staff involved in the study were training to the appropriate level to guarantee standardisation of, for example interviewing of subjects. As the main researcher and the therapist I was by definition able to standardise the study sessions because I was the only person overseeing, massaging and collecting serum samples for each subject. This was possible as only

one patient was recruited into the study at any one time. The senior statistician for the Trust designed the database for collection of all the data and a proforma to ensure all the appropriate information was collected for each subject. All the serum samples were analysed by technicians in the hospital biochemistry laboratory to a strict protocol (see section 3.8.5. of this chapter). These technicians were blinded as to which arm of the study each patient had been randomised to. The nursing staff on the unit were not involved in the trial other than to inform the research assistant of any new patients that had been admitted in order that the information sheet could be offered to them.

With regard to the research assistants, there were three in total, two provided by the university and one by the hospital, all of them had had prior experience in interviewing subjects, but none had previously worked on an isolation unit. Each assistant was thoroughly briefed regarding the aims and protocol of the study, the conditions treated on the ALU, procedures which would be required of them whilst on the unit (such as thorough hand washing techniques before entering a room) and what to expect whilst in a room (type of medical equipment). The above information was backed up with practical experience; they were taken around the unit and I showed them what to do. They had three areas of responsibility, firstly to hand out the information sheets with appropriate explanation of the study; secondly to consent the patients where necessary and thirdly to perform the semi-structured interviews. Prior to working with the patients each assistant went through the information sheet with me, discussing the main issues and possible questions, which may arise. They were also advised that if any concern was raised that they did not feel equipped to deal with, they should tell the patient that they would get back to them with an answer once they had contacted the main researcher. They also conducted a mock interview with me as well as having several 'dummy runs' on patients who had received a massage as part of the normal service (see section 3.12); on these occasions I was present. It was felt that this preparation would ensure standardisation of all procedures.

3.12 Pre-Pilot Study

3.12.1 Introduction

Prior to commencing the trial it was felt important that both the questionnaires and the semi-structured interview be tried out for ease of use and level of appropriateness. One of the drawbacks of the EORTC QLQ C-30 being that it was not created for use with patients in isolation (see section 3.9.2.).

3.12.2 Method

Four patients who had previously received a massage were asked, over a period of a month, if they would mind answering some questions following that day's therapy and also if they would give feed-back regarding how they felt about the questions asked. As well as giving important information about the tools which were due to be used in the study, this exercise also gave the research assistant chance to come to terms with working on a leukaemia unit and gain confidence interviewing patients.

3.12.3. Results

The first patient to be involved in the pre-pilot study (KS) gave some very helpful insights into issues which could influence the quality of life data as well as confirming that neither the questionnaire or the interview were too taxing (the questionnaire took 10 minutes to complete and the interview, approximately 5 minutes). The most important point to come out of this session was the incredibly strong influence that attitude could have over qualitative data of this sort. The lady we were interviewing had relapsed leukaemia but had every reason to want to live (including a 3 year old son) and to be well. Leukaemia is a bizarre condition, patients have no ability to fight off infections for example, therefore are always in the situation of staring death in the face, yet in the absence of such infections the patient can feel as well as any one of the general public. KS had the amazing capacity - in the absence of infection, to totally ignore her leukaemia (though she was not in a classic state of denial) to the point where, when asked about her overall health status in the past 24 hours she graded it as excellent! It was interesting to see how newly diagnosed patients reflected on their disease - whether they were able to normalize it so well, even in the absence of symptoms. Moreover, one would hope that because attitudes are usually traits rather than states, all patients would be consistent in the

way they answered the pre & post session questionnaires thus preventing any biasing of the results. Another issue closely linked with this is that the clinical status of a leukaemia patient can change dramatically in the space of 24 hours. Consequently, the relief of feeling a lot better, or the anxiety of feeling a lot worse, may cause a patient to over-exaggerate their situation when grading a general health scale, a point that needs to be recognised. Finally, some reassuring information gained from KS was that she felt the interview questions were pitched correctly allowing the patient the opportunity of responding from whatever angle they wished without forcing the person to discuss factors regarding their condition which may make them feel uncomfortable.

The second patient interviewed (RP) reinforced some of the issues, which had been raised the previous week, those of perspective and attitude. That is to say, if the patient is answering the questions on the QLQ C-30 from the perspective of what they would be able to do if... then a lot will depend on their attitude to their illness and how they are feeling as to how they answer, because they are expressing what they *think* they could do. For example, in response to the question regarding ability to carry a heavy bag, (RP) thought he could manage this with only a little bit of trouble because he had been on holiday the previous week and carried the suitcases. Despite emphasising that the question was geared to the past twenty-four hours he stuck to this answer yet it was obvious that he was very weak due to a prolonged bout of nausea and vomiting in the previous 48 hours. It maybe that this issue becomes a problem, however since the objective validity of the answers will not be checked it is an interesting point in that it highlighted the patients perceptions of what they think they are capable of, their subjective assessment, and as such how they perceive their health and quality of life. This is of course the important part of quality of life and the aspect it was hoped to improve. One last reflection on this point is that to a certain extent, the objective validity of the patient's answers is irrelevant, because they will, when they repeat the QLQ C-30 following the study session, be answering from the same and therefore a consistent viewpoint. As such, any change in perceived abilities will be real change in quality of life. This session also identified how important it is to go through the baseline questionnaire with the patient, if only to put into context some of the questions (for example, 'Do you have trouble taking a long walk') and to emphasize the fact that it is to be answered from

the perspective of the previous 24 hours.

Emphasis during interview number 3 (SW) was required on the time scale of the questionnaire. There were two issues in this case; firstly the fact that the patient was on a (reducing) dose of diamorphine, which had the side effect of making the patient slightly drowsy. A far more important issue however, appeared to be the patient's focus on returning home. Here was a relatively young mother with a 3-year-old daughter and despite the repeated emphasis on time such as: 'in the last day or so...' she continued to answer in the future tense for example: "I will be able to..." This was reinforced by her tendency to answer in the manner of what would be expected from her rather than what she was actually physically capable of doing, an example being "You have to..." Her responses were taken as an indicator of her determination and positive attitude towards going home - something she was clearly very focused on doing in the near future. It was also suggested that the patient might have thought her answers could have some influence on the medical decision as to when she would be allowed home. This was a valid point and a note was made to reassure patients that their answers would in no way influence medical decisions. (SW) answered the questions on the psychological aspects of quality of life in a similar way in that she did not acknowledge any negative feelings, was this because she was in denial; because it was more socially acceptable to answer in this way or because she was genuinely coping with what is happening with minimal emotional upset? She, like patient No. 1 rated her overall health as excellent.

Once again patient No. 4 (RS) perceived herself as being relatively well despite having been pancytopenic (having minimal blood cells of any lineage) for over 2 months and possibly requiring a Matched Unrelated Donor transplant. She felt so well that she graded herself as having almost no problems whatsoever. This was the case for both the physical and the psychological questions, although it was difficult to tell whether they were the genuine answers or whether she was trying to appear positive. (RS) was the first person to comment that she wasn't sure how she should grade her overall health because although she felt fine she didn't think it would be appropriate to grade it as excellent due to the fact that she had leukaemia - it was almost as if she had to think consciously 'I have leukaemia therefore I cannot be in excellent health' rather than 'I have leukaemia and I do not *feel* in excellent health'.

3.12.4 Summary

In summary therefore, the main lessons that were learned from the pre pilot study were:

- Because patients cannot 'see' their leukaemia and it does not tend to intrude on their ability to perform activities of daily living (unlike the side effects of the treatment), this very distressing diagnosis has in the patients interviewed so far, been marginalized - possibly due to use of the coping strategy of denial.
- Perhaps due to isolation and an inability to 'test out the theory' there appears to be a tendency on the part of the patient to focus on perceived abilities when looking at quality of life rather then to answer objectively. That is, answers seem to rely on the patient's attitude towards their condition. This in itself is an interesting area of exploration and more valid in relation to quality of life than a more objective assessment.
- If there is a strong pull from home such as a dependent relying on them, the above points seem to be reinforced. Such a pull also appears to be a powerful indicator of their overall attitude towards their condition.
- Based on the results of the pre-pilot study it was acknowledged that patients' responses on the QLQ C-30 might not show a vast change from pre- to post session. However it is realistic to expect they will give information about the person's attitudes towards their illness and highlight change in areas such as the perception of pain or quality of sleep, which in itself will offer up a wealth of information - especially if compared to the physiological measures of stress.

3.12.5 Conclusion

In conclusion therefore, it was decided that despite the limitations of the EORTC QLQ C-30, it was still the most appropriate measure of those available, and would offer up valuable information regarding for example patients' perceptions on life and as such was to be used for the trial. The SSI was found to be easy to answer, none-threatening but allowing the patient the opportunity of expressing his or her opinions to their own degree of maximum comfort therefore, there were no changes in the wording of the questions.

3.13 Pilot Study

3.13.1 Introduction

The pilot study had arbitrarily been set as the first 5 patients. However, in the results section (3.13.4), change in hormone levels will be included from the first 6 patients as patient No. 6 was the first to be randomised to experimental arm 2 - massage with essential oils.

3.13.2 Aims

The main aims of the pilot study were:

- To make sure the requirements of the protocol were logistically feasible within the day-to-day running of the unit.
- To identify any difficulties and make minor adjustments to the sessional protocol to ensure smooth running of the trial.
- To monitor blood results from all three arms of the study thus allowing comparison of early data in order to confirm appropriate timing of the samples taken.

The intention was to include the results of the pilot study into those of the main body of data assuming no major changes were required in the running of the study.

3.13.3 Method

The pilot study was run as the main study would also be run, true to the protocol (see sessional protocol, section 3.8.1 and flow diagram, appendix VII, page 286).

3.13.4 Results

The blood results are shown as the mean results for each group. However, to ensure completeness the qualitative results of the pilot study have been separated into individual entries relating to qualitative aspect of each patient's session.

Blood Results: Tables 3.4 and 3.5 show the mean hormone levels for the subjects in the pilot study separated by arm and sample time. The results from subject number 006 were also included as the first patient randomised to receive a massage with essential oils:

Mean Cortisol Levels from Pilot Study Serum Samples:

Sample Time / Study Arm	B/L	30min.	1hr	1.5hrs	2hrs	24hrs
Rest (n=3)	182	177	207	232	236	191
Base Oil (n=2)	295	234	266	256	311	351
Aromatherapy (n=1)	352	287	242	218	181	N/A

Table 3.4

Mean Prolactin Levels from Pilot Study Serum Samples:

Sample Time / Study Arm	B/L	30min.	1hr	1.5hrs	2hrs	24hrs
Rest (n=3)	192	235	221	214	263	255
Base Oil (n=2)	391	402	421	408	424	552
Aromatherapy (n=1)	293	257	248	272	288	N/A

Table 3.5

At this stage there was little to be said about the blood results. However it was interesting to see that there was a dip in the cortisol levels of patients in the 'massage with base oil' group which had disappeared by the end of the two hours. This in addition to the obvious and continued drop in cortisol level of the patient in the 'aromatherapy massage' arm was taken as an indicator that the appropriate time scale had been chosen for the blood sampling; there was an obvious difference between the groups shown in the sample available. The rather more random prolactin results were concerning as they may indicate that despite certain drugs being recognised as affecting prolactin levels and patients taking them excluded from the study (see appendix IV, page 280), the cocktail of drugs inherent in the treatment protocols used on the unit affect prolactin levels enough to make results unusable.

Qualitative Results: The session of patient number 001 (Penny) was fraught with logistical problems. The first difficulty was the fact that there were no demographic details for this subject on the hospital computer system, which delayed being able to randomise her (she was finally randomised to the control group). Secondly, her boyfriend stayed in the room throughout the study session despite the request on the information sheet for no visitors. It was felt inappropriate to ask him to leave so he stayed even though, despite him being quiet throughout, it was less than ideal to have him there. Finally, it was evident right from the start that certain specifications in the protocol were too stringent and not going to work. Wanting the patients to remain on bed rest for 20 minutes for example, prior to having the baseline bloods taken. Instances of situations preventing the bed rest included, the medical team undertaking a ward round and wanting to talk to the subject; the patient deciding they want a shower before the session, or a member of the auxiliary staff coming in to the room to make the bed thus 'getting it out of the way.' The other issue, which had not been thought about was the telephone, it tended to ring just as I was due to start taking bloods or half way through a session. Some people were happy to take the telephone off the hook - others were not, therefore the only realistic solution was to try and note all the times the telephone rang. When Penny was asked about her quality of life within the format of the questionnaire, it once again surfaced how difficult and disorientating life must be for these people - they have a life threatening illness yet feel perfectly healthy a lot of the time and in this case, she was obviously very fed up about having to be in hospital. Penny had a little boy at home (18 months old) and wanted to go home to him. However, she only acknowledged this when asked directly - she clearly resented being in hospital and kept her communication with us (and other staff members it appeared) to a minimum. This actually made it difficult to feel comfortable with her and one kept feeling the urge to apologise for being in the room! This situation was not something which had been encountered previously, because in the pre-pilot phase it had been possible to 'hand pick' the patients we interviewed. As well as appearing quite resentful of our presence we discovered that for some reason Penny tended to answer the quality of life questions in a somewhat contradictory manner. She graded herself for example as having no pain on the QLQ C-30 but then when she filled in the pain scale Penny graded herself as having some pain. Equally, with the SSI, there was nothing she disliked about the session and she would have a rest session again because of the

peace, but then she said she wouldn't because it was boring.

Patient number 002 (Noel) was again randomised to the control group. Whereas with Penny things had felt rather uncomfortable, this week things went far more smoothly. What became very clear however was that the rest periods had to make the patient feel rested and peaceful - even if this meant each session being slightly different from the others. This gentleman was keen to use his session in a proactive way. Therefore although I was aware that if effective, this was likely to reduce proportionally the effects of the massage, he was taught a brief and very simple visualisation technique. The image created centred around him visualising the cells of his transplant (due the same day) growing in his body. He fed back to the research assistant that he had found the experience useful but that he was still looking forward to a massage. As a complete contrast to previous patients, this subject's attitude towards his situation was far more in the victim role and he appeared to need far more nurturing then any other in either the pilot or the pre-pilot phase so far. Interestingly, he has been abandoned by his wife and had no dependents relying on him at home.

Patient number 003 (Lucy) constituted yet another patient for the control arm. Once again the difficulty of enforcing certain aspects of the protocol was highlighted as both of the patient's parents were in residence during the session. It was not easy to see whether this was a problem to her because although she smiled a lot she said very little and her position became more foetal as the morning progressed. This was possibly partly due to some of her parents' comments relating to her sister who was at the same time in the operating theatre donating bone marrow. She attempted a similar visualization exercise to the one Noel had used the week before although it was not clear how successful this was.

Patient number 004 (John) received a massage with base oil only. The main problem with this gentleman was his popularity and as such the number of telephone calls he received. The telephone was taken off the hook for the duration of the massage, but he engaged in calls both before and after the session. An interesting issue to come to light this week was how patients can 'pigeonhole' their problems. This particular patient evaluated himself as having no pain and yet he had been complaining of very

painful shoulders. It could only be suggested that because the pain was not related to his Hodgkin's disease he did not feel it would be relevant. This point highlighted that it was important to emphasize interest in *any* pain when I helped fill in the baseline questionnaires with the patient. The final issue this week occurred during the SSI; whilst the patient dutifully answered all the questions when the tape was running, it was after the cassette recorder was switched off that he relaxed and started giving his real opinion.

Number 005 (Gary) was again randomised to a massage with base oil. The session went well, the patient obviously felt comfortable and I was beginning to feel much more relaxed during the therapy sessions. However, the research assistant was concerned that she still felt 'stilted' when carrying out the semi-structured interview. In her concern to standardize the interviews she was carrying out minimal conversation with the patients. Obviously people are more likely to fully express their views if they feel comfortable with the person interviewing them. It was decided therefore to experiment a little with the research assistant's technique; she was encouraged to carry out a normal conversation with each person but that within the conversation she would ask the three questions in a standardized order and format. This led to greater quantity and quality of information in what was a large part of the qualitative data. The research assistant herself also felt much more comfortable with this interview.

3.13.5 Discussion

The preliminary blood results showed the timing of the samples to be appropriate in that different trends were highlighted in the cortisol levels for each group. A potential problem in the validity of the prolactin levels was indicated in their extreme variance when compared with the trends shown in the cortisol levels. It was felt however that it was inappropriate to stop taking prolactin samples on the results of such a small sample.

The main issue to come from qualitative aspect of the pilot study was that of adaptability. Whilst it was recognised as important for the study to work within the routines of the unit, the expectations of what standardisation was possible had obviously still been too high up to this point. For example, incorporating 20 minutes

bed rest prior to baseline bloods proved almost impossible, stopping visitors was also impossible (especially if they turned up unannounced) and standardising conversations during the SSI was inappropriate. What this information meant in practical terms was that keeping thorough records of each session was extremely important, as unexpectedly high cortisol levels following a massage session may well be due to an upsetting telephone call rather than because the subject didn't enjoy the massage.

3.13.6 Conclusion

In conclusion therefore the protocol was felt to be workable in its present format but it was recognised that it was imperative to keep comprehensive notes on each session in order that any unexpectedly raised hormone levels could be investigated. As such the results from the patients in the pilot study were incorporated into those for the main study.

3.14 Main Study

3.14.1 Introduction

As was stated in the conclusion to the pilot study (section 3.13.6), it was not deemed necessary to make major alterations to the protocol of the trial. Therefore it was felt appropriate to amalgamate the results from the patients in the pilot study with those from the main study. This meant that there was no break between the pilot and the main study and the patient numbers were carried straight on.

3.14.2 Method

Because the study was the basis of this PhD thesis a cut off point was decided on for closing the trial, this was set at 2 years with the first patient randomised on (3.5.01) in order to allocate sufficient time for complete analysis of the data. Although the cut off point was to an extent arbitrary - based on past accrual of patients into the service, it was a time span, which was felt to be realistic in allowing sufficient opportunity to recruit the appropriate number of subjects. Equally, having observed the level of change seen in the cortisol levels following massage in the pilot study it was anticipated that the numbers required to reach statistical significance would be less than originally suggested. This was originally to have been reviewed formally after the first 48 patients had been entered into the trial.

Regarding the protocol for the study, no major changes were thought necessary to the original design of the trial therefore the main study continued as was initially intended using the format laid out in the protocol section above (see section 3.8.1). However, an informal decision was made to allow patients in the control arm the use of visualisation during their session if they requested it.

3.14.3 Data entry and coding

As explained above a proforma was produced for the collection of data (see appendix VIII, page 288) and this was downloaded into a computer programme designed by the head statistician for the hospital. The programme was designed to be compatible with the statistical software package SPSSX, which was to be used for the statistical analysis of the quantitative results of the study. All data was entered in an ongoing fashion except for the blood results, they were downloaded at the end of the trial in

order that I remained unaware of each patient's physiological response to their session. This was necessary as it was me who was responsible for entering all the data onto the programme and awareness of the patients' responses to therapy may have biased my behaviour towards subjects in the different arms.

3.14.4 Essential oil work

One of the aims of this work was to see if there were any additional benefits to blending essential oils into the grapeseed oil used to perform massage therapy on the ALU. The primary way this was evaluated was within the remit of the study by including the use of oils in one arm of the trial. However, essential oils have many alleged properties (Price and Price, 1999); as such a decision had been taken to instigate some parallel, independent work in collaboration with a scientist at Manchester University evaluating the potential antimicrobial properties of the oils used in the main study. Essential oils form part of an aromatic plant's defence against disease, therefore in view of the high level of immunosuppression experienced by the patients in the study, if the oils could be shown to potentially enhance the body's protection against entry from pathological micro-organisms then this would be seen as a valid reason to use them in the massage service. The work was carried out in laboratories based at one of the other local hospitals therefore the methodology is not described here but can be seen in full in the peer review paper which was written describing the work (appendix XV, page 326).

3.14.5 Summary

The study's aims were to look at safety issues whilst measuring physiologically and psychologically any effects of massage with and without the use of essential oils in isolated haematological oncology patients. Results were to be compared to those from patients who spent an equivalent length of time in peace and quiet. That these aims were realistic and achievable using the proposed trial protocol had been shown through pre-pilot and pilot work. Equally the blood results from the pilot study indicated that single sessions of massage had the potential to influence physiological levels of stress. Consequently the study was undertaken as described.

The time span of the study had been set at a maximum of 2 years as this was seen as a realistic time frame to collect sufficient data and then have time to analyse it

appropriately. For several reasons, which will be reflected on in both the results and discussion chapters; this did not prove to be the case. However, in spite of this, substantial amounts of data were produced which showed the benefits of massage for patients being nursed in isolation. In parallel with this trial a collaborating scientist carried out in-vitro assessment of the anti-microbial properties of the essential oils used in the study and confirmed their efficacy.

The results of the main study, including the demographic data of the patients recruited into the trial are presented in the following results chapter.

Chapter 4:

Results

4.1 Introduction

The reporting of results in this thesis necessarily departs from the norm because it includes both quantitative and qualitative elements. The reasons for this and the use of the mixed methods design have already been defended (see section 3.2). A summary being that to elicit comprehensively the benefits of massage for patients with haematological malignancies undergoing potentially curative, high dose treatment, both physiological and psychological aspects of patient response needed to be analysed. The results presented in this chapter demonstrate that single sessions of massage both with and without the use of essential oils can be given safely and benefit patients being nursed on a high dose therapy isolation unit.

This chapter continues with a reflection on the issue of recruitment and the factors, which prevented the majority of patients invited to participate in the study from becoming involved. The demographic details of the thirty-nine patients who did participate are shown, as are the baseline values of variables because they were recognised as being potentially confounding, if they had exhibited statistically significant differences between arms. Evidence that there were no such significant differences is presented. Results of the quantitative analyses of both the physiological data and the questionnaire responses are then displayed followed by the results of the qualitative analyses from the SSI and my therapist's diary entries. Three case studies are presented in which the qualitative and quantitative findings are combined to give full meaning to the data. Finally a brief synopsis of the in-vitro essential oil work is given and the results summarised.

4.2 Recruitment of Subjects

In the two-year time scale allotted for data collection 39 patients were entered into the study. The data collection period ran from May 2001 to July 2003 inclusive. In that time 225 patients were invited to participate in the trial and a total of 74 (33%) were consented. Of the 74 consented, 39 (52.7%) were entered into the trial; 17% of all those asked. Patients were recruited on an intention to treat basis and their results analysed in the arm to which they were randomised. Of the patients recruited there was 100% compliance with the study protocol.

4.2.1 Reasons for Non-Participation in the Study

The sample size calculation was based on a piece research in which the authors had also measured change in levels of cortisol and prolactin before and after intervention (Van Der Pompe et al, 1997). As previously described (section 3.5.5), using the paired t-test formula of the nQuery Advisor V. 3.0 it was calculated that 63 patients per arm would be required to detect a 0.5 standard deviation shift in the mean values. However, because the methodologies of the trials were so different, it was decided that an interim assessment was necessary after 16 patients per arm (see section 3.5.5). Recruitment problems meant that the final figure for patients entered into the trial was 39. Of the original 225 patients asked, 61 stated that they were 'not interested' in massage. However, 25 of these 61 (41%) later went on to take advantage of the massage service offered on the unit. In total 80 of the 186 patients who did not participate in the study (43%) went on to receive massage through the standard service. Of the patients not consented for the study approximately one third gave no reason for their decision. Conversely, for the remaining two thirds there were 23 different reasons for non-participation. Reasons for non-participation of all 186 patients who did not take part in the trial have been presented in table 4.1:

Table of Reasons for Non-Participation in the Study

Reason	Not consented	Consented	Total
No reason given	51	1	52
Not well enough	22	3	25
On maxalon*	5	13	18
Imminent discharge	15	0	15
Wants massage but not on trial	11	1	12
On high dose steroids	9	2	11
On nozinan*	1	7	8
Needed massage (clinically)	3	2	5
Recently had aromatherapy	4	1	5
'Too much going on'	5	0	5
Poor English & didn't want to take part	4	0	4
Doesn't like touch	4	0	4
Asleep / tired	4	0	4
History of depression	2	1	3
Went to ITU/another ward	2	1	3
Confused	2	0	2
MRSA positive**	2	0	2
Doesn't like smells	2	0	2
No central line in place	0	1	1
Skin sensitivity from chemotherapy	1	0	1
On high dose opiates	1	0	1
Nauseated	0	1	1
Deceased	1	0	1
Non-compliance	0	1	1
Totals	151	35	186

Table 4.1

* - Both these drugs are anti-emetics with a long half-life, which falsely raises a patient's cortisol levels for up to 10 days.

** - MRSA or Methicillin Resistant *Staphylococcus Aureus* is a multi-resistant bacterium. To massage a patient with MRSA is to risk cross infection. Consequently these patients were advised that we could not follow up the initial offer of a massage until the infection had cleared. (Both patients went on to receive massage through the standard service).

4.3 Demographic Data

It was important to examine the characteristics of the patients entered into the study in order to identify any statistically significant differences between the subjects in each arm. There were potentially numerous ways in which the subjects could vary such as, numbers of males to females, ages of the patients, clinical condition on entry, or whether they had received massage before. All such variables had the potential to impact on how each subject responded to their session. For that reason, an exhaustive evaluation of baseline descriptives was seen as necessary to ensure homogeneity of the sample prior to carrying out inferential statistical tests. The results of this screening process are laid out in sections 4.3.1 – 4.3.10.

4.3.1 Gender

In total 16 men (41%) and 23 (59%) women were entered into the study. How these were distributed between the three arms can be seen in table 4.2:

Table Showing Gender of Subjects Split by Arm

	Randomised Arm			
Gender	**Rest**	**Base oil**	**Aromatherapy**	**Total**
Male	6 (46%)	7 (54%)	3 (23%)	16 (41%)
Female	7 (54%)	6 (46%)	10 (77%)	23 (59%)
Total	13	13	13	39

Table 4.2

It can be seen from table 4.2 that for two of the arms ('Rest' and 'Base oil') there was an even mix of males and females, unfortunately, for the aromatherapy arm there was a skew with three times more women than men. It is possible therefore that gender mix may have an influence on the results of the inferential statistics, however previous work (Field, 2001) has shown that men respond positively to massage.

4.3.2 Age

As stated in section 3.5.2 in chapter 3, the age range of patients eligible for entry into the study was broad (16 years upwards) so as to include all patients with access to the regular massage service. The youngest patient entered into the study was 22 years

old and the oldest 71 years, giving a range of 49 years. Table 4.3 shows the range of ages for each arm:

Table Showing Age Range of Subjects Split by Arm

Arm	Median Age	Min. Age	Max. Age	Range
Rest	50	22	71	49
Base oil	57	22	70	48
Aromatherapy	51	24	70	48
Total	52	22	71	49

Table 4.3

The median value has been presented as a measure of central tendency because the data were found to be not normally distributed. There was no statistically significant difference between the ages of patients in the three arms of the study (P = 0.787).

4.3.3 Diagnosis

The study sample proved to be a standard cross section of the unit population in terms of diagnoses, 21 (54%) of the 39 were suffering from some form of leukaemia, 7 (18%) from Myeloma and 10 (26%) from Lymphoma. There was no diagnosis available for 1 patient, possibly because he or she had yet to be diagnosed. Table 4.4 shows how these numbers are spread between the three arms:

Table Showing Diagnosis of Subjects Split by Arm

	Randomised Arm			
Diagnosis	**Rest**	**Base oil**	**Aromatherapy**	**Total**
ALL	3	1	0	4
AML	6	4	6	16
CML	0	1	0	1
Myeloma	1	3	3	7
HD	1	2	2	5
NHL	1	2	2	5
Not known	1	0	0	1
Total	13	13	13	39

Table 4.4

4.3.4 Clinical Status

A related issue, which could have impacted on how the patients responded to their session, was their clinical status on entry to the study. This was assessed using the Karnofsky Performance Scale (KPS) as an index of physical functioning (see appendix IX, page 296). All but one patient reached 80 or 90 on the scale indicating good clinical standing. The remaining subject had a score of 60; this participant was randomised to the aromatherapy arm.

4.3.5 Reason for Admission

It was important to identify what treatment each patient had been admitted onto the unit for as this could possibly impact on a patient's physiological response to therapy. A patient admitted for a Matched Unrelated Donor (MUD) transplant would for example be undergoing far more intensive chemotherapy and consequently be prescribed more supportive drugs such as anti-emetics, antibiotics and analgesics than someone admitted for a course of chemotherapy only. It is recognised that some of these drugs may influence levels of stress hormones (Reeder and Lowy, 1993). 20 (51%) patients were admitted for chemotherapy only, 18 (46%) for chemotherapy plus a transplant and 1 (2.5%) patient was admitted with a viral infection requiring high dose intravenous antiviral treatment. Table 4.5 shows how this data is distributed between the three arms of the study:

Table Showing Medical Treatment of Subjects During Admission Split by Arm

	Randomised Arm			
Reason for admission	**Rest**	**Base oil**	**Aromatherapy**	**Total**
Chemotherapy	9	5	6	20
Chemo. Plus transplant	4	8	6	18
Viral infection	0	0	1	1
Total	13	13	13	39

Table 4.5

As can be seen from table 4.5 more patients in the two experimental arms were due to have transplants then those in the control arm. If it is accepted that drug regimes for transplantation are more intensive than those for simple chemotherapy, involve drugs which may falsely raise cortisol and/or prolactin levels and are more likely to

lead to complications that could potentially lead to higher levels of stress, then by definition it can be seen from the figures in table 4.5 that there is no bias in favour of the patients in the experimental arms.

4.3.6 Type of Transplant

There is a wide variation in the drug regimes for the different type of transplants with autologous (self / own cells) transplants only requiring moderately intensive therapy, allogeneic (cells from matched sibling donor) being an intermediate form of transplantation and MUD transplants requiring very intensive treatment. For completeness it was felt necessary to confirm the different types of transplant were evenly spread between the three arms:

Table Showing Type of Transplant Split by Arm

	Randomised Arm			
Transplant	**Rest**	**Base oil**	**Aromatherapy**	**Total**
None	9	5	7	21
Autologous	1	6	4	11
Allogeneic	2	1	1	4
MUD	1	1	1	3
Total	13	13	13	39

Table 4.6

It can be seen from table 4.6 that there is an even spread of the transplants requiring the more intensive chemotherapy regimes and that there are a greater number of autologous transplants in the two experimental arms, therefore there is no positive bias towards the massage groups.

4.3.7 Previous Experience of Complementary Therapies

It was important to document prior experience of complementary therapies for subjects in each of the study arms, as it was possible that familiarity with complementary therapies may condition patients in such a way as to reduce their stress levels through anticipation of relaxation. A total of 15 (38%) patients had prior experience of complementary therapies: 4 in the 'rest' arm, 5 in the 'base oil' arm and 6 in the 'aromatherapy' arm. Of these experiences, all but 2 from the 'aromatherapy' arm had been types of touch therapy (the last two were: reiki and

Bowen therapy). It was anticipated that as the numbers were spread evenly between the three arms they would not bias the results of the inferential statistics.

4.3.8 Baseline Measures of Physiological Stress

For the results of the inferential statistics to be of relevance, it was important to ensure that there were no statistically significant differences in the baseline measures of cortisol, prolactin, heart rate and blood pressure between patients in the three arms. Before looking for differences using parametric tests, the data were visually assessed. Where the mean and median values were seen to be comparable thus showing normal distribution, parametric tests were used. In sets of data were the mean and median values were seen to be disparate then non-parametric tests were used for analyses. The blood values (cortisol and prolactin,) were shown to be skewed, therefore median values and non-parametric tests were used for all analyses. However, heart rate (HR) and mean arterial blood pressure (MAP) values were normally distributed and mean values with parametric tests were used. These baseline assessments are shown in tables 4.7 – 4.9 and are presented using the appropriate values for each measure with the resultant significance values from the 1-way analyses of variance:

Table Showing Baseline Values of Cortisol, Split by Arm

	Physiological Measure of Stress (1): Cortisol*			
Arm	**Median**	**Minimum**	**Maximum**	**Range**
Rest	296.0	054.0	632.0	578.0
Base oil	247.0	166.0	938.0	772.0
Aromatherapy	306.0	160.0	778.0	618.0
Sig. (P-value)	**0.595**			

Table 4.7

* - All analyses were assessed using a Kruskal-Wallis 1-way ANOVA

Table Showing Baseline Values of Prolactin Split by Arm

	Physiological Measure of Stress (2): Prolactin*			
Arm	**Median**	**Minimum**	**Maximum**	**Range**
Rest	195.0	078.0	603.0	525.0
Base oil	245.0	108.0	486.0	378.0
Aromatherapy	143.0	076.0	496.0	420.0
Sig. (P-value)	**0.431**			

Table 4.8

* - All analyses were assessed using a Kruskal-Wallis 1-way ANOVA

Table Showing Baseline Values of Heart Rate and Mean Arterial Blood Pressure, Split by Arm

	Physiological Measure of Stress (3) *			
	Heart Rate		**Mean BP****	
Arm	**Mean**	**S.D.**	**Mean**	**S.D.**
Rest	80.8	10.8	86.3	9.9
Base oil	81.9	14.2	84.7	8.9
Aromatherapy	84.8	15.9	84.2	7.7
Sig. (P-value)	**0.751**		**0.825**	

Table 4.9

* - All analyses were assessed using a Kruskal-Wallis 1-way ANOVA

** - Mean arterial pressure (MAP) was calculated from the blood pressure (BP) reading using the following formula: (2/3*Diastolic BP) + (1/3*Systolic BP). All units in mmHg.

As can be seen from the table above, there are no statistically significant differences in the physiological measures of stress between the three arms.

4.3.9 Other Relevant Comparisons

A large number of other baseline descriptives were collected for each subject. As above, parametric or non-parametric tests were used as appropriate, depending on the distribution of the data, to ensure there were no statistically significant differences between arms for any of the variables. There were no significant differences found for any of the comparisons made as can be seen illustrated in tables 4.10 – 4.16:

Baseline Haemoglobin Levels Split by Arm

	Full Blood Count (1): Haemoglobin*			
Arm	**Median**	**Minimum.**	**Maximum**	**Range**
Rest	9.8	8.1	11.9	3.5
Base oil	10.3	8.4	12.2	3.8
Aromatherapy	9.4	8.3	10.9	2.6
Sig. (P-value)	**0.480**			

Table 4.10

* - All analyses were assessed using a Kruskal-Wallis 1-way ANOVA

Baseline White Cell Count Split by Arm

	Full Blood Count (2): White Blood Cells*			
Arm	**Median**	**Minimum.**	**Maximum**	**Range**
Rest	1.2	0.1	5.5	5.4
Base oil	0.9	0.1	4.9	4.8
Aromatherapy	0.8	0.0	4.1	4.1
Sig. (P-value)	**0.710**			

Table 4.11

* - All analyses were assessed using a Kruskal-Wallis 1-way ANOVA

Baseline Platelet Count Split by Arm

	Full Blood Count (3): Platelets*			
Arm	**Median**	**Minimum.**	**Maximum**	**Range**
Rest	83	7	182	175
Base oil	93	7	343	336
Aromatherapy	33	9	255	246
Sig. (P-value)	**0.620**			

Table 4.12

* - All analyses were assessed using a Kruskal-Wallis 1-way ANOVA

Baseline Neutrophil Count Split by Arm

	Full Blood Count (4): Neutrophils*			
Arm	**Median**	**Minimum.**	**Maximum**	**Range**
Rest	0.3	0.0	4.1	4.1
Base oil	0.2	0.0	4.0	4.0
Aromatherapy	0.1	0.0	4.1	4.1
Sig. (P-value)	**0.710**			

Table 4.13

Baseline Temperature Immediately Prior to Study Session Split by Arm

	Baseline temp.*	
Arm	**Mean**	**S.D.**
Rest	36.72	0.44
Base oil	36.81	0.30
Aromatherapy	36.77	0.38
Sig. (P-value)	**0.825**	

Table 4.14

* - All analyses were assessed using a Kruskal-Wallis 1-way ANOVA

There was no statistically significant difference between the baseline temperatures of patients in the three arms of the study (P = 0.825).

Microbiological Evidence of Infection at Time of Entry to the Trial Split by Arm

	Evidence of Infection at Baseline (no. of subjects)				
Arm	**Bacterial**	**Viral**	**Fungal**	**PUO***	**Total**
Rest	1	0	2	2	5
Base oil	2	1	1	2	6
Aromatherapy	1	1	0	1	3
Total	4	2	3	5	14

* - **PUO** = Pyrexia of Unknown Origin

Table 4.15

There was no difference in the number between patients in the different arms of the study with evidence of infection at baseline.

Time of Wakening on Morning of Study Session Split by Arm

	Time of Waking (Hours)*				
Arm	**Mean**	**S.D.**	**Minimum**	**Maximum**	**Range**
Rest	7.15	1.46	5	10	5
Base oil	6.75	1.87	4	10	6
Aromatherapy	6.08	1.68	3	9	6
Sig. (P-value)	**0.286**				

Table 4.16

* - All analyses were assessed using a Kruskal-Wallis 1-way ANOVA

There was no statistically significant difference between the times of wakening for patients in the three arms of the study (P = 0.286).

4.3.10 Conclusions

The demographic data showed no obvious differences between the patients in the three arms of the study, it was therefore felt appropriate to use inferential statistics to look for any statistically significant differences in physiological response to the study sessions between the subjects in the different arms of the trial.

4.4 Inferential Statistical Analysis of Physiological Data

Although the protocol was set out to include a sixth sample of blood for hormone levels plus blood pressure and heart rate readings at 11am the morning after the study session (24 hours after), these samples were not included in the final analyses as over 50% of them were missing. I was reliant on unit nursing staff collecting the blood; unfortunately they often failed to perform this procedure. The reasons offered as to why this was the case included the relevant nurse forgetting (despite written reminders) and shortage of time.

4.4.1 Analysis of Primary Outcome Measures

A decision was made to use non-parametric tests for the statistical analysis of serum samples in view of the particularly wide variation in hormone levels and occasional extreme values for prolactin (see table 4.8, page 136).

4.4.1.a Between Arms Comparisons

Baseline – 30-Minute Post-Session: Initially the Kruskal–Wallis, 1-way ANOVA was used to identify any drop in hormone levels for both cortisol and prolactin immediately following the study session. Specifically, between baseline and post-session sample one, between the groups. The ANOVA showed a statistically significant difference between groups for prolactin only, although a similar trend was seen for the cortisol results with the arm showing the highest ranking (least change) being the control arm in both cases. The ranking of change for each hormone for the different arms of the study can be seen in tables 4.17 and 4.18:

Table Showing the Mean Ranking of Change in Cortisol Levels from Baseline to 30 Minutes Post Session

Arm	Mean Rank
Rest	24.04
Base oil	17.25
Aromatherapy	17.04
Sig. value	P = 0.192

Table 4.17

Table Showing the Mean Ranking of Change in Prolactin Levels from Baseline to 30 Minutes Post Session

Arm	Mean Rank
Rest	26.81
Base oil	14.50
Aromatherapy	16.81
Sig. value	P = 0.012

Table 4.18

Having identified a statistically significant difference in prolactin levels using the Kruskal–Wallis, the Mann-Whitney U-test was then used to see where the differences lay by comparing the arms in pairs. Using the Bonferroni Correction (Sankoh et al, 1997), a reduced significance level of 0.05/3 = 0.017 was used when carrying out the three-paired comparisons to reduce the possibility of making a Type I error and accepting statistical significance when the result was actually non-significant:

Results of Mann-Whitney U-test:

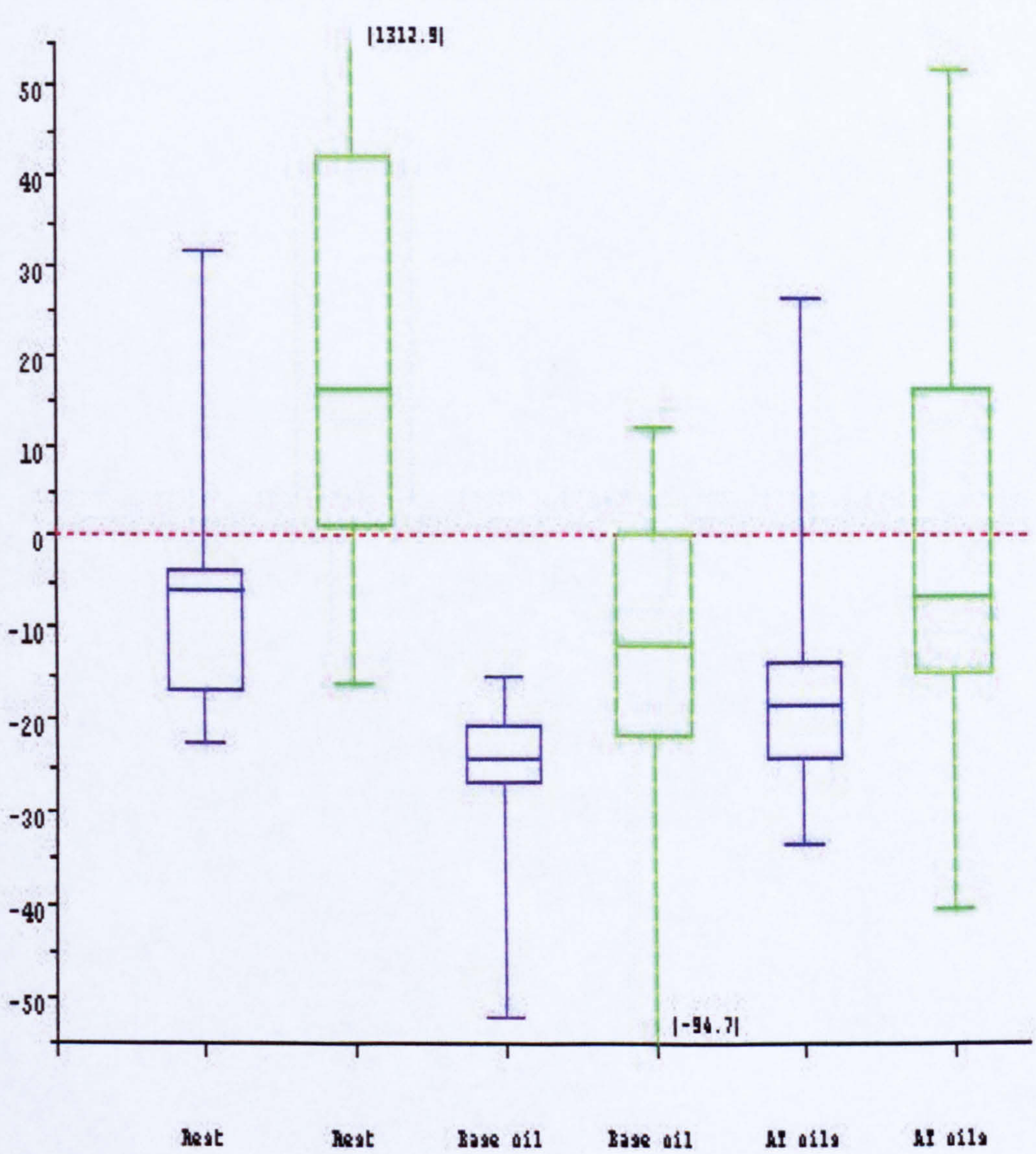
Rest compared with Aromatherapy = P = 0.05

Rest compared with Base oil = P = 0.002*

Base oil compared to Aromatherapy = P = 0.347

* - Significant

It can be concluded from the Mann-Whitney U-test that there was a major difference between the change in prolactin levels in the Rest arm from baseline to 30-minutes post session, and the change in the Base oil arm. A difference in the level of change was also seen between the Rest arm and the Aromatherapy arm although this did not reach statistical significance, however the change in levels in the two experimental arms was seen to be of a similar magnitude. These results are shown in box plot 4.1 (page 142); the median proportional change of level for both hormones in patients within each arm has been portrayed. The median proportional change has been shown because of the wide variance in levels of cortisol and prolactin:


Median Proportional change from baseline to
first post session level for cortisol and prolactin
|1312.9|
50
40
30
20
10
0
-10
-20
-30
-40
-50
|-94.7|
Rest
Rest
Base oil
Base oil
AT oils
AT oils
|Blue - Cortisol| |Green - Prolactin|

Box Plot 4.1

As can be seen from box plot 4.1, the results showed that whilst all three groups displayed a drop in cortisol levels from baseline to first post session sample, the subjects in both massage groups showed a greater drop than those in the rest arm. However there was no statistically significant difference identified between the three arms. With regard to the prolactin levels, there was no drop in levels shown in the rest arm, in comparison, both treatment arms showed a statistically significant drop in levels. However, there was no statistically significant difference noted between the drop in the two treatment arms.

Baseline – 2-Hour Assessment Point: Having identified a statistically significant drop in prolactin levels for one of the two experimental arms when compared to the control arm and a non-significant drop for the other, plus a similar trend for cortisol levels, it was necessary to document whether the observed difference continued for the full 2 hours. Therefore the Kruskal–Wallis 1-way ANOVA was used to identify any continued variation in reduction of hormone levels between arms, by comparing data from baseline with that from the 2-hour assessment. What the analysis showed was that the pattern remained the same as that seen at 30 minutes for the cortisol levels, with the control arm showing the higher rankings; however, the difference was still not statistically significant as can be seen in table 4.19:

Table Showing the Mean Ranking of Change in Cortisol Levels from Baseline to 2 Hours Post Session

Arm	Mean Rank
Rest	21.04
Base oil	17.33
Aromatherapy	18.65
Sig. value	P = 0.696

Table 4.19

In the case of the prolactin levels at two hours, the pattern had disappeared. This data can be seen in table 4.20:

Table Showing the Mean Ranking of Change in Prolactin Levels from Baseline to 2 Hours Post Session

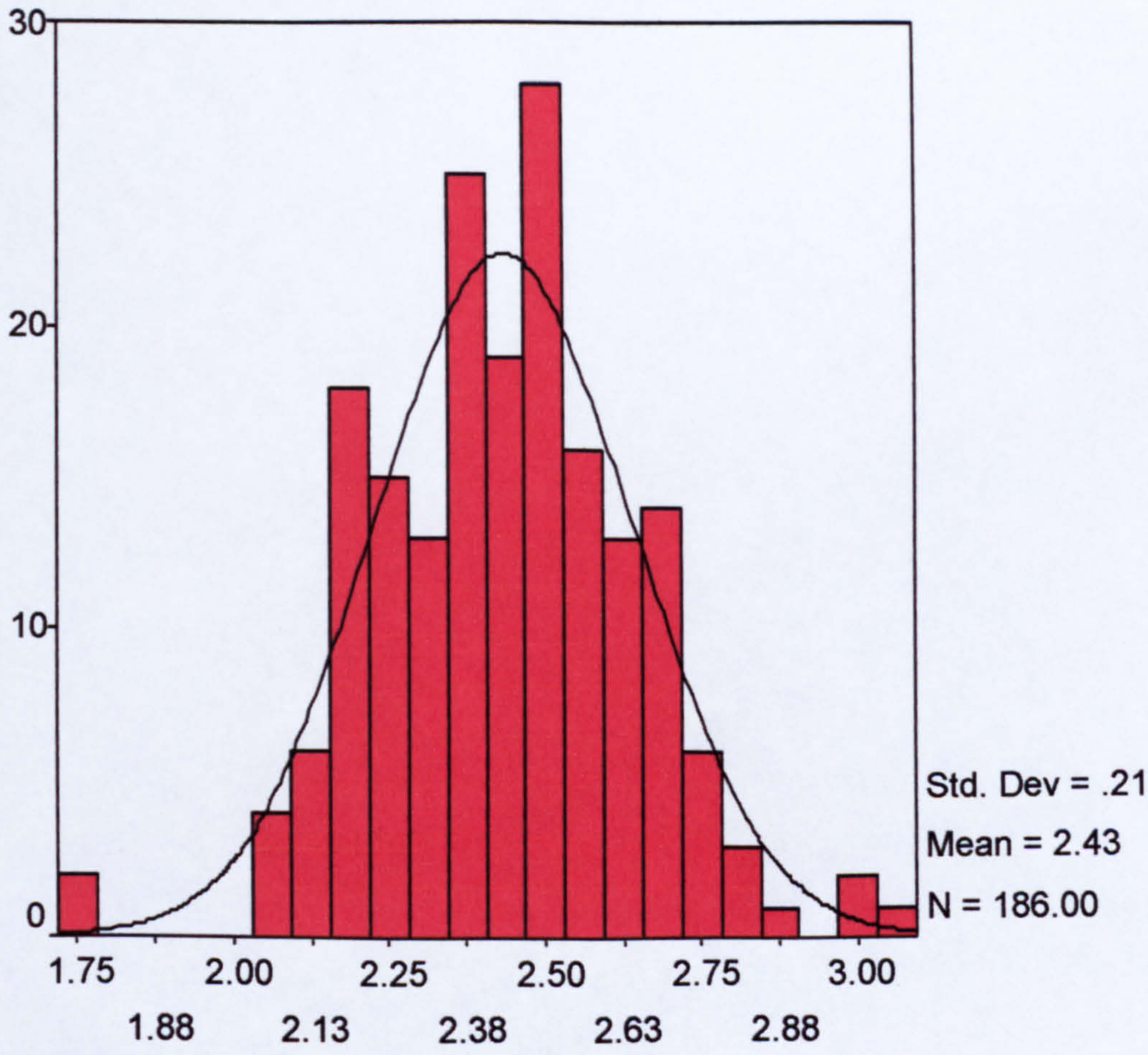
Arm	Mean Rank
Rest	21.04
Base oil	16.21
Aromatherapy	21.00
Sig. value	P = 0.463

Table 4.20

Logarithmic Transformation

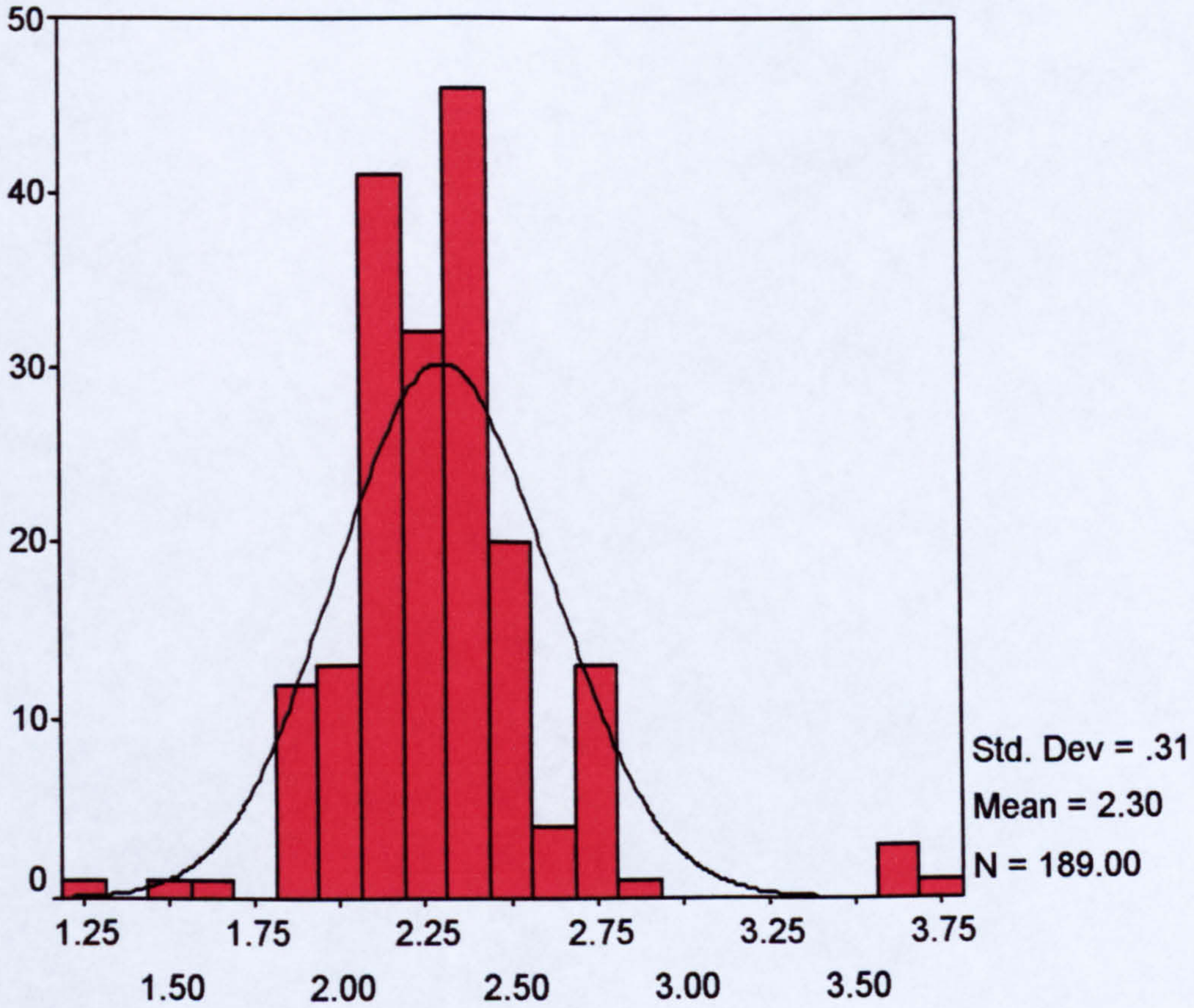
At this point it was decided to assess whether logarithmic transformations would be able to normalise the data. The histograms presented here (graph numbers 4.2 and 4.3) show this was indeed the case:

Histogram Showing Logarithmic Transformations of Raw Values for Cortisol



Graph 4.2

Histogram Showing Logarithmic Transformations of Raw Values for Prolactin



Graph 4.3

Having shown that logarithmic transformation approximately normalised the values, these were then used to validate the results of the non-parametric tests for the between arm comparisons.

Baseline – 30-Minutes: Interestingly although the same pattern was seen between arms with the logarithmic values as with the non-parametric tests, the 1-way ANOVA conducted on the cortisol levels showed a difference between the groups which now reached statistical significance (P = 0.007). The test on the prolactin levels also showed statistically significant differences between groups (P = 0.048). It is suggested that this effect is as a result of the enhanced sensitivity of parametric tests at identifying significant differences between groups.

Baseline – 2-Hours: Both hormone levels showed the same pattern of change from baseline to 2-hours as with the non-parametric tests but the differences between the arms were still not statistically significant, cortisol (P = 0.792); prolactin (P = 0.484).

4.4.1.b Within Arm Comparisons

It was important also, having identified an initial drop in hormone levels which was statistically significant in both treatment arms compared to the rest arm, to see whether a consistent pattern of response was sustained over the 2-hour assessment period within each arm. By looking within each arm rather than across all three arms, any pattern of behaviour will be clearer without the 'noise' from the other arms. Friedman's 2-way non-parametric ANOVA was employed to identify whether the initial differences persisted using the median hormone level at each time point. Tables 4.22 and 4.23 show the resultant P-values:

Table of Significance Values for Change in Cortisol Levels Across 2 Hour Assessment Period Within Arms

Arm of Study	Sig. value
Rest	P = 0.401
Base oil	P = 0.015*
Aromatherapy	P = 0.473

* - Significant, P = 0.05

Table 4.21

Table of Significance Values for Change in Prolactin Levels Across 2-Hour Assessment Period Within Arms

Arm of Study	Sig. value
Rest	P = 0.271
Base oil	P = 0.449
Aromatherapy	P = 0.163

Table 4.22

Wilcoxon matched pairs signed rank test was used within groups for the statistically significant change in cortisol levels, as a post-hoc test to compare each successive assessment point with the baseline level. Results showed that the initial change was not sustained throughout the two hours in any of the 3 arms. One can conclude therefore that the statistically significant change seen in the base oil arm (P = 0.015) is the initial drop in levels.

Whilst the Wilcoxon showed that past the first post sessional samples there was no significant difference within groups, the individual graphs of results indicated that for some patients the initial response was sustained (see appendix XIV, page 324). Patterns of change could be seen most clearly in the cortisol results. Reasons for this and the non-sustainability of the initial response were identified and will be discussed in chapter 5.

4.4.2 Linear Regression

Because of the identified patterns of change seen it was deemed appropriate to use only the change in cortisol levels as a basis for further analysis. It was considered necessary to review the raw data and look for any potentially identifiable subgroups that may have benefited specifically from the interventions. Consequently all the individual graphs, showing proportional change in cortisol levels across the 2-hour assessment period, were classified and coded as either 'responders' or 'non-responders' depending on whether their subsequent cortisol levels remained below the baseline level for the duration of the two hours. The results of this classification

allowed for univariant analysis with factors it was felt could have been of relevance as to whether the patient responded to therapy, the factors chosen were:

Age: The non-parametric Mann-Whitney-U test was used to discover whether people of different ages responded differently to massage. However the test showed no difference between the ages of responders to non-responders (P = 0.509).

Gender: A Chi-square test was used to look for a difference in response to therapy between male and female patients. The results of the test (P = 0.646) indicated that there was no difference in response to therapy between men and women.

Prior Experience of Complementary Therapies: This was the third and final factor identified as having the potential to influence a patient's response to therapy. Once again a Chi-square test was used to look for a difference in response to therapy between patients who had versus those who had not had experience of complementary therapies prior to entry into the study. Once again the test showed no difference in responsivity (P = 0.905) between patients who had and had not had prior experience of complementary therapies.

4.4.3 Calculated Change in Other Physiological Measures

Whilst drop in cortisol and prolactin levels was the primary outcome measure for this study, it was felt important to correlate any change seen in hormone levels with fluctuations in other physiological indicators of stress. The measures used were mean arterial blood pressure (MAP) and heart rate (HR). Initially these two measures were assessed independently, then they were assessed through correlation of all four measures, cortisol, prolactin, MAP and HR.

Median arterial pressure (MAP): Any alteration in MAP across the two-hour assessment period was calculated by subtracting the baseline MAP from all subsequent readings in rotation. This was performed for patients from each arm in turn. The resulting table of median values can be seen below with negative values indicating a drop in MAP and therefore blood pressure, from baseline, the table also includes the significance level of the change from baseline assessed using the Friedman's non-parametric test:

Table Showing Median Change in MAP over 2-Hour Study Period

Arm	30 mins	60mins	90mins	120mins	Sig.
Control	-1.0	0.0	-3.3	-3.3	0.267
Base oil	1.7	-2.7	-0.3	4.0	0.500
Aromatherapy	1.2	1.5	-1.7	0.0	0.927

Table 4.23

Table 4.23 shows that there was no consistent drop in blood pressure over the two hour period – not even at the first post-therapy assessment, therefore the statistically significant drop in cortisol levels seen for both massage groups in the first post-therapy assessment was not a physiological response to massage which was reflected in a similar change in blood pressure. Reasons for this are suggested in the discussion chapter.

Heart Rate (HR): As with MAP, changes in heart rate across the two hour assessment period were calculated by computing change against baseline with baseline value being subtracted from each subsequent value in turn. The median values at each time point have been laid out for each arm in table 4.24. As with MAP the table also includes the significance level of the change from baseline assessed using the Friedman's non-parametric test:

Table Showing Median Change in HR Over 2-Hour Study Period

Arm	30 mins	60mins	90mins	120mins	Sig.
Control	-4.0	-2.0	0.0	-1.5	0.289
Base oil	-3.0	-5.0	-3.5	0.0	0.062
Aromatherapy	-2.0	-2.5	-4.0	-5.0	0.721

Table 4.24

The change in HR over the two-hour assessment period appeared to show more consistency then did changes in MAP. The drop in the HR of patients in the base oil group almost reached point of statistical significance (P = 0.062) although it had risen back to baseline readings at the end of the assessment period. However, whilst the changes seen with patients in the aromatherapy arm were nowhere near statistical significance levels (P = 0.721) the gradual drop in HR over the two hours continued and was sustained at the end of the study period.

The non-parametric Kruskal-Wallis test was then performed on the median rankings of change in both MAP and HR at each assessment point as a factor of arm. The aim was to see whether the readings changed significantly more for patients in one arm than in another at any time point. Table 4.25 shows the resultant statistical significance levels for each of the tests:

Table of Significance Values of Change in MAP & HR Over Time as a Factor of 'Arm'

	30 mins	1 hour	90 mins	2 hours
MAP	0.360	0.320	0.756	0.657
HR	0.600	0.868	0.915	0.622

Table 4.25

Table 4.25 shows quite clearly that the change in physiological variables of MAP & HR was no greater in one arm than another at any of the assessment points.

4.4.4 Correlation of Change Between the Four Physiological Measures

As well as looking at change in values across the two hours in the above measures, it was important to look for correlation in change between all four physiological measures, namely the two hormone levels, blood pressure and heart rate. If close correlation in change was seen between two or more of the variables, then this would go some way to corroborating those measures as reliable physiological indicators of change in stress levels. The correlational calculations were carried out for each arm separately at each time point over the two hours. Because the data was skewed for some of the measures, the non-parametric Spearman's test was used for all calculations.

The 15 tables of P-values laid out on the pages below (tables 4.26 – 4.40) show the significance levels of the correlations between the four physiological measures at baseline and change in readings / values for each time point up to the two-hour assessment as a factor of 'arm':

Tables Showing Significance (P) Values for Correlations of Physiological Measures for the Three Arms at Baseline

Control Arm:

	MAP	COR	PRO	HR
MAP	-	0.29	0.96	0.77
COR		-	0.60	0.47
PRO			-	0.43
HR				-

As can be seen from table 4.26, there are no statistically significant correlations between the four physiological measures at baseline in the patients randomised to the control arm.

Table 4.26

Base Oil Arm:

	MAP	COR	PRO	HR
MAP	-	0.83	0.14	**0.01**
COR		-	0.35	0.73
PRO			-	0.52
HR				-

Table 4.27 shows that in the base oil massage arm the only statistically significant correlation was between change in HR and MAP and they were negatively correlated (rho = ¯0.663).

Table 4.27

Aromatherapy Arm:

	MAP	COR	PRO	HR
MAP	-	0.66	0.22	0.62
COR		-	0.75	0.74
PRO			-	0.82
HR				-

Like the baseline measures of the control group, there were no statistically significant correlations between the physiological measures of patients in the aromatherapy arm.

Table 4.28

The above tables show that the only statistically significant correlation in the baseline physiological measures for the patients in the three arms of this study was the negative correlation between readings of MAP and HR in the base oil arm of the study.

Tables Showing Significance (P) Values for Correlation of Change in Values of the Physiological Measures for the Three Arms at the 30-Minute Assessment Point

Control Arm:

	MAP	COR	PRO	HR
MAP	-	0.61	0.37	0.24
COR		-	0.26	0.46
PRO			-	0.77
HR				-

As can be seen from table 4.29, there are no statistically significant correlations between any changes seen in the four physiological measures at the thirty-minute assessment in the control arm.

Table 4.29

Base Oil Arm:

	MAP	COR	PRO	HR
MAP	-	0.36	0.80	0.55
COR		-	0.98	0.62
PRO			-	0.74
HR				-

It can be seen from table 4.30, there are no statistically significant correlations between any changes seen in the four physiological measures at the thirty-minute assessment for the patients in the base oil arm.

Table 4.30

Aromatherapy Arm:

	MAP	COR	PRO	HR
MAP	-	0.70	0.23	0.28
COR		-	0.39	0.74
PRO			-	0.95
HR				-

It can be seen from table 4.31, there are no statistically significant correlations between any changes seen in the four physiological measures at the thirty-minute assessment for the patients in the aromatherapy arm.

Table 4.31

Tables 4.29 to 4.31 show that there are no statistically significant correlations in changes within the four physiological measures of patients in any of the three arms at the thirty-minute assessment point.

Tables Showing Significance Values for Correlation of Change in Values of the Physiological Measures for the Three Arms at the 1-Hour Assessment Point

Control Arm:

	MAP	COR	PRO	HR
MAP	-	0.80	0.53	0.95
COR		-	0.53	0.97
PRO			-	0.86
HR				-

As can be seen from table 4.32, there are no statistically significant correlations between any changes seen in the four physiological measures at the one-hour assessment for the patients in the control arm.

Table 4.32

Base Oil Arm:

	MAP	COR	PRO	HR
MAP	-	0.400	0.600	0.180
COR		-	**0.001**	0.380
PRO			-	0.100
HR				-

Table 4.33 shows that at the one-hour assessment point in the base oil massage arm of the study, there was a highly statistically significant positive correlation (rho = 0.83) between the change in cortisol and prolactin levels.

Table 4.33

Aromatherapy Arm:

	MAP	COR	PRO	HR
MAP	-	0.88	0.67	0.45
COR		-	0.53	0.49
PRO			-	0.47
HR				-

As can be seen from table 4.34, there are no statistically significant correlations between any changes seen in the four physiological measures at the one-hour assessment for the patients in the aromatherapy arm.

Table 4.34

There was one statistically significant correlation at the one-hour assessment point - in the base oil experimental arm, a positive correlation seen between the changes in the two hormone levels.

Tables Showing Significance Values for Correlation of Change in Values of the Physiological Measures for the Three Arms at the 90-Minute Assessment Point

Control Arm:

	MAP	COR	PRO	HR
MAP	-	0.78	0.86	0.39
COR		-	0.21	0.29
PRO			-	0.96
HR				-

As can be seen from table 4.35, there are no statistically significant correlations between any changes seen in the four physiological measures at the ninety-minute assessment for the patients in the control arm.

Table 4.35

Base Oil Arm:

	MAP	COR	PRO	HR
MAP	-	0.61	**0.03**	0.99
COR		-	0.31	0.93
PRO			-	0.83
HR				-

Table 4.36 shows that at the ninety-minute assessment point in the base oil massage arm of the study, there was a highly statistically significant positive correlation (rho = 0.65) between the median change in MAP and prolactin levels.

Table 4.36

Aromatherapy Arm:

	MAP	COR	PRO	HR
MAP	-	0.61	0.34	0.73
COR		-	0.57	0.80
PRO			-	0.88
HR				-

It can be seen from table 4.37, that there are no statistically significant correlations between any changes, which may have occurred in any of the four physiological measures at the ninety-minute assessment for the patients in the control arm.

Table 4.37

Once again there was only one statistically significant correlation between the changes in physiological measures and again it occurred in the base oil arm although this time it was a positive correlation between the change in prolactin level and the MAP.

Tables Showing Significance Values for Correlation of Change in Values of the Physiological Measures for the Three Arms at the 2-Hour Assessment Point

Control Arm:

	MAP	COR	PRO	HR
MAP	-	0.13	0.18	0.51
COR		-	**0.00**	0.87
PRO			-	0.46
HR				-

Table 4.38 shows that at the 2-hour assessment point in the control arm of the study, there was a highly statistically significant positive correlation (rho = 0.87) between the median change in cortisol and prolactin levels.

Table 4.38

Base Oil Arm:

	MAP	COR	PRO	HR
MAP	-	0.84	0.34	**0.03**
COR		-	0.22	0.69
PRO			-	0.31
HR				-

Table 4.39 shows that in the base oil massage arm at 2-hours post massage the only statistically significant correlation was between change in heart rate and MAP and they were negatively correlated (rho = -0.589).

Table 4.39

Aromatherapy Arm:

	MAP	COR	PRO	HR
MAP	-	0.890	0.770	0.550
COR		-	0.890	0.870
PRO			-	0.052
HR				-

Table 4.40 shows that in the aromatherapy massage arm at 2-hours post massage there were no statistically significant correlations. However, one correlation was nearing significance; prolactin levels and HR were positively correlated (rho = 0.598).

Table 4.40

At the final assessment point of two-hours post massage there was a statistically significant positive correlation between the changes in hormone levels in the control arm, a statistically significant negative correlation between HR and MAP in the base oil arm and a positive correlation nearing statistical significance in the aromatherapy arm between changes in prolactin levels and HR. However, out of a total of 180 possible correlations, only 10 were found to be statistically significant (4 negative & 6 positive). In simpler terms, this gives a ratio of 18:1 between possible correlations and actual statistically significant correlations identified between the changes seen in the four physiological measures over the two-hour assessment period. Implications for these findings in relation to the use of these measures to indicate change in degree of physiological stress are reviewed in the discussion chapter (chapter 5).

4.4.5 Summary of Results from Inferential Statistical Analysis

Of the original 225 patients invited to enter the study 39 were randomised into the three arms of the study (13 patients in each arm). Examination of the pertinent characteristics of the subject population showed no statistical differences between the patients in the three arms of the trial at baseline. Variables compared included age; cortisol and prolactin levels; HR and MAP.

Inferential statistical analysis carried out on the physiological data showed a statistically significant drop in prolactin levels immediately following massage in both treatment arms compared with the control arm, however this was not sustained for the two-hour assessment period. Although this was not mirrored by a significant drop in cortisol levels when the test used was the non-parametric Kruskal-Wallis 1-

way ANOVA, when the data underwent a logarithmic transformation and the subsequent logarithmic values were tested using a 1-way ANOVA, the drop seen in cortisol levels from baseline to immediately post massage also reached statistical significance. This initial drop in hormone levels in the treatment arms as compared with the control arm was the only change to reach statistical significance. However, observation of the individual data graphs showed some subjects to sustain the initial drop in hormone levels (particularly cortisol), therefore linear regression analyses were carried out to try and identify whether there was a discrete subgroup of patients for which the effect from massage was sustained. None of the three variables looked at in this study indicated such a sub-group.

Changes in the physiological variables HR and MAP were explored using non-parametric tests, however although a statistically significant change was documented in HR for the base oil treatment arm, the change was not sustained for the full 2-hours.

Finally, Spearman's test was used to look for evidence of correlation in the change in values between the four physiological variables over the 2-hour assessment period. Only 10 out of a total of 180 possible correlations were found to be statistically significant (4 negative & 6 positive).

4.5 Results of Questionnaire Analyses

The two questionnaires used in this study were chosen to complement each other. The EORTC QLQ C-30 was used to give an overall view of how patients perceived their current quality of life, with the brief pain inventory included to assess specifically how massage impacted on perceived pain.

4.5.1 Raw Scores from EORTC QLQ C-30

The EORTC QLQ C-30 is a 30-question quality of life questionnaire (QLQ), which assesses quality of life by looking at three major aspects:

1. Global health / quality of life (QoL) – measured using two 7 point Likert scales with low scores indicating poor health
2. Functional status (split into five areas) – measured using scales of 1 – 4 with low scores indicating poor level of functioning
3. Symptoms (split into nine areas) - measured using scales of 1 – 4 with low scores indicating low level of problems

By using linear transformation, the raw scores can be standardised so that the scores then range from 0 – 100, in all cases this means that a higher response correlates with a higher score. However, a high score has different connotations depending on the factor being assessed: a high standardised score on a functional scale or one of the global scales represents high level of function or acceptable health / quality of life, whereas a high score on a symptom scale indicates a high level of problems.

Information relating to the patients' quality of life at baseline was available for all patients as every subject completed a QLQ and there were no missing forms. The raw scores given have been laid out with a separate section for each of the three factors, global health/quality of life; functional scales and symptom scales. The tables below show the data for all subjects split into their study arms. The median standardised scores are also presented for each factor. Median scores are used because responses to some of the questions were heavily skewed.

Global health / QoL: These two global scales are assessed using single item 7-point Likert scales with a response of 1 indicating very poor health / QoL and a response of 7 indicating health or QoL which is perceived as being excellent. The raw scores are presented in table 4.41 and 4.42 below:

Table of Raw Scores for Global Health Scale from the EORTC QLQ C-30 Split by Arm

	Global scales (Health)			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
1	-	-	-	-
2	2	-	2	4
3	1	2	2	5
4	4	5	3	12
5	4	5	4	13
6	2	-	1	3
7	-	1	1	2
Total	13	13	13	39

Table 4.41

Table of Raw Scores for Global Quality of Life Scale from the EORTC QLQ C-30 Split by Arm

	Global scales (QoL)			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
1	-	1	-	1
2	3	-	4	7
3	3	1	3	7
4	1	5	2	8
5	3	4	3	10
6	2	1	-	3
7	1	1	1	3
Total	13	13	13	39

Table 4.42

The median combined standardised score for the global assessment of health & quality of life is 58.3. It can be seen therefore that the majority of patients assessed their health and quality of life globally as just above 50%.

Functional Scales: In the functional scales shown below responses of 'not at all' are always seen as good as they indicate a lack of concern by the patient relating to their ability to perform the activity whereas a response of 'very much' would indicate a major problem.

Physical Functioning (PF): Incorporates 5 questions looking at the patient's ability to: perform strenuous activities (Q1), walk a long way (Q2), walk a short way (Q3), need to remain resting during the day (Q4) and perform activities of daily living without help (Q5):

Table of Raw Scores for Q1 of the Physical Functioning scale of the EORTC QLQ C-30 Split by Arm

	PF (1) strenuous activity			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	4	4	4	12
A little	4	4	5	13
Quite a bit	3	3	1	7
Very much	2	2	3	7
Total	13	13	13	39

Table 4.43

Table of Raw Scores for Q2 of the Physical Functioning Scale of the EORTC QLQ C-30 Split by Arm

	PF (2) long walk			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	4	3	2	9
A little	4	3	5	12
Quite a bit	3	5	2	10
Very much	2	2	4	8
Total	13	13	13	39

Table 4.44

Table of Raw Scores for Q3 of the Physical Functioning Scale of the EORTC QLQ C-30 Split by Arm

	PF (3) short walk			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	10	9	9	28
A little	1	4	2	7
Quite a bit	2	-	2	4
Very much	-	-	-	-
Total	13	13	13	39

Table 4.45

Table of Raw Scores for Q4 of the Physical Functioning Scale of the EORTC QLQ C-30 Split by Arm

	PF (4) need to rest			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	8	8	8	24
A little	3	3	1	7
Quite a bit	1	-	2	3
Very much	-	2	2	4
Total	12	13	13	38

Table 4.46

Table of Raw Scores for Q5 of the Physical Functioning Scale of the EORTC QLQ C-30 Split by Arm

	PF (5) help with daily activities			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	13	13	11	37
A little	-	-	-	-
Quite a bit	-	-	2	2
Very much	-	-	-	-
Total	13	13	13	39

Table 4.47

The tables above show that of the 194 responses made relating to physical functioning, 110 (56.7%) indicate no concern relating to this area of functioning. This, plus a median standardised score of 86.7, suggests that the majority of patients did not see reduction in physical functioning as a key problem.

Emotional Functioning (EF): Consists of four items, which reflect a patient's level of, tension (Q21); worry (Q22); irritability (Q23) and depression (Q24):

Table of Raw Scores for Q21 of the Emotional Functioning Scale of the EORTC QLQ C-30 Split by Arm

	EF (21) tension			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	7	9	6	22
A little	3	3	4	10
Quite a bit	2	1	2	5
Very much	1	-	1	2
Total	13	13	13	39

Table 4.48

Table of Raw Scores for Q22 of the Emotional Functioning Scale of the EORTC QLQ C-30 Split by Arm

	EF (22) worry			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	4	6	6	16
A little	6	7	5	18
Quite a bit	2	-	2	4
Very much	1	-	-	1
Total	13	13	13	39

Table 4.49

Table of Raw Scores for Q23 of the Emotional Functioning Scale of the EORTC QLQ C-30 Split by Arm

	EF (23) irritability			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	7	9	10	26
A little	4	3	2	9
Quite a bit	2	-	1	3
Very much	-	1	-	1
Total	13	13	13	39

Table 4.50

Table of Raw Scores for Q24 of the Emotional Functioning Scale of the EORTC QLQ-C30 Split by Arm

	EF (24) depression			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	7	11	10	28
A little	5	2	2	9
Quite a bit	1	-	1	2
Very much	-	-	-	-
Total	13	13	13	39

Table 4.51

Tables 4.48 – 4.51, show that of the 155 responses given in response to questions aimed at assessing levels of emotional functioning by grading emotions usually associated with stress, 92 responses (59.4%) indicated such emotions were not a major concern, as with the physical functioning scales the median standardised score (91.7) confirms this.

Role Functioning (RF): Consists of two items, one assessing limitations in performing activities of daily living (Q6) the other limitations in pursuing hobbies (Q7).

Table of Raw Scores for Q6 of the Role Functioning Scale of the EORTC QLQ C-30 Split by Arm

	RF (6) activity limitations			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	6	9	10	25
A little	2	2	1	5
Quite a bit	1	1	-	2
Very much	4	1	2	7
Total	13	13	13	39

Table 4.52

Table of Raw Scores for Q7 of the Role Functioning Scale of the EORTC QLQ C-30 Split by Arm

	RF (7) hobby limitations			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	5	5	6	16
A little	1	1	2	4
Quite a bit	2	3	2	7
Very much	5	4	3	12
Total	13	13	13	39

Table 4.53

Of the 78 responses required relating to role function, 41 (52.6%) indicated that patients saw no limitations to their ability to function normally, although overall the median score for this factor was 66.7, which although higher than 50 does seem to imply a level of impediment.

Social Functioning (SF): Two items looking at the impact of the patient's situation on family life (Q26) and social activities (Q27):

Table of Raw Scores for Q26 of the Social Functioning Scale of EORTC QLQ C-30 Split by Arm

	SF (26) impact on family			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	1	4	2	7
A little	1	-	1	2
Quite a bit	2	1	1	4
Very much	6	8	9	23
Total	10	13	13	36

Table 4.54

Table of Raw Scores for Q27 of the Social Functioning Scale of the EORTC QLQ C-30 Split by Arm

	SF (27) impact on social activity			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	-	3	3	6
A little	2	1	-	3
Quite a bit	-	2	1	3
Very much	9	7	9	25
Total	11	13	13	37

Table 4.55

Five responses were missing in the social functioning scale this maybe due to patients not being sure how to grade the impact isolation had on these two aspects of their life. Of those that did respond it is not surprising to see that 48 of the 73 replies (65.8%) felt their situation had the highest level of impact on them socially. That the median standardised score for impact on social activity was 0.00, confirms patients as seeing their situation caused them an extremely high level of social impediment.

Cognitive Functioning (CF): Consists of two items assessing difficulty concentrating (Q20) and problems with memory (Q25):

Table of Raw Scores for Q20 of the Cognitive Functioning Scale of the EORTC QLQ C-30 Split by Arm

	CF (20) concentration			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	7	7	5	19
A little	1	2	3	6
Quite a bit	3	3	4	10
Very much	2	1	1	4
Total	13	13	13	39

Table 4.56

Table of Raw scores for Q25 of the Cognitive functioning Scale of the EORTC QLQ C-30 Split by Arm

	CF (25) memory			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	11	9	10	30
A little	-	3	1	4
Quite a bit	1	1	1	3
Very much	-	-	1	1
Total	12	13	13	38

Table 4.57

Of 77 responses relating to levels of distraction, 49 responses (63.6%) indicated no problems; the median score is 83.3, which confirms patients did not appear to perceive reduction in cognitive functioning as measured here to be a cause for concern.

Symptoms: In the nine scales assessing the patient's symptoms, a response of 'not at all' indicates an absence of symptoms whereas a response of 'very much' suggests the symptom is a major problem to the patient. The symptom scales are split up into the following multi-item scales:

Fatigue: A three-item scale asking about need to rest (Q10), feeling weak (Q12) and feeling tired (Q18):

Table of Raw Scores for Q10 of the Fatigue Sub-Scale of the EORTC QLQ C-30 Split by Arm

	Fatigue (10) needing rest			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	5	2	6	13
A little	3	4	2	9
Quite a bit	2	5	2	9
Very much	3	2	3	8
Total	13	13	13	39

Table 4.58

Table of Raw Scores for Q12 of the Fatigue Sub-Scale of the EORTC QLQ C-30 Split by Arm

	Fatigue (12) feeling weak			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	4	6	4	14
A little	6	3	5	14
Quite a bit	1	4	2	7
Very much	2	-	2	4
Total	13	13	13	39

Table 4.59

Table of Raw Scores for Q18 of the Fatigue Sub-Scale of the EORTC QLQ C-30 Split by Arm

	Fatigue (18) feeling tired			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	2	4	3	9
A little	6	3	3	12
Quite a bit	3	4	5	12
Very much	2	2	2	6
Total	13	13	13	39

Table 4.60

Of the 117 responses relating to fatigue, just under a third (30.8%) denied fatigue was a problem, another 30% graded it as a minor issue whilst 47.9% of responses recognised fatigue to be a major issue. Interestingly this balance of raw scores led to an overall median standardised score of 33.3 suggesting fatigue is not a major problem generally, but for a considerable minority it is an issue that requires addressing.

Nausea & Vomiting (N&V): A two-item scale asking about the patient's level of nausea (Q14) and vomiting (Q15):

Table of Raw Scores for Q14 of the Nausea & Vomiting Sub-Scale of the EORTC QLQ C-30 Split by Arm

	N&V (14) nausea			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	4	7	7	18
A little	4	2	2	8
Quite a bit	4	1	2	7
Very much	1	3	2	6
Total	13	13	13	39

Table 4.61

Table of Raw Scores for Q15 of the Nausea & Vomiting Sub-Scale of EORTC QLQ C-30 Split by Arm

	N&V (15) vomiting			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	7	8	10	25
A little	3	2	3	8
Quite a bit	3	3	-	6
Very much	-	-	-	-
Total	13	13	13	39

Table 4.62

Of the 78 responses to queries about the two symptoms, 43 (55.1%) indicated they were not a problem, the median score of 16.7 confirms this generally.

Pain: Another two-item scale looking at whether the patient has experienced pain (Q9) and whether it interfered with their daily activities (Q19):

Table of Raw Scores for Q9 of the Pain Sub-Scale of the EORTC QLQ C-30 Split by Arm

	Pain (9) experienced?			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	10	10	6	26
A little	2	-	4	6
Quite a bit	1	2	2	5
Very much	-	1	1	2
Total	13	13	13	39

Table 4.63

Table of Raw Scores for Q19 of the Pain Sub-Scale of the EORTC QLQ C-30 Split by Arm

	Pain (19) interfered with activity?			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	11	12	8	31
A little	1	-	3	4
Quite a bit	1	1	2	4
Very much	-	-	-	-
Total	13	13	13	39

Table 4.64

The responses given to items in the above symptom scales would suggest that pain was not seen as a problem to patients as a total of 57 out of 78 responses (73%) graded it as having no impact, this was confirmed with a median score of 0.00.

Single Item Scales: Finally there are six single item scales looking at, Dyspnoea (Q8); insomnia (Q11); appetite loss (Q13); constipation (Q16); diarrhoea (Q17) and financial difficulties (Q28):

Table of Raw scores for Q8: The Dyspnoea Sub-Scale of the EORTC QLQ C-30 Split by Arm

	Symptoms (8) dyspnoea			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	8	10	11	29
A little	5	2	2	9
Quite a bit	-	1	-	1
Very much	-	-	-	-
Total	13	13	13	39

Table 4.65

Table of Raw Scores for Q11: The Insomnia Sub-Scale of the EORTC QLQ C-30 Split by Arm

	Symptoms (11) insomnia			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	9	6	6	21
A little	1	3	1	5
Quite a bit	1	4	2	7
Very much	2	-	4	6
Total	13	13	13	39

Table 4.66

Table of Raw Scores for Q13: The Appetite-Loss Sub-Scale of the EORTC QLQ C-30 Split by Arm

	Symptoms (13) appetite loss			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	2	3	4	9
A little	3	4	4	11
Quite a bit	5	2	-	7
Very much	3	4	5	12
Total	13	13	13	39

Table 4.67

Table of Raw Scores for Q16: The Constipation Sub-Scale of the EORTC QLQ C-30 Split by Arm

	Symptoms (16) constipation			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	8	12	11	31
A little	3	1	1	5
Quite a bit	1	-	1	2
Very much	1	-	-	1
Total	13	13	13	39

Table 4.68

Table of Raw Scores for Q17: The Diarrhoea Sub-Scale of the EORTC QLQ C-30 Split by Arm

	Symptoms (17) diarrhoea			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	9	8	4	21
A little	2	3	3	8
Quite a bit	2	1	5	8
Very much	-	1	1	2
Total	13	13	13	39

Table 4.69

Table of Raw Scores for Q28: The Financial Difficulties Sub-Scale of the EORTC QLQ C-30 Split by Arm

	Symptoms (28) financial diff.s			
Responses	**Rest**	**Base oil**	**A / T**	**Total**
Not at all	7	9	11	27
A little	1	3	1	5
Quite a bit	3	1	-	4
Very much	-	-	1	1
Total	11	13	13	37

Table 4.70

In order to get an idea of the degree to which the symptoms measured are an issue to these patients, all the single items have been displayed together. Looking at table

4.67, it can be seen that appetite loss causes the main problems. However, when taken together 138 of the 232 responses (59.5%) indicated that general symptoms were not perceived to be a major problem.

4.5.2 Variation in EORTC QLQ C-30 scores between arms

It can be seen when reviewing the tables above, which all relate to the baseline scores of the EORTC QLQ C-30 that in some cases there appeared to be a variation in level of response between subjects from the three arms of the study (see for example table 4.63, pain). It was felt necessary therefore to use inferential statistics to ensure there were no statistically significant differences between groups at baseline as such differences would have biased the post-test results. The appropriate statistical test to use in such a situation was the Kruskal-Wallis (K-W) 1-way ANOVA, as the scores are ordered groups, which therefore have a ranking position (1 – 4), this allowed for application of the K – W to compare scores between the three arms. The results from question number 9 – 'Have you had pain' were chosen to analyse as they showed what appeared to be a sizeable difference between the three arms. It was recognised that there would be many tied rankings, however the test takes that into account. The result showed that there was no statistically significant difference between the responses of the patients in the three arms when asked about the amount of pain they were experiencing at baseline ($P = 0.228$). It can be concluded therefore, because the variable chosen on which to carry out the K –W 1-way ANOVA showed greatest variation between the arms on visual assessment, that there were no statistically significant differences at baseline between the arms for any of the variables measured by the EORTC QLQ C-30.

4.5.3 Analysis of Raw EORTC QLQ C-30 Scores

The first analysis to be carried out looked at the raw scores of each question and compared responses at baseline with those 24 hours later through cross-tabulation. Cross-tabulation allowed us to see whether individual patients' quality of life as measured by this questionnaire, was perceived by the patient as better, worse or the same 24 hours after receiving the study intervention. Unfortunately, seven of the repeat forms were not received therefore analyses could only be carried out on 32 of the 39 patients.

Global health / QoL: The global health scale scores for the 24-hour QLQ C-30 assessment ranged from 1 – 7, namely they covered the full range of answers. The majority of patients' responses (18 or 56.25%) remained the same; 7 (21.9%) responded that their health was better and 7 (21.9%) that it was worse. With the global QoL scale the 24-hour responses again covered the full range of responses from 1 – 7. This time 15 patients responses (46.8%) remained the same whilst in 8 cases (25%) patients responded that their QoL had deteriorated and in 9 cases (28%) that it had improved.

Functional Scales: The functional scales are all multi item scales aimed at assessing a person's level of functioning from different perspectives:

Physical Functioning: For all five questions in this scale the majority of patients' responses remained the same. Interestingly however, for the first three questions, which required a hypothetical response relating to their abilities to walk / carry heavy bags, four patients (12.5%) gave a more positive response following the study session whereas 2 subjects (6.25%) in response to the first two questions and 3 subjects (9.4%) in response to the third question felt they would have more trouble. For the fourth question, which looked at their need to stay in a bed / chair, 20 patients' (62.5%) responses remained the same and 14 (43.75%) of those claimed they had no need to stay in the chair / bed. Of the remaining 12 responses, 6 (18.75%) patients stated that their need had got greater since the study session and 6 that it had become less. Finally, for the fifth question, which examined their need for help with activities of daily living, 30 (93.75%) continued to respond that they had no need for help whilst 2 (6.25%) patients moved from needing quite a bit of help to needing a little help.

Emotional Functioning: There are four items in this scale, the first focuses on how tense the patient is feeling, 16 patients (50%) continued to respond that they did not feel tense at all. Of the remaining 16 patients, 6 (37.5%) did not change their response, 6 (37.5%) shifted their response in a positive direction whilst for 3 patients (18.75%) their responses reflected a worsening of tension. The second item explored how much patients felt they were worrying, 11 (34.4%) of them (as at baseline) felt they did not worry at all whilst another 9 (28%) gave the same response as at

baseline. However, 8 patients (25%) responded that they worried less than at baseline whilst in 3 cases (9.4%) the level of worry had risen. For the third item, measuring irritability, 19 patients (59.4%) responded that, as at baseline, they did not feel irritable; a further 4 (12.5%) did not change their response. Of the remaining patients, 6 (18.75% of all responders) claimed to be less irritable whilst 2 (6.35%) stated they were more irritable. The final item dealt with feelings of depression; 19 patients (59.4%) felt they were not at all depressed either at baseline or 24 hours after the session 5 other patients (15.6%) did not alter their grading of their depression. Of the remaining responders, 4 patients (12.5%) answered that their feelings of depression were greater whilst 3 (9.4%) that they were less.

Role Functioning: The aim of this scale is to examine how patients perceive their ability to continue functioning at the same level as before their period of hospitalisation. The scale consists of two items, the first measuring limitation in ability to carry out activities of daily living; 13 patients (40.6%) graded the limitations the same at both record points, 13 patients graded limitations as worse after 24 hours (40.6%) and 4 patients (12.5%) graded limitations as less at the second assessment point. The second item assessed the patients' limitations in pursuing hobbies; 18 patients (56.25%) gave the same response at both assessment points, 6 patients answered that the limitations were greater at 24 hours whilst 5 patients (15.6%) said they were less.

Cognitive Functioning: This scale was based on two items assessing firstly, ability to concentrate. 11 patients (34.4%) answered on both occasions that this was not a problem at all, a total of 17 patients (53.1%) did not change their assessment, 5 patients (15.6%) felt it had got worse but 9 patients (28.1%) felt their ability to concentrate had increased in the past 24 hours. The second item was based on memory; 18 patients (56.25%) answered that they had no difficulty and this did not change. 24 patients in total (75%) answered that their memory had not changed over the 24 hour period, 5 patients (15.6%) answered that their memory problems were worse after the 24 hours whilst 2 (6.25%) answered that they were better.

Social Functioning: Again this scale consisted of two items; one asking how the patient's condition interferes with their family life, the other with their social life.

Understandably, 11 patients (34.4%) maintained a response confirming that their condition interfered with their family life 'very much'. 21 patients (65.6%) in total did not change their assessment of how their current condition interfered with family life, 1 patient (3.1%) graded it as having more interference at the second assessment point whilst 7 patients (21.9%) assessed it as being less disruptive the second time. With regard to the item asking about influence to social life 15 patients (46.9%) stated a disruption of 'very much' whilst 22 patients (68.75%) did not alter their assessment. 3 patients (9.4%) graded the disruption as worse after 24 hours and 5 patients (15.6%) that it was less.

Symptom Scales: There are nine symptom scales, some multi item scales, others single items.

Fatigue: The fatigue scale is a scale consisting of three items; the first looked at a patient's need to rest. For seventeen patients (53.1%) this did not change in the 24 hour assessment period, five patients (15.6%) felt their need for rest had increased but for 10 patients (31.25%) the need had reduced, so much so in one case that a patient who had initially graded their need for rest as 'very much' assessed it at the end of the study period as 'not at all'. The second item asked whether patients felt weak: 16 patients (50%) claimed the same level of weakness, 7 (21.8%) that they felt more weak at the end of the study assessment period and 9 (28.1%) that they felt less weak. For the third item, which looked at how tired the patients felt, 19 (59.4%) documented no change in the level of tiredness, 6 patients (18.8%) documented that they felt more tired whilst the final 6 (18.8%) claimed to feel less tired.

Nausea & Vomiting: This is a two-item scale with one item measuring nausea, the other vomiting. In relation to the nausea item 12 patients (37.5%) answered that they didn't experience any nausea, a total of 19 patients (59.4%) did not alter their assessment of their level of nausea, 6 (18.75%) felt it had got worse whilst 7 (21.8%) answered that it had lessened over the 24 hours. Whilst 19 patients (59.4%) responded that the had suffered no vomiting either at baseline or at the 24 hour assessment with a total of 22 patients (68.8%) not altering their assessment, 6 patients (18.8%) graded their vomiting as worse after the study whilst only 4 (12.5%) graded it as having improved.

Pain: Pain is another symptom assessed on a two-item scale. The first item asks whether the patient has experienced any pain, 16 patients (50%) answered that they had suffered no pain at either assessment point, with a total of 19 patients (59.4%) not changing their assessment of their pain after the study. However, only 4 patients (12.5%) claimed their pain was worse whereas 9 patients (28.1%) said it was better. The second item measured how much any pain experienced interfered with activities of daily living. 22 patients (68.8%) responded at both assessment points that there was no influence on activities of daily living with a total of 24 patients (75%) not changing their assessment of its influence. Four patients (12.5%) claimed their pain had greater influence after the session whilst 3 (9.4%) assessed it as having less impact.

Single Item Scales: The remaining symptom scales are all single item scales assessing specific problems:

Dyspnoea: For this item 17 patients (53.1%) claimed not to have any shortness of breath and a total of 18 patients (56.25%) did not alter their assessment of this symptom. However, 9 patients (28.1%) assessed their breathlessness as have improved whilst 5 patients (15.6%) graded it as being worse.

Insomnia: Surprisingly perhaps, considering the subjects' situation, 14 patients (43.8%) answered that they did not have any trouble sleeping (although this could be with the aid of a sleeping tablet) and a total of 20 patients (62.5%) did not alter their assessment of any sleeping difficulties. 3 patients (9.4%) graded their sleeping difficulties as worse after the study whilst 9 patients (28.1%) claimed their sleeping to have been better.

Appetite Loss: Twenty patients (62.5%) did not alter their assessment of appetite loss with 8 patients (25%) grading it as very much of a problem. Seven patients (21.8%) graded the problem as worse after the study whilst 5 patients (15.6%) graded it as better.

Constipation: Twenty-eight patients (87.5%) did not alter their assessment of this symptom and 23 of these (71.9%) stated it was not a problem at all. Two patients

(6.25%) graded the problem as worse after the study period whilst one patient (3.1%) graded it as better.

Diarrhoea: Fifteen patients (46.9%) felt diarrhoea was not a problem and a total of 22 patients (68.8%) did not alter their assessment of it. Three patients (9.4%) graded the problem as better with one patient's assessment improving by 3 points, and 6 patients (18.8%) felt the problem had got worse.

Financial Difficulties: Eighteen patients (56.25%) stated that their condition had given them no financial difficulties and did not change their opinion; a total of 26 patients (81.3%) gave consistent answers at both assessment points. However, 3 patients (9.4%) graded their difficulties as worse after the study session whilst 2 (6.3%) graded them as better.

4.5.4 Inferential Statistics on EORTC QLQ C-30

In order to identify whether any of the changes noted between the baseline and post session scores were statistically significant when the arms were split, the K-W 1-way ANOVA was performed on the data: The null hypothesis for this aspect of the study being that the median change in EORTC QLQ C-30 scores between the arms would be similar. The post scores were paired with the baseline scores to provide a single value equating to the difference between scores. These values were then split into the three arms and the new scores / values were compared between arms using the K-W 1-way ANOVA. It was recognised however that as with the analysis of baseline scores, because the test required ranking of the scores and there were many instances of tied scores (e.g. '0') it maybe difficult to identify differences.

The K-W results showed no statistically significant difference in level of change between the three arms with the mean ranks as follows: Rest = 13.7

BO = 16.3

AT = 19.8

Consequently the null hypothesis could not be rejected.

The K–W 1–way ANOVA was next used to look for differences between the arms in the baseline to post session changes for each of the multi-item subscales using the

standardised scores. Significance values have been presented for each of the subscales:

K-W Significance Levels for Baseline to Post-Session Change Between Arms in Multi-Item Subscales of EORTC QLQ C-30:

Global health / QoL: K-W significance level: P = 0.41
Physical functioning: K-W significance level: P = 0.01*
Emotional functioning: K-W significance level: P = 0.51
Role functioning: K-W significance level: P = 0.03*
Social functioning: K-W significance level: P = 0.04*
Cognitive functioning: K-W significance level: P = 0.75
Fatigue: K-W significance level: P = 0.34
Nausea and vomiting: K-W significance level: P = 0.24
Pain: K-W significance level: P = 0.35
* - Significant results

There were three subscales identified which showed statistically significant differences between the arms in the amount of change shown from pre- to post session measurement. It was therefore important to identify where the differences lay, consequently median rankings for each arm were highlighted:

Median Ranking of Change in Scores of Multi-Item Sub-Scales of the EORTC QLQ C-30 that Showed Significant Differences Between Arms

Arm	Physical functioning	Role functioning	Social functioning
Rest	9.10	19.10	13.44
Base oil	19.27	16.25	18.95
Aromatherapy	19.30	9.06	11.72

Table 4.71

For standardised scores in the functioning subscales of the QLQ C-30 a higher score (and therefore also a higher ranking) collates with a high level of functioning. It can

be seen by looking at table 4.71 that there was no consistency in the change seen following the trial sessions. This inconsistency will be reflected upon in chapter 5 (section 5.2.3).

In order to assess whether there were any specific aspects of the QoL data that were more greatly altered than others by the interventions it was necessary to do a 3 way cross-tabulation of the raw scores: version 1 (V1) x version 2 (V2) x arm, for the individual items and to then perform the K-W on the results for each item. With some items it was clear by looking at the initial cross-tabulations across all arms that there would be no difference, as many of the scores remained the same at both assessment points. Therefore, an arbitrary cut off of only items that showed a level of variation of >10 patients changing their score was chosen to identify items, plus items which were recognised as highly relevant to the original study aims. This further analysis was consequently performed on 16 items:

K-W Significance Levels for Baseline to Post-Session Change Between Arms in Highly Relevant Items of the EORTC QLQ C-30:

Q4:	Need to stay in bed / chair:	K-W significance level: P = 0.009*
Q6:	Limits on activities of daily living:	K-W significance level: P = 0.016*
Q8:	Were you short of breath:	K-W significance level: P = 0.626
Q9:	Have you had pain:	K-W significance level: P = 0.144
Q10:	Need to rest:	K-W significance level: P = 0.273
Q11:	Trouble sleeping:	K-W significance level: P = 0.149
Q12:	Have you felt weak:	K-W significance level: P = 0.537
Q14:	Have you felt nauseated:	K-W significance level: P = 0.346
Q18:	Were you tired:	K-W significance level: P = 0.745
Q20:	Difficulty concentrating:	K-W significance level: P = 0.890
Q21:	Feeling tense:	K-W significance level: P = 0.353
Q22:	Are you worried:	K-W significance level: P = 0.805
Q23:	Level of irritability:	K-W significance level: P = 0.408
Q24:	Level of depression:	K-W significance level: P = 0.891
Q29:	Global health:	K-W significance level: P = 0.783
Q30:	Global quality of life	K-W significance level: P = 0.530

* - Significant results

It can be seen that with the K-W performed for individual items across groups most of the tests proved insignificant due to the small numbers and the limited ranking. Only two tests proved to show statistically significant differences between the groups: Q4 & Q6. The mean ranks of Q4 (R = 22.10, B.O. = 12.14, A/T = 14.15) indicate that patients in the two experimental arms had less need for rest in the 24 hours following their session. However, the mean ranks of Q6 (R = 9.75, B.O. = 16.50, A/T = 20.67) seem to indicate that patients in the control arm had less difficulty performing activities of daily living in the 24 hours following their trial session. The ambiguity of these results will be reflected upon in the discussion chapter.

4.5.5 Pain Scale

The pain scale used was a version of the Brief Pain Inventory (BPI) developed by Cleeland and Ryan (1994) for assessment of pain by patients with cancer. Reduction in perception of pain was included in the analyses for this study on the basis that during an audit carried out as part of the pre-pilot work certain patients commented that massage eased their pain. I felt however that anecdotal evidence tended to show pain as a problem for only a minority of patients with haematological malignancies. This theory was backed-up by the results of the pain assessment:

The second question on the BPI was; 'How often have you had pain in the last week?' This question was the only one, which was answered relatively consistently:

- 23 of the 39 patients answered at baseline that they had no pain and another 2 did not answer at all. This amounts for almost 2/3 of all subjects (64.1%). Only 13 patients went on to answer the rest of the questions.
- In the post session questionnaire (24 hours later) only 29 patients answered question two and of these 15 answered that they had no pain. 15 of these patients went on to answer the rest of the questions.

In total there were 12 patients who answered both the baseline and post session questionnaire in full. A cross-tabulation of their responses was performed and of these 12, one answered that their worst pain was '0', of the other 11 responders 6 graded their pain lower in the post session assessment and only one graded it as worse.

Because of the low level of response it was inappropriate to use inferential statistics on the results. However this low response rate is useful as it shows that, as suggested pain is not a major problem to the majority of these patients.

4.5.6 Summary

The rationale behind the use of the EORTC QLQ C-30 and the BPI in this study has been defended in the methodology chapter of the thesis. The results presented show that change was identified for some patients in the QLQ C-30 from the pre to post-session assessment. In three of the multi-item subscales and two individual items the change was shown, through inferential statistics, to be significantly different between arms; the implications of these findings have been considered in chapter 5. It was deemed inappropriate to perform inferential statistics on the BPI scores as not enough of the post-session questionnaires were completed.

4.6 Qualitative Results

4.6.1 Introduction

The qualitative section of the thesis describes the psychological effects of the study sessions. This component of the results chapter has been written partly in a reflective style. The reason for the use of reflective style being, that it was my intention to take the reader into the hearts and minds of the patients on the isolation unit whilst trying to understand what, if anything can be done through massage to alleviate some of the physical and psychological suffering they experience. The purpose for this journey was to gain a greater understanding from these results of how massage maybe helpful in making the patients' stay at hospital less distressing. Sections of text were incorporated verbatim from the patients' interviews, in order to demonstrate the wealth of material within the data.

This work centred on evaluation of the psychological and physical effects of using massage with and without essential oils, on patients nursed in a high-dose therapy isolation unit. As stated, the results presented in this section focus primarily on the psychological issues and are derived from the topics highlighted during the semi – structured interviews (SSI's) as well as my therapist's reflective sessional diary entries; they will be reviewed in that order.

Scoring of the QoL and pain questionnaires provided numerical data and was analysed in a quantitative fashion (see section 4.5 above). However, the questions asked had psychological implications for the patient. Certain issues arose during the acquisition of the patients' quality of life data – particularly comments reflecting their attitudes to different aspects of life, which were pertinent to this section and were incorporated as appropriate. In some cases comments from the interviews and the diary entries have been used in more than one section, if the same point was relevant to more than one issue.

The main aim of this part of the thesis was to look at data, which showed what the subjects and I as the researcher / therapist felt about their session; how they perceived it as impacting on their psychological and physiological well-being.

It is suggested that an important aspect of the therapy, which will influence what each patient gained from their session is how they felt about and related to me as the therapist. However, it is equally dependent upon their attitude towards both their situation and life in general, as well as how external influences (such as noise or visitors) may have impacted on them. My therapist's perceptions are combined with those of the patients' in the reflective section in which some of findings presented in the earlier sections are explored in greater detail. The chapter will continue with a presentation of these findings. Finally I will bring all the results together in the format of three case studies aimed at highlighting certain issues and integrating the different results pertinent to that patient.

Because similar issues were expressed by patients in both massage arms and in some cases the control arm also, excerpts of text have been used from all three groups interchangeably to illustrate points. In each case a pseudonym has been used to identify patients and the arm of the trial they were in documented (see appendix XII, page 302, for a list of pseudonyms and associated trial number and arm).

4.6.2 Results of Thematic Analysis of SSI and Therapist's Diary

Following the thematic analysis of the SSI and my sessional therapist diary, 13 themes emerged. Twelve of the themes are presented and discussed here, the final theme 'therapist's reflections' is addressed and integrated in the final, reflective part of this chapter:

Psychological Issues	Physiological Issues	Environmental Issues
1. Positive emotions 2. Negative emotions 3. Issues around 'control' 4. Attitude of patient 5. Comments re. therapist 6. Comments about oils 7. Comments about session 8. Prior concerns 9. Future sessions	Physiological change	1. Conversation 2. Disturbances

Once the themes had been identified the text was reviewed to ensure nothing had been missed. Finally all the relevant comments within each patient file were cut and pasted into a new file under the appropriate headings and subheadings as laid out above. This ensured all the data was together in the same place; it was then possible to see not just what was said but how frequently certain comments were made.

It became obvious that whilst some comments were categorised under one subheading, they were also equally relevant to others, for example an almost universal comment relating to the massage was that it was gentle. Any comments of this nature were listed under the subheading of positive emotions, as they would often be linked to other adjectives such as nice or soothing. The implication being that the comment was relating to the massage technique used, this is a generalisable point, which could have been attributed to any massage therapist. However, depending on the context of the sentence, such comments could be taken to imply how the patient felt about me as the therapist and on occasions also needed to be discussed from that angle. As much as possible such factors have been accounted for in the presentation of the findings.

4.6.2.a Psychological Issues

Positive Emotions: Patients in all three arms made positive comments about their session; table 4.72 is an attempt to quantify these comments. Although emphatic words (for example: very, extremely) have not been included, if a patient repeated a word in more than one context (such as: the room was calm, I felt calm) that word would be entered twice:

Positive Emotions Described by Subjects Following Study Session During the SSI

	Arm of Study				
Comment	**Rest**	**Visualisation**	**Base Oil**	**A/T**	**Total**
Gentle / soft			3	3	6
Enjoyable /pleasant		2	3	1	6
Peace / Quiet		1	1	4	6
Motivating		1			1
Calming / soothing		1	3	7	11
Relaxing		2	17	18	37
Reduced emotional stress		1		1	2
Felt better in myself		1			1
Great / fine / nice / good			12	7	19
Lovely/wonderful/blissful			4	7	11
Brilliant / excellent			3	1	4
Comfortable			2		2
Nice/beautiful smell				2	2
Nice sensation			1		1
Feel asleep / sleepy			3	3	6
Sense of wellbeing			1		1
Not intrusive				1	1
Beneficial / constructive		2		1	3
Positive		1			1
Gave focus		2			2
Hypnotic				1	1
Invigorated			1		1
Nice being pampered				1	1
Allows you to forget				2	2
Took my mind off it ...				1	1
Total	0	14 (11%)	54(42%)	61(47%)	129

Table 4.72

When compiling table 4.72 it was necessary in a few cases to adapt slightly what the patient said in order to use it in the table, for example 'you can just let go and relax' became simply 'relaxing'. Equally some statements would have lost their meaning if they had been para-phrased so had to be left out completely, for example: 'I felt

extremely chilled out afterwards, it was just that extra little special feeling'. Most of these comments have been used in the more descriptive part of the chapter. Of the positive comments it was possible to list in the table above, none were attributable to the patients in the standard rest arm, interestingly however 14 (11%) were attributable to the 5 patients in the visualisation subgroup. Of the remaining positive comments 54 (42%) were attributable to patients in the base oil arm and 61 (47%) to those in the aromatherapy arm.

The most striking thing once the comments had been collated was the frequency with which the word relaxing appeared. Within this group of subjects it was an adjective that was used universally to describe the massage both with and without essential oils. The word relaxing is quite a small insignificant word but the definitions of relax given by the Oxford dictionary shows how powerful it becomes in this context: "make or become less stiff or rigid or tense..." (Swannell, 1986). What was most potent was the fact that the word obviously described how the patients felt so completely, that the only way they could emphasis that feeling was by adding adverbs such as 'so' or 'very' to the description, for example:

- It was very, very relaxing (Carol)
- I did find it very, very relaxing (Nancy)
- Well, it was so relaxing, really relaxing; I fell asleep (Diane)
- Just made me feel good, very, very relaxed (Wendy)
- I'm just very relaxed (Isabel).

In some cases subjects were able to further clarify and expand on the sentiment. One patient was able to be very concise in what it meant to her and her comments described perfectly what a therapist would hope to achieve for all patients:

"That was wonderful, it allows you to completely forget everything for a while" (Carol).

Equally, the level of relaxation was such that six patients in the experimental arms (23%) either went to sleep or felt sleepy, an example of one of the comments describing this sensation can be seen here:

'If you've enjoyed something there is not a lot you can really say is there? I was almost asleep, I knew when she went out of the room but I just didn't want to open my eyes' (Paula).

Three other patients (12.5%) identified an associated benefit – that the massage took their mind off their condition. The implication of this and other identified benefits are discussed in the reflective section of this chapter.

Negative Emotions: Patients in all arms of the study made negative comments relating to some part of the study process, these have been laid out in the table 4.78:

Negative Emotions Described by Subjects Following Study Session During the SSI

	Arm of Study				
Comment	**Rest**	**Visualisation**	**Base oil**	**A / T**	**Total**
Boring	1				1
Not different/significant	2	1			3
Feel no different			1		1
Difficult to relax	1			2	3
Didn't like finishing				1	1
Session not long enough				1	1
Too regimented	1				1
More agitated (bloods)	1				1
People always in & out	1				1
Don't like seeing blood	1				1
Don't like blood tests	1		2	1	4
Blood's being wasted	1		1	1	3
Doesn't like oil			1		1
Has a problem with touch			1		1
Light headed after m.				1	1
I.V. machine noisy			1		1
Noisy on unit				1	1
'Alcowipes' (smell)	2	1	2	2	7
Couldn't smell oils				1	1
Total	12 (35%)	2 (6%)	9 (26%)	11 (32%)	34

Table 4.73

It was anticipated that patients' remarks relevant to safety issues regarding the use of massage and essential oils would be identified in this section. Observations, for example, relating to massage making the patient more rather than less agitated. Whilst one patient did make a similar comment, it was in relation to the taking of blood not the therapy session. In fact there were no responses, which could be interpreted as identifying an issue that may throw concern over the use of massage in the subjects randomised to this study. There were however, two concerns relating specifically to the therapy sessions. Firstly two patients in the aromatherapy arm

found it difficult initially to relax, in one case this was due to the noise on the unit, in the other because she was unsure what to expect. Secondly, one patient admitted to feeling no different at the end of the evaluation period. This statement however, does need to be put into context; the same man exuded positive comments about the massage and about how relaxed he felt. The only other negative comment directly relating to the massage was relating to it finishing – two patients didn't want it to! For one of these two (Ann) the comment appeared slightly light hearted but in the other case the lady brought it up as a very pertinent point relating to her ability to relax:

> "It wasn't long enough. I thought it could have gone on a bit longer and have other parts of your body done as well. It takes you about five minutes to relax. Next time I have a massage maybe I'll relax earlier, knowing what to expect." (Jean)

An associated topic was that of maintaining the feeling of relaxation. A couple of patients acknowledged noise as a problem with one lady stating clearly that it inhibited her ability to relax:

> 'Noise outside (people talking and walking about) made it hard to concentrate on relaxing the body... in a quieter situation I could have relaxed more.' (Helen)

Another lady also acknowledged that the level of activity prevented her from maintaining her initial feeling of relaxation:

> 'I'm not so calm as I was when it was going on. I suppose because there is so much going on it's like out of your mind again now, busy and bustling again.' (Norma)

There were also two issues, which regrettably but quite understandably, impacted noticeably on patients in all three arms of the trial. These issues are related to and revolve around the taking of blood. Firstly, some subjects were clearly concerned about the series of blood samples being taken even though the blood samples taken were small and with respect to the patient's clinical condition, insignificant. That more than one sample would be taken was reinforced to all patients whilst obtaining informed consent, unfortunately the information was obviously not always taken in. Equally the fact that the samples were explained to be clinically insignificant was not

enough in some cases to completely reassure the patient - although no patient expressed concerns at the time of consent. Nine patients in total made comments that reflected their concern over the blood being taken and to show what an emotive subject it was for a number of patients, several of the comments have been displayed in full:

- She commented that she soon would not have any (blood) left (Paula)
- 'Didn't like all them blood tests.' (Roger)
- Asked how long it would take to regenerate the blood. (Molly)
- She did make the comment that she thought all four, post session bloods were going to be taken at once. (Alice)

The other, related issue was that of the alcohol wipes (Alcowipes). Because the central lines feed directly into the patient's heart any access into them must be under aseptic conditions. In order to maintain sterility of blood taking procedures Alcowipes were used to swab the end of the line. Unfortunately they smell very strongly and for patients who may be nauseated, they can cause major problems. This proved to be a principal concern with at least seven patients and in a couple of cases it impacted on their physiological wellbeing:

- 'Alcohol Wipes when doing blood makes me a bit heady, something seems to build up in my head, more sensitive to it the more I used it.' (Paul)
- 'The Alco swabs, the smell of them absolutely turns me over and there's been rather a lot of them in the last few minutes!' (Teresa)

From the point of view of the study, it is suggested that the main impact of both these issues would be to reduce any benefits or the sustainability of any benefits relating to the massage. With regard to the Alcowipes, one lady expressed that this was the case very succinctly: 'It (the smell) was taking away the lovely smell of the oils.'

One negative point, which was raised by some patients in the control arm was quite an obvious one and has been highlighted in the following reflections:

- 'Boring' (Penny)
- 'It's not much different to what I do each day anyway so...' (Lucy)
- 'The trouble is, I mean, you're doing it all the time in here anyway, and that's the only thing you can do in here, is rest.' (Cyril)

The fact that it was not an issue raised by patients in the experimental arms suggests that massage offers something different, something to take away the boredom, the sameness of what happens every day.

Issues Around Control: An overwhelming issue for many patients was that of control. Two patients identified general lack of control over their situation to be a major problem and expressed their feelings in a very explicit way. One of the two patients was in the standard rest arm; he made his resentment at his sudden life change very clear:

> 'You do feel you are at the mercy of everybody who wants to come and do something at you all the time... The worst thing about being in these rooms is actually the fact that you have got so little control.' (Cyril)

'The other patient was in the aromatherapy arm and whilst the second and third post blood were being taken started talking about his lack of control, about not wanting to 'buzz' the nurse to make him a cup of tea, yet being frustrated because he couldn't go and make one for himself. Other patients expressed similar frustrations in a more implicit way; a good example came from one of the ladies in the aromatherapy arm: 'I've not been allowed to go out of this place; I get stressed out just sitting in here'. As a contrast to such a show of aggravation, other patients would display a quiet determination to regain control in whatever way they could. In one such case the patient (in the aromatherapy arm) conveyed adaptation to her situation with a certain amount of acceptance, but that acceptance was active:

> 'See, I'm very low at the moment and I'm more susceptible to infection, so to try and combat that I'm using the tea tree and I also soak my toothbrush in water and 2 drops of tea tree oil.' (Nancy)

Comments from patients in all arms of the study appeared to indicate that interventions such as massage might be useful in combating feelings of loss of control; again sometimes this was expressed explicitly as in the following excerpt:

> 'You would have more control then wouldn't you, if you had a chance to put the 'do not disturb' out. Obviously it has got to be within reason, but you do feel you are at the mercy of everybody who wants to come and do something at you all the time.' (Cyril)

More often however, the comments simply implied the patient regaining control such as the observations below:

> 'I found it quite constructive. It's something that if I feel a bit worked up and panicky which I do do, I can lie there and visualize it doing me good.' (Beryl)
>
> - Very pleasant lady, keen to help but also keen to do anything, which may help her. (Molly).

Attitude and Coping Strategies: Different attitudes shown by patients in relation to their illness and current situation were highlighted particularly during the baseline collection of quality of life data. Although the scoring of the questionnaire has been dealt with elsewhere in the thesis (section 4.5.) it was felt to be appropriate to integrate these extra findings with the results of the SSI as they related more specifically to issues raised here. There were certain questions within the questionnaire, which were not directly relevant to the patients' current situation such as how they would cope with going on a long walk - in these cases subjects were encouraged to answer subjectively by reflecting on how they felt they would cope. Some patients appeared to reject the idea that they may experience problems, for example one man in the base oil arm had a heightened expectation of what he was physically capable of; it became obvious as the session continued that physical strength was very important to him. This coping strategy was clearly identifiable in three male patients. In the same vein there were some patients who graded their health as excellent on the global health question as if in denial of their illness. Others however seemed to adopt the illness role and went into a lot of detail about the problems they were experiencing; again, this type of focus was documented for three patients particularly. Because, for reasons previously explained (see section 3.9.2), my therapist's diary entries were not standardised and the patient's attitude was not always mentioned. However one patient was mentioned in relation to how directly she coped with her condition in that when she was asked about her overall health, she responded 'I've got cancer' between guffaws of laughter. The topic of attitude and its relationship to reduction of stress is a complex one and is dealt with in greater detail within the reflective part of this chapter.

Comments About the Therapist: One question, which was very important, was how much of any therapeutic effect was down to my influence as the therapist? It was accepted that all patients must have trusted me and felt comfortable enough with my presence to allow me to touch them in the intimate way required of massage therapy. However, the same could be said of any massage therapist from whom a massage was requested, consequently that does not afford me qualities, which cannot be generalised to other units. Whilst there was no question in the semi-structured interview enquiring directly into what the patient felt about the therapist, the questions were worded in a manner broad enough to allow comments about me if the patient wished, the table below lists the comments made:

Comments About the Therapist Expressed by Subjects Following Study Session During the SSI

	Arm of Study				
Comment	**Rest**	**Visualisation**	**Base oil**	**A / T**	**Total**
Calming	1	1			2
Soothing		1			1
Gentle				1	1
Sensitive			1		1
Warm hands			1		1
Gentle hands			1		1
Made me relaxed				1	1
Nice / pleasant	1	2	4		7
Lovely			1	1	2
Good masseuse			1		1
Informative			1		1
Total	2 (10.5%)	6 (31.6%)	10 (52.6%)	3 (15.8%)	19

Table 4.74

Less than 1/3 of all study subjects (12 patients) made comments about me as the therapist during their interview: 7 in the base oil arm, 2 in the aromatherapy arm, 2 in the visualisation subgroup and 1 in the rest arm. Between them they made 19 comments relating to the therapist. Over 50% of the remarks came from patients in the base oil arm. The subject of a therapist's influence is extremely important and will be addressed again in the subsection looking at the amount of time during the sessions was spent in conversation and again in the reflective part of this chapter.

Comments About the Oils: It was important to look for any extra benefits brought to the process by the essential oils. Two of the seven comments specifically relating to the oils pointed to the fact that the patients in question found it difficult to smell the oils as much as they would have liked. However, the other five comments reflected on how beautiful, pleasant and de-stressing the oils had been.

General Comments About the Session: Comments have been incorporated into this section that don't easily fit into any of the other subheadings. Four statements related to patients approval of massage and its evaluation, including assessment of its benefit when used alongside orthodox medicine. A short example of such approval is included here:

> 'I just felt the whole idea was very good, it was a really good idea, and I'm glad I can help with what she's doing.' (Diane).

At the time of the study, massage was only available to the patients on one day a week. Several patients mentioned that they would like to be able to access a massage service more regularly than once a week but one patient in particular made clear the reasons why she felt a daily massage service should be available:

> 'It was a lovely experience and it would be nice to just (have a massage), when you wanted it ... if you've got stuff on that day and you can't do it you're going to miss out, be nice to be able to say I'll have one tomorrow instead. Especially when you're stuck like this, you haven't got much else to look forward to as it were.' (Olga)

This matter will be reflected on in greater depth in discussions relating to implications for clinical practice in chapter 5.

Prior Concerns: It was interesting to note that although all patients who received massage expressed the desire to repeat the experience (see section on future sessions), five of them did in fact confess to prior concerns regarding massage. One gentleman linked the idea to going to a massage parlour, which he had not previously been brave enough to do (Ian), whilst another stated that he would only feel comfortable being massaged by a female (Brian). These issues both highlight the

fact that for some patients at least, the sex of the therapist may be an important factor in whether they decide to take up an offer of massage. Two patients confessed that they had agreed to go into the study despite the fact that up to that point they did not 'really like being touched' (Nancy and Fiona). Related to this, another perhaps more ambivalent subject confessed to thinking of massage as, 'Rub it and that's that' (Mike), again the study session reassuringly changed his views. The final concern to be expressed, related to discomfort around undressing - although the patient concerned requested a back massage (Nancy) which required her to get undressed. Embarrassment about taking ones clothes off is an understandable concern and one that may well put many patients off having a massage.

Future Sessions: Several patients commented in a general fashion on the benefits of the session – most of them were subjects in the massage arms, and mainly they were spontaneously reflecting on how they would like to be able to receive massage on a regular basis. One example of such comments is given in the box below:

> 'I just think it should be a regular thing for anybody that wants it. It can only be beneficial can't it if you are relaxed and accepting a nice, calm atmosphere. Yes, I think it's brilliant. I think it is a very necessary service really, I think it's time people saw that side of medicine as being important, you know, holistic or whatever approach.' (Ann).

Enquiring as to whether subjects would want another session had in fact been one of the questions asked during their interview as a way of gauging how pleasurable they had found it. The following number of patients from each arm gave a positive response:

Number of Patients in Each Arm Wanting a Repeat Study Session

Rest	**– 3**
Visualisation	**– 3**
Massage	**– 13**
A/T massage	**- 13**

Box 4.1.

As can be seen in box 4.1, 100% of patients in both massage arms wanted to receive further massage. More then that, rather than just answering with a simple yes, the majority of them went on to emphasize the point. It was interesting that 3 of the 5 patients who had made use of the visualisation technique (60%) also wanted to repeat the experience. Of the 3 patients in the rest arm who answered in the affirmative, only one answered out-right, another appeared ambivalent and the third one qualified it by saying this was the case only if he got peace and quiet.

4.6.2.b Physiological Issues

Physiological Change: Probably the most important finding in this section was a negative finding; the lack of comments indicating harmful side effects of either the massage or the use of essential oils. Remarks relating to for example tenderness over the massaged area or itching and/or rash formation following the use of essential oils would have made me seriously apprehensive about the safety of the therapy; reassuringly no such remarks were forthcoming. Apart from safety, the focus of the trial was the reduction of stress; however, a patient may experience this in many ways. So far the results in this section have reflected on comments by the subjects that appeared to indicate reduction in psychological stress (feeling more relaxed for example). Here, comments will be reported that seem to suggest reduction in physiological stress. Table 4.75 lists all the remarks made which indicate relief of physiological distress:

Comments Relating to Physiological Improvement by Subjects Following Study Session During the SSI

	Arm of Study				
Comment	**Rest**	**Visualisation**	**Base oil**	**A / T**	**Total**
Reduced pain		1			1
Shoulder better			1		1
Feel much better				1	1
Dry skin now smooth/soft				2	2
Back more supple			1		1
Feet less tender			1		1
Ankles feel better			1		1
Shoulders less tense			1	1	2
Neck less tense				1	1
Back less tense				1	1
Legs more relaxed			1		1
Nausea & vomiting disappeared				1	1
Total	0	1 (7.7%)	6 (46%)	7 (54%)	14

Table 4.75

Table 4.75 shows that 46% of patients in the massage with base oil and 54% of the patients in the aromatherapy arm identified physiological benefits to the massage they received, whereas only one patient (7.7%) in the visualisation subgroup and none of the patients in the standard rest arm, identified any physiological benefit.

The first patient to comment on physiological gain was a subject in the visualisation subgroup (Noel). This particular gentleman stated that the session 'Took away some of the pain,' however it was difficult to interpret what he meant by this as his grading of pain was erratic and he appeared to down grade his pain in response to conversation. It may be therefore that this subject was an example of pain being far more than a physiological experience and that it was more a reflection of his state of being. Another issue relating to pain came soon after (John), this patient gave a good example through his baseline assessment using the pain scale of how patients can 'pigeonhole' their problems. John evaluated himself as having no pain and yet he had been complaining of very painful shoulders, it is suggested that because the pain was not related to his condition he did not feel it would be relevant. As can be seen in table 4.75, there were also comments relating to relief of muscular tension,

generalized remarks about feeling physically relaxed or contemplating on smoothness of skin, which also tied in to a better body image. One man reflected specifically on his 'restless legs':

> 'Feet are on fire, feel champion, fine.' Paul is due a knee replacement [R] and the other is aching due to overcompensating therefore, legs it is for massage, especially since he is also suffering from restless legs. He commented after I'd finished the first leg that it felt a lot more relaxed.' **(Paul)**

Symptoms such as these can become overwhelming if the person has nothing else to focus on. By drawing a patient's attention away from their physical aches and pains it was hoped to enable them to relax in the full sense of the word, with a resultant drop in stress levels.

4.6.2.c Environmental Issues

Conversation: It was important to document the amount of conversation which occurred during a study session as it had implications for what the patients found beneficial within the session; was it the therapy or was it spending time talking with me as the therapist? My therapist's sessional diary entries were standardised to the extent of always documenting the approximate percentage of each session in which there was ongoing conversation, and in a general manner, what that conversation consisted of. The logic being that if there was no conversation during the therapy, then my influence as a person could be minimised more easily than if there was two-way discussion throughout the session. These issues were only relevant for patients in the experimental arms as I was not in the room of the patients in the control arm during the 20-minute sessional period. To review my influence as the therapist in a measurable way, the amount of patients who talked to me during their session were documented:

- 14 patients (> 50%) - no conversation
- 3 patients - minimal conversation (5 – 10% of the session)
- 5 patients* - conversation during most of the session
- 2 patients* - conversation during 100% of the session

* - In some of these sessions the topics of conversation were emotive.

It can be seen from the numbers presented above that for approximately 2/3 of the patients massaged, conversation was not necessary or of minimal importance. However, in 1/3 of cases the patients felt it necessary to talk through most of the massage. In three of those subjects the topics of conversation were obviously emotive and related to either their own diagnosis or that of a close relative. One patient commented specifically about talking to someone who was not part of his or her primary care team:

> 'It was a good time to talk – with someone who was independent, not one of my nurses or doctors.' (Mike).

There were 5 of the patients who felt the need to talk through a large part of the massage session who also mentioned the therapist specifically during their interview; two of those offered general comments about liking me - these were both patients who had talked of very emotive things during the massage (both in the base oil massage arm). The other three commented on very specific things; the first two commented on being made to feel comfortable, one in a very general way (aromatherapy arm) the other in relation to my perceived sensitivity to their discomfort about getting undressed (base oil arm), the final one spoke of my 'gentle hands' (base oil arm). The implication of the type of conversation is discussed in the reflective part of this chapter (4.6.2.d).

Disturbances: Evidence of external disturbances came primarily from my therapist's sessional diary; this objective documentation of the number and type of disturbances that occurred during the study sessions has been quantified and listed in table 4.76:

Disturbances Encountered by Subjects During Study Session Split by Arm

	Arm of Study				
Disturbance	**Rest**	**Visualisation**	**Base oil**	**A / T**	**Total**
Relative(s) in room	1	1	1	3	6
Relative(s) arrive	1	1	1	5	8
Friend(s) arrive			1	2	3
Pt. coughing in session			1		1
Doors banging		1			1
General noise on unit				2	2
Phone ringing x1			1		1
Phone ringing >1		3			3
Machinery noise				1	1
Doctors ward round				2	2
Administration of drugs	1			3	4
Staff enter (other reasons)	2	1		6	9
Problems taking blood			2		2
Total	5	7	7	24	43

Table 4.76

As each arm had only 13 patients, it can be concluded from table 4.76 that some patients (in the aromatherapy arm at least) must have been disturbed by multiple distractions. To look at this in greater detail table 4.77 clarifies how many patients in each arm suffered a disturbance and how many disturbances occurred:

Breakdown of Number of Sessions to Encounter Disturbances Split by Arm

	Number of distractions / disturbances per patient			
Totals	**Rest**	**Visualisation**	**Base oil**	**Aromatherapy**
	1 (1)	1 (2)	1 (4)	2 (6)
	4 (27)	3 (3)	1 (5)	1 (8)
		1 (32)	1 (14)	1 (15)
		2 (33)	1 (20)	**9 (17)**
			1 (22)	2 (19)
			2 (24)	4 (23)
				4 (28)
				1 (37)
Total no. pts effected	**2 (25%)**	**4 (80%)**	**6 (46%)**	**8 (62%)**
Multiple distractions	**1 (12.5%)**	**2 (40%)**	**1 (8%)**	**5 (38.5%)**

Table 4.77

Note: Figures in brackets indicate patient's study number.

On examination of table 4.77 it can be seen that the subgroup that endured the largest percentage of patients encountering disturbances was the visualisation subgroup. However the arm of the study that suffered the highest number of disturbances per head was the aromatherapy arm, with one patient being disturbed nine times. The number and type of disturbance may be an important factor in how each patient responded physiologically to therapy; therefore these findings will be reviewed in relation to drop in hormone levels in both the case studies and the discussion chapter.

4.6.2.d My Reflections as Therapist/ Researcher

Introduction: What I wanted to do, as part of the investigation, was to relate my own reflections on each session with those of the subject, as I was interested to see whether we identified similar issues. Consequently my therapist diary entries and contemplation on patients' comments have not been standardised – except to document approximately how much conversation occurred during each of the massage sessions. For continuity, this section has been presented under similar sub-headings to those used for the thematic analysis. Matters, which appeared to stand out as relating to a particular subject, have been commented on, for example remarks suggesting coping strategies or attitudes and interruptions to the session. However, reflections relating more to the study process as a whole have also been addressed. The themes explored are not exhaustive, and whilst greater attention has been paid to the most commonly occurring issues, it is the intention to reflect also on factors which may have impacted substantially on only a few patients – especially if the importance can be seen to be potentially relevant in future situations and / or was seen as impacting on the subject's cortisol levels.

Because of the mixed methods design of the study, deciding on the layout of the results was challenging. For a standard thesis the author's reflections would be presented as an integral part of the discussion chapter. However for this study those reflections also formed a fundamental part of the results. For that reason, a verdict was reached to present reflections that arose and were included in the sessional diary within the results chapter, whilst reflections that arose as a result of examining the data were included within the discussion chapter.

Positive Emotions: The main focus of this work was to look for potential benefits of massage on patients in isolation. To reflect for a minute on the philosophy of PNI; the interconnectedness of mind, body and immune function, if such a link is accepted, then to allow someone the space to escape through massage from the distress of their situation is to give them space for healing. Precious time in which they are not swamped by the anxieties of illness and the threat of death, time in which the stresses of hospitalisation are not overwhelming the body's natural defences. That the mind and body are intimately connected appears to be confirmed when one notes comments such as this one:

> 'Very relaxing, relaxed my mind, it was hypnotic, went into my own world. Took my mind off my nausea, sickness disappeared for a while'. Now he feels: 'emotionally stable, fine, no worries.' (Mike).

One of the failings of me acting as both therapist and researcher in the study was that at times the nurse and therapist aspect of the role impinged on the researcher part of the role, this is something I will reflect on in greater detail. The clearest example of this was seen when I was asked by five patients in the control arm (independently) to provide an alternative to massage. I agreed, teaching them a simple visualisation technique. In doing so, I accepted that any extra benefit to the patients in this subgroup would reduce any difference seen between the experimental and control arms. However, the comments from these five patients I feel vindicated the decision. The visualisation proved to be beneficial to the patients and potentially provided the staff on the unit with a simple tool, which they can learn and offer to patients as a way of empowering themselves. Some of the relevant topics were highlighted in excerpts from the interview with subject Beryl:

> 'I found it quite beneficial; I found it quite positive. As it happened I was quite weary before she came in anyway. I did visualise the chemo working; it's not quite such a traumatic thing – more a friendly thing, working on my behalf assisting the bone marrow going round absorbing all the bad cells... Relaxed, quite a bit better, it's given me something to focus on and the fact that she's taught me, instead of just lying there she said try and visualise, I found quite constructive. It's something that if I feel a bit worked up and panicky, which I do do, I can lie there and visualise it doing me good. So I'm probably better for it, before I was a bit down in the dumps, a bit negative.' (Beryl)

It needs to be emphasised at this point that when suggesting visualisation, it was always explained to the patient that such techniques may help encourage their body to be receptive to the treatment, however they do *not* make the patient responsible for whether the chemotherapy / transplant succeeds or fails

Negative Emotions: It has been suggested that the multiple roles I was required to take on for this study meant that at times the therapist and nurse aspects of the job got in the way of the research. Unfortunately, and it is debatable whether this is also unethically, the research sometimes obstructed my usual standards of nursing care. The clearest way to explain this is to give an example:

This particular concern tied into many of the negative comments made by patients in the SSI and had implications on patients' ability to remain relaxed throughout the two-hour assessment period. It centres on the study protocol requiring me to take several samples of blood from each subject. It is understandable that patients would feel concerned about this when their lives revolve around blood counts and they can only be discharged once these counts reach a certain level. Consequently there is the feeling that every drop of blood is precious. The amount of blood taken from each subject was negligible in terms of clinical impact a fact that was explained at the time of consent. However psychologically it obviously worried several patients, who commented on it when asked about their dislikes relating to the study process. An example of such a comment can be seen below:

> 'I don't like seeing my blood pouring out. It feels like it's being wasted, it's precious. I think that's probably what it is. Especially when your life's in a bit of a poor show anyway.' (Cyril).

An associated problem related to the smell of the Alcowipes, the alcohol wipes used to swab the end of the central line prior to taking blood. Unfortunately they smell quite strong and induced feelings of nausea in some patients; several patients made it quite clear how they felt:

> 'Oh, the Alcowipes, they are horrible; yes that was the worst bit. It just makes me feel... not very well, yeh. Something needs to be done about that.' (Tom)

Unfortunately it was difficult to solve the problem, because once the trial had started the protocol was fixed and if I had started changing the procedure for taking blood half way through the trial, that in itself would have had implications for the results of the two cohorts of patients. However, continuing the study in the original format in spite of these concerns felt uncomfortable from the nurse / therapist perspective and will be discussed in greater detail in the section of chapter 5 dealing with the limitations of the study (section 5.3).

Another issue, which may have influenced patients' ability to relax, certainly two patients commented on it, was the length of the session – that it was too short. The sessions were standardised at 20 minutes for several reasons (see section 3.8.3), which include not wanting to over-stimulate the patient. On reflection, it is surprising that the subject of time did not come up more often, as for most of the patients in the study this was their first experience of massage. It is probable that they would not know what to expect, and as a consequence it could have taken a little time for them to relax into the therapy. However, one patient's own thoughts suggested a solution, she did find it: 'relaxing', 'beneficial' and 'soothing,' therefore proposed the idea that she would relax earlier next time. This is logical, as the memory of the pleasant sensations from the previous occasion would put her in a receptive frame of mind for relaxation in future. If there had been more comments relating to the time of the sessions being too short then I may have considered reviewing my normal practice, of standardising massage times to approximately 20 minutes. However, because only two patients out of twenty-six commented on the length of the massage I took it more as confirmation that the timing was approximately correct, not wrong.

Several patients in the rest arm stated that they felt their session was boring and insignificant; 'The only thing you can do.' In making comments such as these they were implying that the massage was something different. When discussing the positive issues raised by the patients, I focused on the element of relaxation as something to reduce stress. However, another powerful weapon against stress as I have already implied, is distraction. If someone is bored then their mind is free to focus on their situation and the associated anxieties. If however they are distracted then their mind is taken off their situation – they are literally given something else to

think about. By offering massage, not only might one be helping to relax the patient directly through touch but also indirectly by 'taking their mind off it,' giving them something positive to reflect on, if only for a short while. One patient clarified this point beautifully with her comments:

> 'Can you describe where, how you feel relaxed?' Just am really, not like I was yesterday. I've not been allowed to go out of this place; I get stressed out just sitting in here.' (Enid)

An interesting contrast to this perspective came from another patient who thought of himself as a non – worrier (Brian), he quoted a wonderful saying from his mother-in-law 'worry is interest paid on trouble which may never happen.'

Control: A very important issue relating to a patients acceptance of their situation and as such their ability to relax is that of control. As I reflected on the section of my data which highlighted patients' attitudes to their illness and life in general I was intrigued to see how many contrasts there appeared to be. One overwhelming issue for many patients was that of control. When someone is admitted onto a unit such as this one, it is fair to say that they are metaphorically stripped of all control over their day-to-day life. However, their ways of dealing with this very dramatic change in their life are vastly different and range from ineffectual raging against it to making the best of it and working towards regaining a certain element of control. The two excerpts below are examples of two very different attitudes; the first man is very explicit in his resentment of his sudden life change:

'You would have more **control** then wouldn't you, if you had a chance to put the 'do not disturb' out. Obviously it has got to be within reason, but you do feel you are at the mercy of everybody who wants to come and do something at you all the time. Even if it's just giving you your lunch or whatever, it's not quite the same as you going down getting your lunch at home whenever you get hungry. The worse thing about being in these rooms is actually the fact that you have got so little **control**. I mean you can't do anything without asking somebody to do it, you know you really are so dependent on other people all the time'. Talking about having bloods taken; 'Then again, it's the **control** thing, I like to feel in **control** and again when they are doing that you are a passive thing aren't you. You just have to sit there while this is all done to you. The whole thing of being in these rooms is that you have no **control**, or not enough **control**. I mean, I know it's going to be like that but, it makes you feel like I'm just sitting here, I'm just the patient, it's still done to you, isn't it. It's not - major stress or anything like that, it's just another we're coming to take bloods, it's just on and on and on isn't it?' (Cyril)

Although this excerpt of the interview is a long one, it has been included in its entirety as it clearly illustrates what a major issue the lack of control was for this subject and how it obviously inhibited his ability to cope with the situation in which he found himself – it also very clearly summarised the way of life on the unit.

The second example highlighted an attitude more in line with the majority of patients in that whilst this patient did not mention the word 'control' explicitly, her actions expressed her approach; a calm resolve to reclaim control in whatever way she could. She also implied adaptation to her situation with a certain amount of acceptance but that tolerance was in no way passive in that she was proactive in helping herself:

'Well, the only oils that I actually use at the moment are lavender and tea tree, and I don't put them on my skin, I put them on my blanket, so that they are in the atmosphere, and the tea tree, that's a natural antiseptic. See, I'm very low at the moment and I'm more susceptible to infection, so to try and combat that I'm using the tea tree and I also soak my toothbrush in water and 2 drops of tea tree oil'. (Nancy)

This lady saw her leukaemia as a message to change. One related and interesting point was that although she was not yet fully comfortable with the blood-taking aspect of her stay on the unit she was at the same time at pains to reassure me that she didn't mind me taking blood for the study, equally she always took her own

blood pressure (with an automated BP machine). It seems that perhaps these decisions and her choice to be in the trial were signs of her trying to maintain some control over her life.

It is interesting to see how many patients did appear accepting of their situation. Obviously they may not always be expressing what they felt; they may not feel comfortable describing their frustrations to one of a team of people here to help them. The general tone of many of the interviews was one of resignation. One of the reasons for setting up the service was to try and help patients regain an element of control in their lives and judging by some of the comments made by subjects in the study the reasoning was appropriate and the service beneficial. One example of such remarks can be seen below:

> 'I just feel that whatever you can do to help yourself get better you should take advantage of. I think these trials are excellent things; if you don't try them you never make any progress.' (Wendy)

Attitude and Coping Strategies: The comments patients expressed in relation to attitude gave a lot of insight into how they coped with their condition. It was unfortunately beyond the remit of this thesis to fully explore the implications of different coping strategies and their influence on levels of stress as it is a major field of research in its own right (Cooper and Watson, 1991). However, I intended to explore the issue to a certain extent especially since the contrasts between the different methods of coping were so obvious. I noticed for example when discussing the quality of life questionnaire with subjects, that many of them did not acknowledge their disease process at all. When asked about overall health or quality of life they would grade it in relation to how they felt and this may be as high as 7 (top score available). To an observer this may seem a little confusing in light of their condition, but in relation to the use of denial as a coping strategy it was understandable. Denial is used when the full impact of a situation is too much for a person to cope with; this can be seen for example when someone is coping with bereavement. Equally however, trying to cope with a life threatening diagnosis and being separated from friends and family to go through the very intensive treatment required to cure their illness maybe too much for some people. As a very dramatic

contrast to this approach, one of the subjects had a coping style almost directly opposite – she approached the situation head on. The lady in question had coped well with her chemotherapy so far and was keen to be part of the study. She appeared to understand everything that was expected of her perfectly and when she filled in the QLQ no clarification of the context from which to answer the questions was required. She responded very realistically with an almost objective realism in her answers, for example when asked to grade her health she expressed amusement and bluntly pointed out that she had cancer. In comparison to this, most patients answered the questions in the QLQ from a subjective standpoint. The contrasting attitudes illustrated here demonstrate the point that whilst one lady coped with things by facing them head on with full acknowledgement of their implications, the results of the study would suggest that most people cope in a more reactive way, that is by dealing with the symptoms they feel from the illness / treatment and suppressing or ignoring the cause of these symptoms. It is possible that they can respond in a more positive manner towards what is happening if they suppress their knowledge.

Comments About the Therapist: To look at the influence of me as the therapist objectively: as has already been stated earlier in this chapter (section 4.6.2), less than 1/3 of all study subjects (12 patients) made comments about the therapist during their interview and 3 of them were patients who had used the visualisation technique during their rest session. With visualisation, the support was primarily verbal as the visualisation technique required description. With the massage subjects, the only conversation started by me focused on a discussion of what part of their body they wanted massaging and what oils to use. That is, the patient initiated all other verbal communication and even then only responses were given, I did not build upon the conversation. However, there were 5 of the patients who felt the need to talk through a large part of the massage session and who also mentioned me specifically during their interview; two of those offered general comments about liking me - these were both patients who had talked of very emotive things during the massage, the other three commented on very specific things. The first two commented on my making them feel comfortable, one in a very general way the other in relation to my perceived sensitivity to her discomfort about getting undressed. This must be a very important issue for people who have already given away much of their dignity and control to others - although it ought also to be part of basic massage training for all

therapists, perhaps something to be reinforced in this setting but not something which is unique to me. Equally, the final comment whilst gratefully received and very reassuring; 'Gentle hands – the most gentle hands you've ever felt really' (Brian) and an issue that came up many times in the comments listed under 'positive emotions,' is more a reflection of technique then of me as a person and something which can to a great extent be taught to others. What was pleasing to see was that there were not masses of comments reflecting on what a good listener I was, how it was great to talk to someone who was not looking after them medically (though one patient did say something similar; Mike) or how I understood all their problems, as this would have put a question mark over what was the primary reason for the benefits described here; the massage or me as the therapist. In fact there were only two comments, which I felt I could own; one reflected on my commitment and ability to massage generally, the other described me as a person: 'Jacqui has a nice, calming, soothing influence on people. She has got an aura about her' (Noel). This description is accepted with humility; if this is how people see me then it will help to reduce their stress levels. However, I am honoured patients see me this way and would not want to change it. Equally, I am sure most therapists have similar gifts they bring to a session.

Comments About the Oils: As well as wanting to find out what influence if any I had on the therapeutic effect, it was also important to look for any additional psychological benefits brought to the process by the essential oils. If there was shown to be no advantage to using the oils – either physical or psychological then the consideration would have to be whether to stop using them during the regular service as they require metabolism through the liver and could be seen as just a burden to the body. Because of the large quantities of drugs these patients have to metabolise, only low concentrations of essential oils are ever used (equivalent to treating a baby), thus reducing the potency of their smell. It was therefore understandable that of the seven comments specifically relating to the oils two reflected the fact that the patients in question found it hard to smell the oils as much as they would have liked. However, the other five observations reflected on how; 'beautiful', 'pleasant' or 'de-stressing' the oils were. It maybe therefore, in light of the fact that chemotherapy can alter both taste and smell, that the patients who had trouble smelling the oils had a generalised reduced sensitivity to smell. Obviously, whatever the reason, these

reductions in sensation may still have an impact on the patient's whole experience and need to be noted.

Prior Concerns: The unanimous affirmation by patients receiving massage that they enjoyed it was reassuring – especially in light of the fact that several of them had entered the trial with reservations about some aspect of massage therapy; two patients for example confessed that they had agreed to go into the study despite the fact that up to that point they did not really like being touched, one of these same two people was also anxious about getting undressed (Nancy). My normal way of dealing with this situation would be to initially offer massage to peripheral parts of the body such as the feet when undressing is not necessary. However, in this case, the patient wanted a back massage. It was gratifying to see that both these ladies were able to overcome their concerns about touch sufficiently to benefit from the massage. Even if full relaxation was not achieved, the positive feedback they both gave about the session and the fact that they wanted to make use of the service again, adds validity to the idea that even with patients who hold fundamental concerns, appropriate touch can be a powerful therapeutic tool.

Future Sessions: 100% of patients in both massage arms answered during the SSI that they wanted to receive further massage. It is possible that even though it wasn't me conducting the interview, some patients answered this way for reasons of social acceptability. However, the results would suggest that that was not the case as the majority of subjects rather than just answering with a simple 'yes', went on to emphasize the point with words such as 'definitely' or 'any time.' It was interesting that 3 of the 5 patients who had made use of the visualisation technique also wanted to repeat the experience. If this proves to also reduce cortisol levels then it may be that offering such a service can be piloted on a regular basis, as it would be something that patients could then make use of when ever they wished.

Conversation: It has been intimated that distraction may be an important part of the therapeutic effect of massage in this environment. Obviously, as well as the diversion of the actual massage, interaction with a therapist may have been an important mode of distraction. Equally, conversation could have benefited patients in other ways such as allowing them to off load some of their concerns. It was

therefore important to reflect on the implication of emotive conversation during a massage session. In order to understand what impact this type of discussion may have had on a person's stress levels, the issue will be revisited in relation to individual changes in hormone levels shown at the end of this chapter in the case studies. It is suggested however, that one of two things may happen: either the patient will become more relaxed having been able to talk about concerns in a safe environment whilst being physically nurtured; or the conversation will prevent them from relaxing as they remain hooked into their problems. My own thoughts are that each patient will show a different physiological response and that this response will be intimately tied up with his or her own inherent coping mechanisms.

General Comments: Sometimes during the SSI, patients would make comments that didn't seem to fit into any particular theme; they seemed to be general comments about some aspect of either the standard service or the study process. Two rather large sections of text have been included here because they showed the importance some patients attached to complementary therapies. For me they are confirmation that we owe it to all patients to recognise their needs and make sure they are addressed within a safe service; they are a very powerful reminder to me of my motivation, and reassure me that relevant aims underpin this work. The first is a statement of how gratefully such input is received:

> 'I just think it should be a regular thing for anybody that wants it. It can only be beneficial can't it if you are relaxed and accepting a nice, calm atmosphere. Yes, I think it's brilliant. I think it is a very necessary service really, I think it's time people saw that side of medicine as being important, you know, holistic or whatever approach.' **(Ann)**

The second goes further and shows that whilst patients see such therapies as beneficial it is reassuring to them to know they are being studied using scientifically rigorous methods:

'I do think it's a good thing that they are doing clinical trials of these things because I'm a big believer in the whole body thing. You do get all the medical treatment there's no doubt about that, when it comes to the emotional you don't find anybody with time enough to deal with that and I think something like this does allow you to unload your feelings if you like, unwind yourself and if it's done in a proper clinical trial, if it's part of the whole treatment then I think it's a good thing for you, it's working along with the orthodox stuff, I can't see that it couldn't benefit somebody, if they're able to relax enough to allow it to do it. Because you get so much stuff going inside you that makes you feel rotten that you just want someone to make you feel better.' **(Beryl)**

4.6.3 Summary of Qualitative Results

To summarise, the aim within this section has been to present a comprehensive description of the qualitative results of the study by reflecting on the main themes addressed by the patients and tying those into my own interpretations. The data presented above is not exhaustive with the main focus being on the information, which was seen as having potential impact on stress levels. However, in order that any interested reader may review the results independently, the raw thematic data is presented in appendix XIII (page, 303).

As has been highlighted (section 3.10.3), integration of physiological and psychological data from individual patients was a central objective in this work to facilitate understanding of the way in which massage can enhance the wellbeing of isolated patients. Consequently section 4.7 comprises of three case studies chosen to illustrate the relationship between physiological and psychological responses to therapy.

4.7 Case Studies

4.7.1 Introduction

Because of the mixed methods design of this work the separate facets of the results have been presented in different sections of the results chapter, to help give the reader a clear picture of each segment. However, rather like the facets of a diamond, their true beauty is seen most clearly when they are viewed in their entirety as they are when combined in the presentation of a case study. Although each subject had a file compiled containing all the aspects of their results, it was not feasible to submit each subject as a separate case study. However, neither would the thesis be complete if a small sample of results were not described in detail, as it is in this way one can truly understand how massage and the use of essential oils can be of benefit to isolated patients, particularly when used as an integral part of their package of care.

A case study has been presented from each arm of the study. They have included descriptions of how, for example, the patients coped with interruptions to the session and whether such disturbances impacted on their ability to relax:

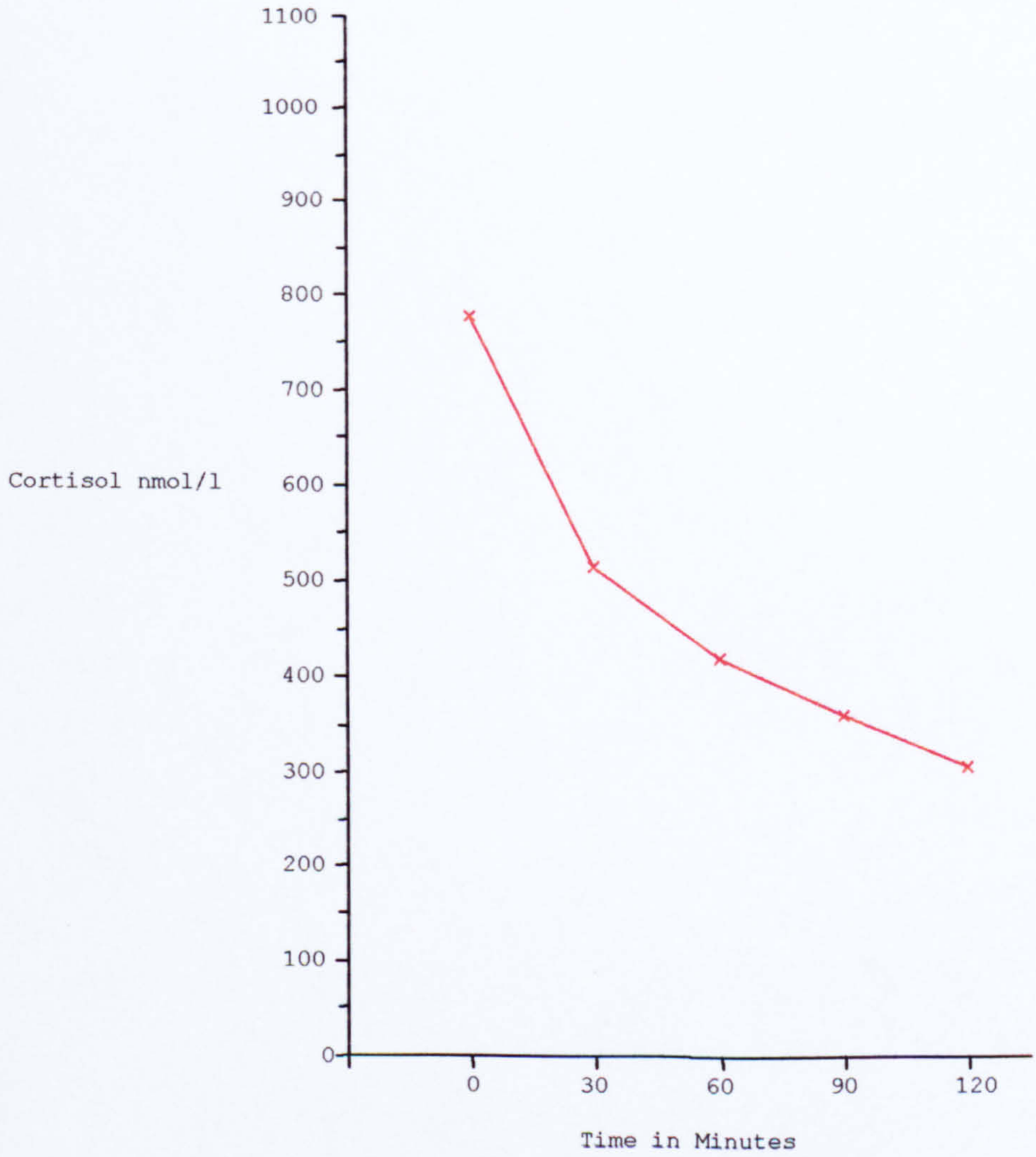
4.7.2 Case Study (Mike) – Aromatherapy Massage.

This gentleman identified several problems whilst I was collecting baseline quality of life data; he complained of big problems sleeping and it was noticed that he acknowledged lots of concerns usually associated with stress, such as feeling tense, lack of memory, poor concentration and inadequate sleep. He also observed that he was still (post chemotherapy) having problems with nausea and vomiting. During the post-massage blood sampling sessions he started talking about the lack of control he currently had over his life and gave examples such as not being able to go and make a cup of tea; not having a choice regarding when his blood pressure was taken or drugs brought into his room – he said it made him feel 'niggly.' Mike had never experienced a massage before and confessed to feeling very pessimistic about the benefits.

The patient had an old football injury to his left knee, that plus the fact that I did not want to go too near his face with new smells due to his nausea, indicated that his feet and calves / knees would be the most appropriate areas of the body to massage.

Equally, in order to address Mike's nausea the essential oils of lemon (2 drops) and peppermint (1 drop) were chosen for his blend, he found the aroma very pleasant. During the semi-structured interview at the end of the two hours Mike described himself as feeling 'very relaxed, it relaxed my mind'. He also said; 'it took my mind off my nausea; the sickness disappeared for a while'. At the end of the session the patient was awake but very relaxed and summarised the session by saying 'it was hypnotic, I went into my own world'. Graph 4.4 showing his drop in cortisol levels can be seen below:

Graph Showing Raw Cortisol Levels for Case Study 1(Mike)



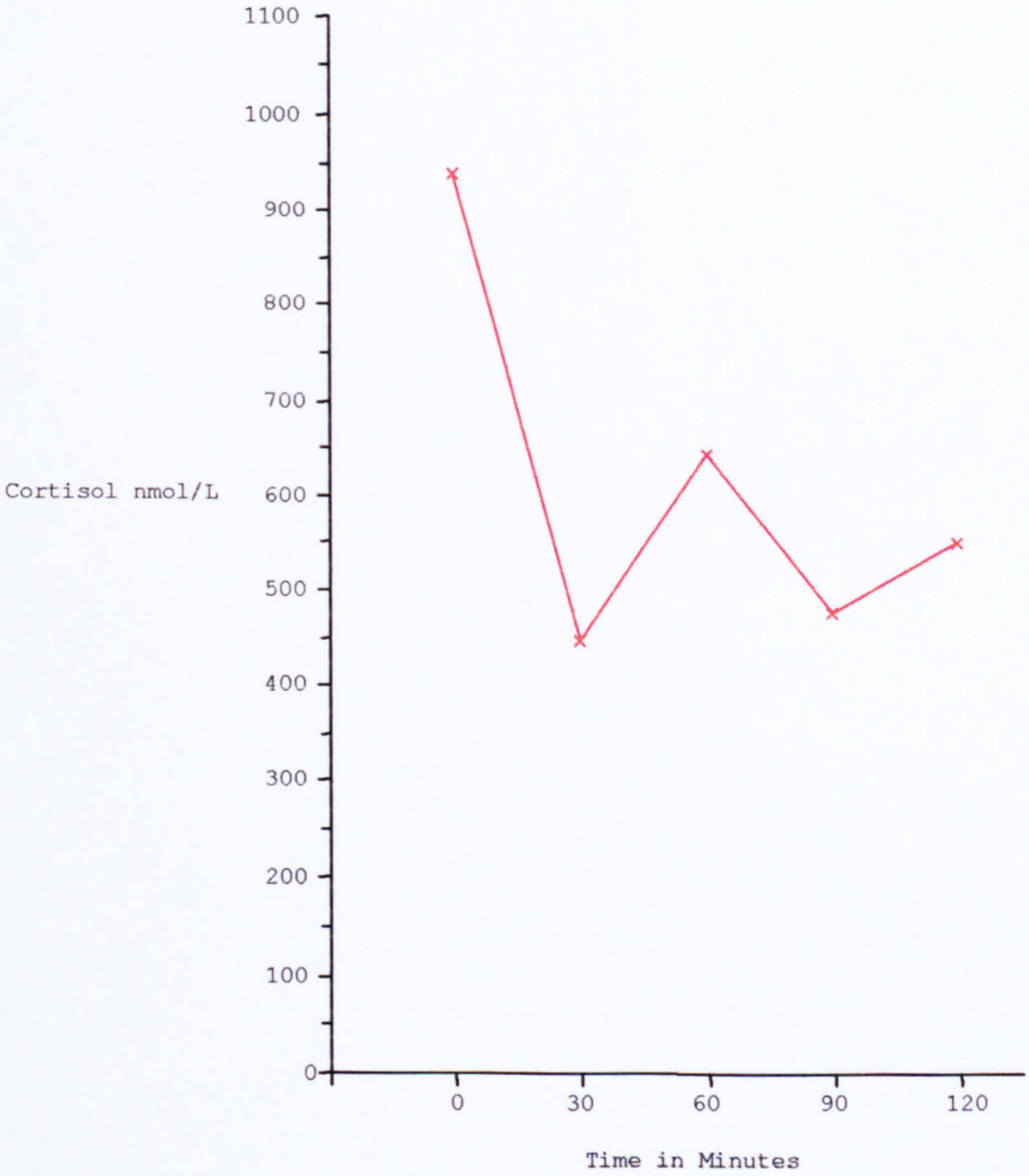
Graph 4.4

This particular patient was a good example of how, despite being slightly apprehensive about the idea of massage and bringing up emotive subjects (his lack of control) during the session, massage therapy still had the power to reduce his cortisol levels, improve his physical wellbeing (eradicating his nausea), and give him a sense of peace.

4.7.3 Case Study (Molly) – Base Oil Massage.

This lady listed several problems during her baseline assessment, both physiological and psychological; she complained of nausea, pain - especially through her back and the tops of her arms (identified as being due to injections of GCSF), the soles of her feet felt chronically tender with tightness running through her big toe. She also acknowledged that she was naturally a 'stiff' person with 'jumpy' legs who finds it difficult to relax. In this case the patient had no preconceptions about possible benefits of massage although she had not experienced such therapy before. Because of her nausea, physiological symptoms and lack of prior experience with massage, I decided with the patient that the best and least threatening site for her first massage would be her feet. By the end of the session the patient was asleep. During feedback within the SSI the subject described herself as feeling much less jumpy and very relaxed (which she commented was unusual), her feet were no longer tender and the tension in her big toe had eased. Unfortunately (as can be seen from the graph below) the patient's husband turned up approximately 20 minutes after the massage had ended and appeared quite irritated by her being asleep so kept trying to talk to her. Despite this hiccup and corresponding rise in her cortisol level, she managed to regain her level of relaxation as can be seen in graph 4.5:

Graph Showing Raw Cortisol Levels for Case Study 2 (Molly)



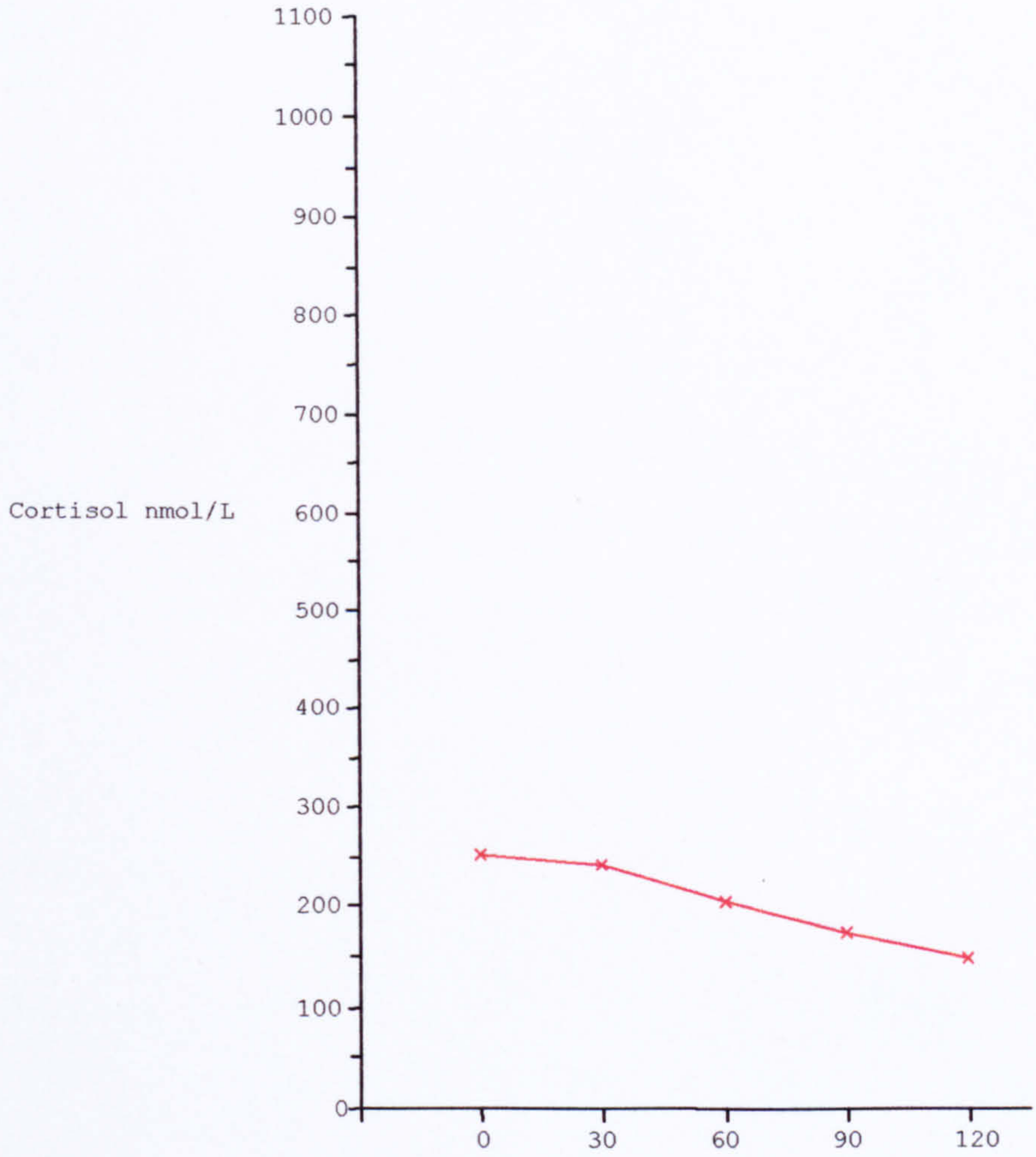
Graph 4.5

This lady was of a generally anxious disposition and asked many questions both of a nurse who came in and took one of the blood samples and myself. Her concerns included queries regarding how long it would take to regenerate the blood we were taking. In spite of this she relaxed sufficiently during the massage to go to sleep and kept drifting back off to sleep between blood samples being taken.

4.7.4 Case Study (Emma) – Rest (Visualisation).

Patients in the control arm were randomised to undisturbed bed rest. However, some of this group (5/13) requested something extra. I decided, as the researcher, to concede to this request as any effect would reduce the magnitude of the massage effect rather than enhance it. Consequently these patients were taught a simple visualisation technique in which they saw their chemotherapy as a gardener helping to clear their 'garden' (bone marrow) of weeds (leukaemic cells). If they were due for a transplant they were encouraged to visualise the new cells as seeds in their fresh, clean soil, which they saw growing into strong plants (for example, a field of corn). It was reinforced to all five patients that whilst this was a tool for them to use if they felt comfortable doing so, it did not make them responsible for curing their own leukaemia. This lady was part of the visualisation sub-group. Although she verbalised not feeling directly stressed about her illness and felt she was dealing with it head on, she was troubled by the fact that both her son and husband were struggling to cope. As this patient was due for her transplant she had the whole visualisation described to her, then she was left to work with it for the duration of the twenty-minute study session. During the SSI she confirmed that she had enjoyed the experience, seeing it as something to focus on and relate to. The exercise tapped into her hobby – gardening, and she saw herself as clearing a particularly large, prickly weed in her own garden. She had two telephone calls during the session but worked them into the visualisation process by describing to the caller what she was doing. It can be seen from graph 4.6 below that despite her cortisol level being low at baseline, it still reduced by half over the course of the two hours:

Raw Cortisol Levels for Case Study 3 (Emma)



Graph 4.6

This lady responded to the visualisation with enthusiasm and adaptability in that she was able to incorporate the telephone calls into the process. Although she described herself as being 'calm' and 'laid back' both before and after the session, she still recognised the benefits of the visualisation technique and was keen to repeat the session.

4.7.5 Summary

The case studies presented above give only a brief view of the impact massage with or without essential oils can have on both the physiological and psychological well being of the isolated patient. They also show that teaching patients tools such as visualisation can be of benefit.

Although only three out of thirty nine patients have been represented here they are in many ways generalisable to the rest of the subjects. For example, five patients had prior concerns about massage (as did the gentleman in the first case study), yet all of them showed evidence of psychological benefit. All but one of the five commented specifically on physiological improvement and in four cases, cortisol levels were seen to drop – in the fifth case the blood samples were unfortunately missing. A number of patients expressed anxieties and frustrations about their own condition or concerns about loved ones, during the study period - as again was the situation in the first case study described here. One may expect such conversations to prevent full relaxation, yet it can be seen here not always to be so. Equally, many patients had to contend with interruptions of various kinds, as demonstrated in the second and third case studies. Some patients were able to override the disturbances, as was the situation here for both patients. Unfortunately for some patients the disruptions did limit the length of time for which they felt the benefits of the intervention. The third case study, Emma, not only illustrated a subject adapting to disturbance, she also incorporated those disturbances into her visualisation. Emma also expressed feelings described by others in the same sub-group that the visualisation technique helped by giving them something to focus on. Interestingly, although patients in this sub-group confirmed psychological benefits from the visualisation, none of them mentioned physiological benefits and the drop in cortisol levels was not as great as in the massage arms.

4.8 Essential Oil Work

It was one of the aims of this work to look at whether the use of essential oils in massage was appropriate for this population of patients. Properties of oils, which may lead to psychological benefits (such as pleasant aromas), could be adequately assessed within the remit of the clinical study. However it was recognised that oils may impact on the massage process in other ways, for example by enhancing the patients' protection against pathogens. Unfortunately, whether any oils provided such superior resistance could not be easily assessed clinically. For this reason independent laboratory studies had been commissioned to enhance the findings of the clinical work. These in-vitro studies were carried out in parallel with the main clinical trial and were set up to look at anti-microbial properties of the oils used for the study. This work provided some interesting results. Several of the oils commonly used on the unit such as geranium were shown to kill organisms of high clinical importance such as: Methicillin resistant *Staphylococcus aureus* (MRSA), vancomycin resistant *enterococcus* (VRE), *Candida albicans, Aspergillus fumigatus,* and *Pseudomonous aeruginosa,* when used in very low concentrations – levels much lower than would be used in the clinical setting.

Because I didn't carry out the in-vitro work myself but rather commissioned a collaborator to perform the studies, it was inappropriate to include the results in full within the main body of the text. However, a peer review paper was written describing the work and results in full – including tables of anti-microbial activity for all the relevant oils; this has been included in its entirety in appendix XV (page, 326). It was necessary to include acknowledgement of this work within the thesis as it has major implications for using essential oils in clinical practice.

4.9 Summary

The results chapter has been used to present all the findings of this work from both a physiological and psychological perspective. The primary outcome measures (drop in cortisol and prolactin levels) showed a significantly greater initial fall in hormone levels for patients randomised to the experimental arms as opposed to the control arm ($p < 0.05$). Possibly because of the small number of patients recruited on to the study, these were the only statistically significant physiological changes documented. Psychological response to massage showed universal feelings of relaxation following the therapy session as well as other indicators of enhanced wellbeing. Interestingly the majority of the patients in the visualisation sub-group of the control arm also appeared to benefit from the intervention.

In order to collate and consolidate the various facets of the results chapter three case studies (one from each arm of the study) were presented illustrating the different dimensions of the benefit seen from such interventions. Issues such as the impact of disturbances on the physiological response will be further reviewed in the discussion chapter.

Finally, a brief overview of the results from the parallel laboratory work carried out looking at the anti-microbial effects of the essential oils was presented. These results indicated some potentially clinically relevant findings suggesting oils could be used in a therapeutic setting for reasons other than that they smell beautiful.

Chapter 5:

Discussion

5.1 Introduction

The principal aim of this study was to identify whether physiological and psychological benefits of massage could be achieved safely, with and without the use of essential oils, in patients receiving treatment for haematological malignancies on a high dose therapy isolation unit. Benefit was measured primarily through the reduction of the stress hormones cortisol and prolactin. This involved an appraisal of whether massage with essential oils was more effective than massage with base oil or time for peace and calm at reducing physiological and psychological symptoms of stress. A secondary aim was to confirm that single sessions of massage either with or without the additional use of essential oils could induce a clinically relevant change in cortisol and prolactin levels in this patient group. It was felt that the most appropriate way of assessing the potential benefits of massage in this cohort of patients was by using a mixed methods design of study in order that the quantitative and qualitative elements of the data could be awarded equal value.

The patients on the adult leukaemia unit were chosen as subjects for this project because until the commencement of the massage service, patients undergoing high-dose chemotherapy whilst being nursed in isolation had no access to complementary therapies. It has been suggested that socially isolated patients with cancer are at higher risk of relapse from their disease and that social support can buffer the stress of isolation. Spiegel et al (1998) reviewed studies looking at the potentially protective influence of social support in preventing cancer progression, with stress and its effect on immune function as the mediator. They concluded that whilst psychosocial interventions have the facility to help in adjustment to a diagnosis of cancer, and there is evidence to suggest an influence on cancer survival, more work is required. The implication of such evidence for patients undergoing high dose chemotherapy is profound; in order to treat such patients safely, current medical knowledge would suggest that they have to be nursed in isolation, yet research suggests this is an emotionally high-risk environment, which leads to immunosuppression through the mediation of stress. A related concern for patients under a chronically high level of psychological stress is that there is a growing body of evidence suggesting that such stress affects the immune defences in a way which leaves the cancer patient more vulnerable to infectious diseases – potentially fatal in

haematology patients. Bovbjerg and Valdimarsdottir (1998) looked at the evidence suggesting ways psychosocial factors can have an impact on patients with cancer and highlight the fact that psychological stress alters both susceptibility to infectious diseases as well as severity and duration of the illness. There has been a possible model proposed offering a link between stress & some haematological malignancies (Keicolt-Glaser et al, 2002). Chronic suppression of immune defences through emotional distress is suggested by Keicolt-Glaser and colleagues (2002), to lead to recurring infections. Such infections are accompanied by persistent inflammatory changes, which in turn have been linked to the development or progression of certain conditions including some haematological malignancies. To find ways of reducing stress levels therefore in such a highly stressful environment might possibly be a way of breaking the cycle. The results from this study suggest that for some patients massage may be a way of reducing psychological stress through the therapeutic effects of touch and because the therapists themselves form a buffer against the stressful effects of social isolation (Heinrichs et al, 2003). There is also work suggesting that the presence of a caring practitioner improves mood (Post-White et al, 2003).

Because of the mixed methods design of the trial a large quantity of data was created. Consequently there were numerous avenues for exploration and many have been encompassed within the remit of this thesis. Some examples of issues raised by the work have been listed below although the list is by no means exclusive:

- The influence of psychoneuroimmunology (PNI) on health and well being of patients on an isolation unit.
- The influence of stress specifically (linked to PNI) on health and well being of patients on an isolation unit.
- Implications of the altered sleep patterns and fasting common for patients on an isolation unit, on physiological indicators of stress.
- Relaxation and its physical and psychological effects (linked to PNI)
- Issues relating to the isolation of patients and the impact of reduced social support.
- How generalisable are these results due to the influence of isolation and the high dose drugs?

- The problems (and theory) around the dual / triple role of a research / health care practitioner.
- The challenges of performing research within the field of complementary therapies.
- Ethical issues around withholding supportive care from needy patients.
- The potential role of massage and essential oils in the integral care of the immunosuppressed patient.
- The use of visualisation by patients to regain a level of control.

Some of the factors in the list above form an integral part of the work such as the influence of PNI and have been addressed in great detail throughout the thesis. However other issues, whilst they are equally important, such as the problems arising around a researcher having to perform multiple roles, are too big a subject to do justice to here and it is beyond the remit of this work to address them all in detail, although all matters have been reflected upon to a varying degree.

This discussion chapter continues with an appraisal of the results in light of the original aims and of issues relevant to the results. Also factors of consequence to the clinical trial and my contemplations relating to a number of issues, which have arisen during the study and have implications for this and future work will be considered. Then there is an important section reviewing the potential consequences of some of the study findings on the clinical practice of the nurse, therapist and researcher. Problems relating to the trial are discussed and future work proposed. Finally, a summary of the discussion chapter will be given.

5.2 Discussion of Results

The results of this study have verified the first experimental hypothesis. They have shown that massage, both with and without the additional use of essential oils, can safely enhance the physiological and psychological wellbeing of patients with haematological malignancies, being nursed on a high dose therapy isolation unit, after only a single session of massage. The second hypothesis, that the effectiveness of both interventions would be relatively short lived also proved to be true. However, the third hypothesis that aromatherapy massage would be more effective than massage using purely base oils at reducing signs and symptoms of stress could not be accepted on the basis of the results of this study.

5.2.1 Safety issues

Whilst there is now a small quantity of recent data coming through the literature relating to the use of massage in patients with haematological malignancies (Field et al, 2001), none of the work identified addressed issues of safety. Because of the vulnerabilities of this subject group it is imperative that any evaluation or exploration of the use of massage and essential oils also incorporates a measure of safety. In this study I included a question in the SSI, which encouraged patients to reflect on any negative aspects of their session, they were also prompted to tell the research assistant how they were feeling currently (two hours after the massage). It was anticipated that these questions would be a platform for patients to express any physiological concerns such as their skin feeling sore and/or itchy, or their muscles feeling tender. Equally it was hoped that psychological worries, for example if they had felt more rather than less anxious after the massage, would also be raised. Patients in the experimental arms of the study highlighted no such concerns. Although these results are not sufficient on their own to guarantee the safety of massage they have given encouraging preliminary data. It has to be recognised of course, that patients may have responded to the SSI by giving socially acceptable responses, however there were no signs of skin irritation after any of the massages and nurses on the unit would often relay to me, comments made to them by the patients – these only ever reflected how calm or relaxed they felt following their session.

5.2.2 Physiological Results

The results from the inferential statistics showed that patients in the two experimental arms demonstrated a significantly greater fall in the primary outcome measures of serum cortisol and prolactin levels at the 30-minute assessment point compared with those in the control arm. A continuation or enhancement in this drop was observed throughout the two-hour assessment period for a larger number of patients in both experimental arms (14/26 or 54%) than in the control arm (5/13 or 38%) (See appendix XIV, page 324, for graphs showing individual results). However the difference in change between groups across the two-hour period was not statistically significant. This apparently rapid decline in the initially significant change in response to the massage was anticipated (see section 3.4.1), and the finding that a statistically significant drop in cortisol and prolactin levels can be induced through massage is none the less an important finding and a powerful motivator for future research (see section 5.5.3).

Several reasons can be suggested for why the physiological response seen in this cohort of patients was short-lived including the number of interruptions the patients endured. Cassileth and Vickers (2004) assessed over 1,000 cancer patients for reduction in symptoms including fatigue and anxiety following massage over a three-year period. They observed 'major, clinically relevant and immediate improvements in symptom scores.' However, they also documented that the effects were smaller and less persistent for in-patients than outpatients. The first reason Cassileth and Vickers (2004) posed for the variation, was that in-patients are subject to more 'intervening events' such as undergoing procedures or changes of medication. For the patients used in this study, such intervening events may also include: general noise on the unit, telephone calls, staff putting up IV drugs / dealing with monitoring equipment, and visitors. I was aware of all these potential problems when setting up the study but it was felt that because this was the reality of working on the unit, it was important to identify whether massage could still influence stress levels in spite of such problems rather than when the patient was protected from them. Interestingly the patients in the aromatherapy arm of the study had to cope with over three times as many disturbances as those in the base oil massage arm (24:7) and twice as many disturbances as the patients in the rest arm (24:12). That the reduction in cortisol levels observed in patients from the aromatherapy arm was statistically

equivalent to those of patients in the base oil arm – it was in some of the patients randomised to the aromatherapy arm that some of the most powerful responses were seen, suggests that without the interruptions or with an equivalent number of interruptions aromatherapy massage would be the more effective of the two therapies.

Another issue related to level of response, concerned the fact that more patients in the experimental arms had been admitted for transplants as opposed to chemotherapy. In total, 4 patients in the rest arm; 8 in the base oil arm and 6 in the aromatherapy arm had been admitted for transplants. The chemotherapy and support drugs (such as cyclosporine and campath) required by a patient during the transplantation process are much more intensive then those used during the induction phase of chemotherapy. Therefore massage may have appeared less effective then it actually was due to the influence of the drugs on hormone levels. Certain drugs are recognised as altering hormone levels and patients known to be on 'problem' drugs such as metaclopramide and high-dose steroids (Parfitt, 1999) were excluded from the study. However, it came to light through discussion with drug companies that drugs less well recognised for their influence might also have a considerable impact on prolactin levels (for example, cyclosporine). A concern here was the validity of the prolactin results seen in the trial. The initial results from the pilot study (see section: 3.13.4) indicated that there might be a problem, however at that time the numbers were too small to come to a decision to stop monitoring prolactin levels. Unfortunately these early indicators for concern appear to have been legitimate as there was no consistency in the prolactin results after the initial response. An alternative suggestion relating to the lack of consistency in prolactin changes may be that although prolactin and cortisol are both indicators of stress levels, they may react differentially depending on which emotion is elicited by a situation. Recent work suggests that cortisol 'responds consistently and intensely to shock and intimidation' as would be seen in the environment of the unit, whereas prolactin surges are associated with feelings of rage which may not be as common in this situation (Sobrinho et al, 2003). Because of these issues it was felt more appropriate to focus primarily on results relating to cortisol levels when reflection on change in hormone levels was required.

Possibly the most compelling reason offered for why the response to therapy in some patients was so short-term relates to the repeated blood sampling. Whilst felt to be the best way of documenting changing hormone levels (see methodology chapter) repeated blood sampling is suspected to have impacted in a major way on the patients' length of response both through the act of taking the blood and because of the smell of the alcohol wipes used to swab the line, which some patients found offensive. Kirschbaum and Hellhammer (1994), in their overview of salivary sampling of cortisol levels, confirm the taking of blood as potentially stressful. Unfortunately, for reasons discussed in the methodology chapter (chapter 3), it was inappropriate to use salivary sampling of cortisol for this study despite its obvious advantages and the fact that there appears to be high levels of correlation between serum and salivary cortisol Kirschbaum and Hellhammer (1994). However, in light of the number of negative comments relating to the blood-sampling element of the study protocol, it is almost certainly true to say that without that, the relaxation effect of the massage would have persisted for longer.

Regardless of the apparently temporary nature of change in hormone levels observed in this study, the clinical relevance of that initial reduction in cortisol levels cannot be over-stated. Sephton et al (2000), identified that in women with metastatic breast cancer (N = 104), a flattened or abnormal diurnal cortisol rhythm predicted shorter subsequent survival times (P = 0.0036). Sephton and colleagues (2000) explored the possibility and found tentative links to suggest that flattened cortisol rhythms may reflect chronic stress, such as that seen through the loss of marital support. This suggestion is validated to a degree by the work of Cacioppo et al (2000), who showed that chronic loneliness in a subject sample of approximately 130 students was characterised by elevated mean cortisol levels *across the day*, and that loneliness as a concept was open to manipulation. The data presented here offers preliminary results suggesting that massage therapy can enhance a patient's diurnal cortisol slope through the reduction of stress and as such may offer the potential for enhanced survival. By standardising the number and time of treatment sessions, ensuring all patients were nursed in isolation during the study period and providing both comparison experimental arms and a control arm, this study has gone some way in compensating for the weaknesses noted in previous research looking at the benefits of massage for patients with either haematological malignancies or potentially life-

threatening conditions (Field et al, 2001; Smith et al 2003; Kite et al, 1998; Nixon et al, 1997).

That massage in this setting can influence cortisol levels is a good foundation for exploring whether the change is sufficient to have an effect on the patient's immune function. More precisely, whether such a modification can influence the rate of cell regeneration following chemotherapy. This idea is further explored and expanded in section 5.5.3 of this chapter, which looks at ideas for future work in the area.

In an attempt to identify a subgroup of patients who may have benefited to a relatively greater extent regression analyses were carried out (see section 4.4.2 of the results chapter). However, none of the three factors explored (age, sex and prior experience of complementary therapies) were useful in predicting patients who would respond to massage. Conversely it was interesting to note that in this study patients' coping strategies did seem to have a powerful influence over the outcome of their session as measured by reduction in cortisol levels. One patient for example, appeared to have a very optimistic attitude and evaluated the aromatherapy session to which he had been randomised in a very positive way. However, he kept up a stream of banter during the whole of the session; his feet (the site of the massage) remained rigid throughout and he insisted on his wife staying in the room. His cortisol levels went up despite his enthusiastic reflections on the session. It is suggested that the reason for these conflicting results was that he coped with his situation by: 'holding himself together,' not by relaxing. In terms of the stress literature (chapter 2), he was ready for fight or flight. One could anticipate that because of this, despite the patient in question having gained pleasure from the massage, it actually made his task more difficult. The qualitative section of the results (section 4.6) showed that massage helped patients to relax and forget everything for a while. For this gentleman such a response would make 'holding himself together' much more difficult and it would be reasonable to expect his stress levels to rise. However, it is worthy of note that this particular patient went on to have massage on a regular basis. It is suggested that if he experienced a rise in cortisol levels on each occasion then this would lead to physiological and psychological discomfort, one can only conclude therefore that he adapted his coping strategy to accept a degree of relaxation. The issue of pre-morbid coping as an important factor for how patients deal with their condition has been

recognised for a long time (Cooper and Watson, 1991). In 2003, Antoni considered potential avenues for exploration in relation to psychoneuroimmunology and cancer, he also highlighted coping as an important topic. Data from this study (such as the example presented here) has been able to endorse this notion by showing a relationship between the way a patient reacts to a situation and their physiological response.

When the trial was designed, four physiological indicators of stress were used (cortisol and prolactin levels, HR and MAP) in an attempt to corroborate any findings suggesting that massage reduced cortisol levels and therefore stress levels. A correlation between changes in the four measures had been anticipated as all four have been used in prior research as indicators of variance in levels of stress (Van der Pompe et al, 1997; Moyer et al, 2004). However, the results of the present study showed no consistent correlation between the different physiological measures. One reason put forward to account for these findings is the size of the study sample. Having a relatively small sample size meant only large treatment effects were identifiable. Interestingly the median change in HR over the two-hour assessment period for the patients in the aromatherapy arm showed a trend indicating a steady decrease in heart rate, which at the two-hour assessment correlated with change in prolactin levels. The idea that the study sample was too small to identify statistically significant changes does not however, account for the fact that some of the correlations seen, for example in the aromatherapy arm at the 60 minute assessment, resulted in small non-significant *negative* correlations between MAP and blood levels (cortisol, $P = 0.88$; prolactin, $P = 0.67$). There are several possible reasons for this, firstly the massage could be normalising an abnormally low blood pressure (low through the effects of for example, drugs or sepsis). Secondly the physiological measures chosen may not generally correlate well in this subject population. This suggestion is supported by the fact that there were very low levels of correlation observed in the majority of the comparisons made. However, there are potentially important issues, which could be addressed through the correlation of variables in light of current research. Waking times for example have recently been shown to influence cortisol levels (Bower et al, 2005; Williams, Magid & Steptoe, 2005; Hucklebridge et al, 2005), therefore an exercise correlating drop in cortisol levels

with time since wakening, blood pressure and pulse in this cohort of patients may throw up interesting pointers for future studies (see section 5.5.1).

5.2.3 Quality of Life

The EORTC QLQ C-30 was the quality of life questionnaire chosen for this study for a number of reasons (see section 3.9.2) including its validity in measuring subjectively relevant aspects of quality of life (Osoba et al, 1998) over which massage could potentially have an influence. One of the unexpected findings of the present investigation therefore was the general lack of improvement in quality of life as measured by the EORTC QLQ C-30. There were statistically significant baseline to post session changes noted between arms for three of the multi-item subscales (physical functioning, $P = 0.01$; role functioning, $P = 0.03$ and social functioning, $P = 0.04$). However, the changes were inconsistent. The alteration with the highest level of statistical significance; physical functioning, showed an enhanced level of functioning for both experimental arms compared to the control arm post session. This is one of the areas massage would be expected to have the highest level of impact on quality of life. However, it is important to recognise the limitations of the findings, as changes in the role functioning subscale would imply the control arm as having the greatest level of positive change post session and with the social functioning subscale, it was patients in the base oil arm who showed the most positive change. It may be that there were too few subjects in the study for the changes to show statistically significant and clinically relevant shifts. Equally, whilst I sought and was granted permission to use the QLQ C-30 to monitor change in quality of life overnight rather than over a week (see appendix X, page 297), the questionnaire may not have been sufficiently sensitive to monitor change effectively over such a short period of time.

It must be considered that the questionnaire was not created for patients in isolation and is aimed at patients who have ongoing physical problems. Many of the patients in this trial were admitted onto the unit in good physical health as was shown by the generally high KPS scores. What was more of an issue for this cohort of patients was their presence or absence of clinical symptoms, for a patient suffering from acute leukaemia this can change dramatically in the space of 24 hours. Consequently the relief of feeling a lot better, or the anxiety of feeling a lot worse may cause a patient

to over exaggerate the situation when grading a general health scale. This point needs to be recognised particularly because when these patients were grading their quality of life, they were doing so with nothing else to think about, therefore any health related issue would feel 'larger than life,' (see results of pre-pilot study in methodology chapter). To take this a step further some researchers have suggested the experience of cancer is equivalent to an emotionally traumatic event as defined by the DSM-IV, which results in 'extreme fear, helplessness, and horror' (Yehuda, 2003). In such a situation it is hardly surprising that for some patients at least, a rapid change of clinical condition, may lead to emotional exaggeration of the condition. Interestingly, when answering the sub-scale of emotional functioning, which required the patient to grade emotions usually associated with stress, for example whether they felt tense and depressed, 59.4% of all responses indicated such emotions were not something that bothered them. The same level of unconcern was seen in the cognitive functioning sub-scale with 63.6% of patients indicating they had no problem with concentration or memory, again symptoms often associated with stress. This finding is remarkable yet is equally, understandable. If it is accepted that patients have trouble accepting their condition as is often the case with extreme trauma – especially with a diagnosis of leukaemia when there is nothing for them to look at and identify as the focus of their condition, then denial is an appropriate coping strategy and such responses may well be an integral part of such denial. Equally they might have lacked insight into the degree factors such as their mood had changed, possibly if their main carer had answered the questions, the responses would have been different. Similar results were found for the role and social functioning sub-scales. However, slightly more patients acknowledged a level of impediment, which is understandable as isolation obviously inhibits social functioning and prevents all but basic role functions. Conversely, the results of the social functioning scale are ambiguous as they could show the impact of isolation or they could be confounded by it.

As previously discussed, a large number of subjects in each arm scored themselves in a very positive manner at baseline for many of the subscales, suggesting either that their condition had a minor impact on their quality of life, that the impact it did have was not measured effectively using this scale or that they were in denial. These results corroborate findings by Wettergren et al (1997). Wettergren and colleagues,

(1997) examined the quality of life of 20 patients with haematological malignancies using questionnaires, which included the QLQ C-30, prior to transplantation, and again following discharge. They observed that patients scored highly on the functioning scales and low on presence of symptoms at baseline and that this did not change over time. The way the subjects scored the QLQ C-30 in this study meant that it would be hard for the intervention to enhance the measures of quality of life to any substantial degree. It was therefore not surprising that the patients' responses for most of the questions did not alter from pre- to post session. There were only two individual variables, which changed post-session with a statistically significant level of difference between the arms. The first measured the patient's need for rest and indicated that subjects in the experimental arms had fewer requirements for rest than those in the control arm 24 hours after the study session. One reason suggested for this was that following the massage patients had better nights sleep and so felt more rested and alert the next day. This proposal is in part corroborated by the fact that five patients in the aromatherapy arm of the study documented enhancement in their quality of sleep; three graded their sleep as having improved by *three* points; one by two points and another one by one point. This compares with two patients in each of the other two arms grading their sleep as having improved by one point each. Reduction in level of fatigue is perhaps one very powerful way in which massage can influence the quality of life of these patients. A descriptive study carried out by Molassiotis and Morris (1999) which identified long-term quality of life issues encountered by 28 patients following unrelated bone marrow transplantation, identified that fatigue was the symptom interfering with the daily life of most patients (78.6%). Consequently to discover an intervention capable of alleviating such a troublesome symptom would be to potentially enhance the quality of life of patients on a long-term basis.

The second question showing statistically significant differences in response between arms looked at limitations on activities of daily living. It indicated that patients in the experimental arms perceived themselves as having greater difficulties in performing activities of daily living then those in the control arm. This result appears ambiguous in light of the proposed reduction in fatigue highlighted previously; one would expect a person who felt rested to have more energy for performing activities of daily living. A suggestion to account for the conflict would be if relatively more of the

patients in the experimental arms had started treatment overnight, which required them to be confined to bed, or attached to an intravenous drip. Another suggestion could be that the patients were not consistent in answering questions or that their responses reflect their mood combined with the high level of intervening factors including change in clinical status. This is a proposal which is validated by the view that 'quality of life is dependent on the client's perception' (Eilers and King, 2003), and is confirmed to a certain extent in that five patients from this study altered their answers to a question enquiring about financial difficulties imposed by their condition, yet it would be anticipated that their response to such a query would remain the same overnight.

5.2.4 Pain

Interestingly, although results from the pre-pilot audit (see appendix I, page 285) suggested that pain was an issue for this group of people, the results from this study suggest this not to be the case. One of the initial questions on the questionnaire allowed the patients to identify whether they had any pain. Those who graded themselves as not having pain were not obliged to fill in any more of the questionnaire. Because of the small number of patients who did fill in all of both pre and post-session questionnaires it was felt inappropriate to statistically analyse the data.

5.2.5 Qualitative Results

One set of results, which did show universal association were the results of the semi-structured interviews in relation to the effects of the massage. Each interview included comments relating to feelings of relaxation and/or easing of tension. Such comments echo findings by other researchers in the related area of palliative care (Cassileth and Vickers, 2004; Dunwoody et al, 2002; De-Valois and Clarke, 2001). The fact that the massage was a powerful enough tool to induce effects such as patients forgetting about their current situation, suggests that perhaps the most important factors leading to the apparently short-lived physiological response was the small sample size and the series of blood samples required.

Two important issues, which are relevant to and may help one to understand the psychological impact of massage, are firstly coping and conditioning, and secondly

body image. These topics will now be discussed and reflected upon in light of the relevant literature and the findings of this study:

5.2.5.a Coping and Conditioning

Control: One aspect of coping, which is recognised as having an effect on a patient's ability to deal with their situation, is their locus of control (Watson and Ramirez, 1991). It is suggested that a person with an internal locus of control (active in dealing with their situation), is more likely to cope effectively then someone who has (either by choice or circumstance) an external locus of control (the person passes control over what is happening to them to someone else) and has developed passive coping strategies (Watson and Ramirez, 1991). Campos de Carvalho and colleagues (2000) highlighted that of 19 patients interviewed whilst undergoing bone marrow transplantation, 55.6% felt their need for control over what was happening to them was not satisfied. Patients in the current study also identified lack of control as an issue of concern. This was sometimes expressed in implicit statements such as '...Apart from the bloods, but that sort of thing is being done to me all the time, its nothing new' (Colin). Whilst other patients were very explicit in their frustrations at having to pass control of their lives over to others 'The worst thing about being in these rooms is actually the fact that you have got so little control' (Cyril). By offering massage to patients, not only do they have choice over whether they accept thus enhancing their feeling of control, but also when to have the massage and what part of their body they want massaging. Olga highlighted this when reflecting on her choice to take up the offer of a massage, 'If you've got stuff on that day and you can't do it you're going to miss out, be nice to be able to say I'll have one tomorrow instead.'

Distraction: A large part of the misery people suffer on a high dose chemotherapy unit such as this one comes from the constant barrage of side effects inflicted upon them by the chemotherapy. Nausea for example is often intractable – despite the powerful drugs available. Perhaps in some situations, what is required is that the cycle of thought be broken, that the focus of thought be changed. Think for a minute of the saying 'Chinese torture.' Chinese torture was a method of torture whereby something relatively inconsequential – like water dripping on the forehead, continued for hours, relentlessly grinding the prisoners will down as it overwhelmed

all other sensory input and became the one single focus of their mind. Such a method of torture would not have been nearly as effective if the prisoner had a way distracting him or herself from the relatively minor physical discomfort. It is proposed that in the situation these patients find themselves, they are undergoing a very similar process. They are isolated, unable to escape and they have to suffer a relentless procession of drugs, which cause constant side effects such as nausea. If ways can be found in which patients can change the focus of their thoughts away from the side effects then hopefully they will not have the same power to distress them; massage may be one of those ways. Partly because it is soothing and calming as many patients described it, but also because it is a distraction. Many of these patients (quite understandably) feel depressed, as a consequence they may loose their ability to focus or concentrate (Evans et al, 2000), so normal distractions such as television or reading become ineffective as a diversion. Massage on the other hand is something that is given to them; their only job is to receive it. One patient described this very eloquently:

> "It's nice and relaxing because sometimes when you're in a situation like this you can't really get in to a book, you don't really sometimes want to concentrate on something, whereas when you're just being massaged you don't have to concentrate on anything, you know mentally it's just relaxing, you can just let go and relax." (Alice)

Denial: Denial is used when the full impact of a situation is too much for a person to cope with (Heim, 1991); this can be seen for example when someone is coping with bereavement. Equally however, trying to cope with a life threatening diagnosis and being separated from friends and family to go through the very intensive treatment required to cure their illness maybe too much for some people. Especially as physically, the patient often feels no different to normal; they have nothing, which distinguishes them as being ill that could otherwise help them accept their condition. They do not for example have a tumour to be felt or a plaster cast to indicate a broken limb. Consequently they 'pigeon hole' off the actual diagnosis and instead focus their energies on; getting through the treatment, dealing with the side effects and surviving the isolation. To reiterate, there is much useful information relating to how patients cope with incarceration on a leukaemia unit within this section of the results, however only that directly relevant to the primary issue of whether and how

massage can help reduce stress levels can be addressed in any detail within this thesis.

Conditioning: It has been suggested, that a factor which may lead to heightened levels of stress for the patient in isolation could be the use of maladaptive coping strategies, including for example, anticipation of worst-case scenarios and reliving stressful situations - rumination (Heim, 1991). This is something patients would be especially prone to, as being isolated they often have nothing to distract them. It has been proposed (Caudell, 1996) that because leukaemia patients suffer such high levels of symptom distress they need interventions, which will improve their level of coping and/or adaptation skills throughout their journey. However, the impact of any situation depends largely on a person's perception of threat, in other words how threatening they perceive a certain thing - including their environment, to be (Reiche et al, 2004). Any perception of threat can quickly escalate due to behavioural conditioning (Hucklebridge, 2002). Conditioning is a situation whereby something happens to a person, for example they are given some chemotherapy, and it has an effect on them such as making them feel ill. If that feeling is bad enough and is consistently paired with a neutral stimulus, often environmental, for instance their isolation room, in time the neutral stimulus will start to trigger the same response as the stimulus, which prompted the original reaction. This is known as Pavlovian or classical conditioning. Unfortunately, conditioning can lead to the patient feeling unwell purely through being in the isolation room. Such conditioning has been shown as powerful enough to influence immune function in some cases and the compelling evidence for this can be seen in a chapter by Hucklebridge (2002). However, in their meta-analysis of the relevant literature, Miller and Cohen (2001) conclude that psychological interventions may have the capacity to modulate such effects. It might be therefore that as well as reducing stress levels; interventions such as massage could find a use in blocking the initiation of negative conditioning in patients undergoing high-dose therapy by introducing a positive focus to override the negative stimulus.

The idea of inappropriate conditioning of patients through the regular pairing of negative events (such as undergoing bone marrow aspirations) with an unchanging environment – the isolation room, activating negative responses to the room alone

has been discussed above. Equally the idea of massage blocking the effect has been reflected on. However it may be that the use of essential oils in the session could enhance the benefits of the massage and eventually provide a focus for positive conditioning. In other words when the patient smells the oils he or she feels more relaxed even before the massage has started. An indication that this might be the case for some patients can be seen by comments made in the SSI. One patient for example reflected that she 'didn't want to get rid of the smell, when that's wafting over it's really nice' (Ann). This correlated with a cortisol level that dropped and stayed low for the duration of the two-hour assessment period. The benefit of the oils in this situation therefore maybe to prolong rather than deepen the effects of the massage. Such a conclusion ties in with the fact that approximately 30% of patients in the aromatherapy arm of the trial documented greatly enhanced sleep patterns following their massage session (see section 5.2.2).

Individual differences: The impact of individual differences in characteristics such as response to stress are important factors to include when looking to identify the influence of interventions such as massage on stress (Turner-Cobb, 2002; Heffner et al, 2003). It is important to recognise the possibility that massage does not fulfil the same role for any two patients. To the point that any reduction of stress seen following massage may come through a variety of reasons, for some patients it may be due to the comfort of touch, for others the escapism of forgetting their situation and for another group the security of time with a caring professional. Anything, which the patient responds to that can induce the benefits seen through massage is relevant but may not be equally important to each patient, making it difficult to tease apart the essential elements of such complex therapies. It is suggested that the reality is, massage with or without essential oils is a multi-factorial therapy and to try and identify the one pure essence of its success is the wrong research question. It is more appropriate to assess whether massage, which can be seen as an essentially passive aid to coping or for example, visualisation as a more active way of coping would be most appropriate for a particular patient. It is suggested that in a number of cases patients would appreciate both levels of intervention and support at different points along their journey.

5.2.5.b Body Image

Another benefit of massage, which has not so far been discussed in great detail within the thesis, relates to problems with body image. One of the side effects caused by chemotherapy is dry skin. For some patients (women particularly) this can be a problem, especially as they have to cope with many other issues relating to body image such as weight loss and the insertion of long-lines. Massage can address such anxieties in several ways; the fact that a therapist is prepared to work on their body without comment shows acceptance of the person as they are, equally massage offers practical support in some situations by directly addressing the problem (in the case of dry skin for example). One patient commented: 'My legs feel nice and smooth as I get dry skin on my legs especially being in here, they've gone quite dry' (Paula). Paula's cortisol levels dropped and stayed low for the duration of the assessment period. Other researchers who have found similarly that massage can have a beneficial effect on the body image of cancer patients support this finding. Bredin (1999) conducted a qualitative study looking at the impact of a series of six massage sessions on three ladies with adjustment problems relating to body image following mastectomy. Her results show that the massage had a profound impact on their situation with one of the patient's comments being that the massage helped her (numb) arm 'to feel part of her body' once again.

5.2.6 Visualisation

The most unexpected result from the trial was the positive impact the visualisation exercise had on the small sub-group of patients in the control arm who made use of it. This finding opens up avenues for future work looking at more self-centred styles of coping and relaxing, which are independent of whether a therapist or other professional is available to give support. These few patients have provided many potent insights regarding the benefits of using visualisation through their sessions, yet it is not within the remit of this work to explore such benefits fully. However, it feels appropriate to finish with another quote, this time out of my therapist's diary entry for Emma:

> She enjoyed doing the visualisation – she gave herself a challenge as she has one big prickly weed in her garden, which she hasn't been able to remove and she saw herself getting rid of it. I encouraged her to use the technique whenever she felt like it as it obviously worked for her – bloods went down and stayed down. (Emma)

5.2.7 Summary of results

In summary, the quantitative data from this study have shown that in this cohort of patients, massage resulted in a statistically significant short-term drop in physiological indicators of stress, as measured by reduction in cortisol and prolactin levels. Equally the qualitative results have confirmed the psychological benefits of massage to patients under chronic stress. The statistically significant reduction in 'need for rest' for patients in the experimental arms shown in the QLQ C-30, suggested massage as a potential medium through which to improve the patients' sleep pattern. The importance of this work comes from marrying both physiological and psychological responses to massage, as it allows us to begin to understand how complex is a patient's response to stress and how their different coping strategies might be enhanced through massage.

5.3 Limitations of the Study

There have been several major difficulties encountered whilst carrying out this work and these will now be reviewed:

5.3.1 Multiple Roles

Throughout the study, issues relating to my multiple roles within the trial caused difficulties. For example it was very challenging for me as the therapist to detach from the needs of the patient, particularly when they were randomised to the control arm of the study. It was reinforced to all patients (prior to randomisation) that if they did not receive a massage during the trial that they would receive priority treatment next time the service was available. Equally, emphasis was put on the importance of the control arm for experimental purposes in order that patient randomised to that arm of the trial could gain some sense of benefit from taking part. Finally, those who voiced a need to 'do something' during their session were offered (once they have been randomised) the opportunity to work with basic visualisation or relaxation techniques. However, all these compensations did not detract from the fact that the patients in the control arm often showed or expressed disappointment at not receiving a massage and this impacted on me as guilt and concern.

There were also issues, which centred round my sensibilities at depriving subjects in the control arm of massage yet still having to take their blood. The logic behind using serum samples has been validated in that many patients were suffering from some degree of mucositis whilst on the trial, therefore would not have been able to produce the series of salivary samples that would have been required, without discomfort. However, it does not prevent the concerns around taking the serum samples. This unease was particularly relevant, as my own sensitivities were in some cases backed up by patients' comments as has been illustrated within the results chapter (see section 4.6.2). My thoughts regarding these anxieties have been presented here in a manner comparable to the way they were written in the sessional diary at the time, as they are quite explicit in describing how I felt. The first episode is a summary of my interactions with a gentleman in the rest arm:

'Although Cyril and I had nice little chats each time I went in to take his blood (including the financial effects of him being in hospital as he is self employed) it became fairly obvious by the 12.45 bloods that he was finding the procedure somewhat of an irritation as he muttered something to the effect of 'This is a bit of a con, I thought you'd take the blood in one job lot.' Interestingly, this was in spite of him insisting he'd read and understood the information sheet and me reinforcing the point that there would be several blood samples over a relatively short period of time. I can only assume that if one is getting a massage, even if you're not sure initially whether you will enjoy it, that is a reasonable payoff for having the bloods taken. Whereas with nothing in return the novelty soon wears off and despite being prepared to take that gamble the reality is somewhat more of an irritation than was expected. However, it does throw up another concern relating to informed consent. Information relating to the schedule of serum sampling was reiterated on several occasions yet obviously not absorbed in some cases at least. Unfortunately although most patients kindly give up their time and blood with minimal concern (as far as I am aware), it did not assuage my guilt at taking from them and giving nothing in return.'

The incident above was disturbing and highlights obvious issues relating to the validity of informed consent. The patients all received written information sheets (see appendix V, page 281) and had several opportunities to discuss any concerns either on their own or with family present, prior to signing consent forms. As such it is difficult to know what other safeguards could have been put in place to prevent such misunderstandings.

Whilst the incident with Cyril was upsetting, the episode described below with Alan was far more emotionally challenging for me personally. The diary entry here clarifies the distress felt by a professional trying to integrate the various fractions of her role and highlights the many ethical concerns, which are provoked by such a situation. Once again the diary entry is presented as it was initially written in order to enhance understanding of the situation:

'Alan, despite having a positive attitude appeared to be encountering lots of problems and was, I quickly realised during the assessment period, now finding it hard to maintain his positivity. I found this hard because despite his reassurances on Monday that he had not had a massage before and didn't mind if he was in the control arm I felt as if I had let him down and increased his catalogue of disasters. From a purely personal point of view, if someone is in pain, physical, psychological or spiritual, the instinct is to nurture him or her and protocol did not allow for this. Instead I found myself taking his precious blood (he is pancytopenic and getting no increments from blood or platelet transfusions) with no benefit to him - is this ethical? I was asked by one of the staff if I would take 30mls of blood for HLA antibody screening during the second session, which didn't help my feelings of making his situation worse - especially when he asked if all the blood I was taking was for the trial. Although it was not, it made me acutely aware once more of how precious the patients' blood is to them and how generous is the spirit that would let me take extra to clinical requirements under such circumstances. Finally, when I went in at the end of the two-hour assessment to give him the repeat QLQ for the next day, he looked so sad that I sat down and listened properly without being distracted by the trial. I desperately wanted to make it better for him and to give him a big hug but of course that is not appropriate except under the guise of a massage. When I talked to my clinical supervisor about how I was feeling, she pointed out that I was carrying out all the research, and maintaining a very busy service by myself so it was bound to affect me at times. I knew she was right but at the time I was still not sure how I felt about continuing.'

The impact of my experiences with Alan are highlighted in this final, related section which describes what happened the week following Alan's entry into the study and draws attention to the consequences of such an incident:

'Today should have been a study day but I couldn't, I didn't have the heart to allow Harry, the only potential candidate, to commit himself to the chance of not getting a massage when it was blatantly obvious that he both wanted and needed an abdominal massage as he was suffering from constipation due to part of the chemotherapy regimen. The memory of my misery when talking to Alan last week in his distress but not being able to treat him was still too raw and fresh in my mind. Besides, I didn't think it would have been ethical - it certainly wasn't to me. Of course my experiences of the last two weeks throw up a major short - coming of the study design; patients who *really* need the service can't by definition be included because one cannot take the risk that they are randomised to rest. So, the patients with newly diagnosed leukaemia who are finding it difficult to cope, those with physiological or psychological problems, those who have relapsed and are finding it hard to deal with the implications, these are the people the service was set up to help yet they are, by necessity, being excluded from a trial aimed at evaluating the service.'

As can be seen from the accounts above, the multiple roles of therapist / nurse / researcher caused me great personal difficulties at times. However as far as I am aware, other than its implications for who was enrolled onto the trial, it did not have a negative effect on the study.

For the initial part of the study all these worries were compounded by the fact that as a researcher I was handicapped by lack of the practical support from a research assistant. This was help, which had been promised by the university but because of unforeseen circumstances was not forthcoming. This did cause enormous problems in the beginning because it was for inappropriate for me to undertake parts of the study work myself. For me to carry out the semi-structured interviews for example might have led to biasing of qualitative results through patients' not wanting to respond in a negative manner in case they upset me. Equally for me to carry out the initial consent might have been looked upon as biasing recruitment. A research assistant was eventually supplied by the university and regular support offered by the hospital.

5.3.2 Recruitment

Another major concern throughout the duration of the study was that of recruitment. The initial sample size calculation estimated that 48 patients (16 per arm) were required to be entered into the study in order to perform the interim analyses. When the trial closed 39 patients (13 per arm) had been entered, therefore the study was underpowered. Several reasons are offered to account for this and will now be discussed. There are certain drugs used regularly on the unit, which falsely raise either the prolactin or cortisol levels of the patients. For that reason, it was often the case that although a patient had signed the consent form, I was not able to use them in the study because of their prescribed medication. Equally, because the trial protocol required the use of patients who have never or not for a long time, had experience of massage, the patients recruited were unsure of what to expect and were sometimes wary of participating - especially if their chemotherapy was also trial based. The decision to decline entry was understandable; however many of these same patients went on to take advantage of the standard massage service offered. In order to monitor the situation, a list was kept of all patients given an information sheet and reasons for them not entering into the trial, plus a note was made of whether they went on to make use of the standard service. An additional challenge, which compounded the problem of patient recruitment into the study during the early months of 2002 centred on the fact that the ALU had to re-locate to another ward. This ward had the lay out of the old Nightingale wards with beds up either side of the ward separated only by curtains; therefore none of the patients were in isolation. Because of this it was felt to be impossible to continue the study during this period as one of the main bases for the work was the fact that being separated from significant others accentuates loneliness and vulnerability and therefore stress. The patients moved back to the ALU in May 2002 but all was still in chaos and I did not feel comfortable randomising anyone initially as it was felt that the disorganisation on the unit might transmit itself to both the patients and myself as either stress or anxiety. As a consequence a decision was made to restart proceedings on Monday, 10th June 2002.

5.3.3 External Disturbances

The next issue related to a factor, which was an ongoing concern throughout the whole of the study and is an issue in the running of the regular service; external disturbances. These came in many different forms and ranged from friends and relatives remaining in the room of the patient whilst they received a massage (despite gentle hints that they could go and get a drink), to members of staff shouting up and down the unit to each other. With regard to the relative scenario, many of them were very quiet, respectful and were no trouble. Unfortunately however, some had the compulsion to talk or ask inappropriate questions in front of the patient. An example from the study was when one patient Jean, had a friend arrive who started asking me why she couldn't have any more chemotherapy (she was suffering from relapsed lymphoma). To look at these disturbances from the most rational perspective is to see them from a realistic point of view. They are part and parcel of offering massage on a unit such as this. There is no quiet room and if there were, neutropenic patients would not be allowed out of their rooms to make use of it anyway. Consequently if massage is to reduce stress levels it must do so in spite of the chaos. However, it is interesting to reflect on the fact that although there were many disturbances which were documented by me as the therapist (43 in total), only one patient explicitly commented on the disturbances as specifically influencing his session (doors banging, Noel). It is intriguing to know why. There are several reasons why this might be the case, it maybe that most patients didn't see the disturbances as something directly relevant to the study process therefore did not mention them during the interview. It may be that most patients can filter them out as part of the background noise of the ALU, especially as much of the chaos revolved around staff coming into the room to change intravenous drugs. Perhaps they didn't like to mention disturbances for fear it might be seen as complaining, or perhaps they simply didn't mind and the disruptions didn't prevent them from relaxing. Certainly, two patients in the aromatherapy arm who were subject to multiple interruptions (Wendy and Norma) both showed physiological evidence of relaxation which was maintained for the full two hours – although Norma commented at the end of the two hours that she was 'Not so calm as I was when it was going on. I suppose because there is so much going on.' Some disturbances it was possible to pre-empt such as telephone calls, by taking the telephone off the hook - assuming the patient was amenable to this. If calls were taken then they were documented as well as (if the

information was offered) what the conversations were about (were they emotive issues?). Other disturbances however were more difficult to deal with, the most distressing of these for myself and in some cases the patient, being a certain member of staff. This particular nurse appeared to see me as someone who was taking her patients from her, so despite regular reassurances to the contrary and despite a large 'Please Do Not Disturb' notice on the door felt it necessary to bang very loudly into the room in which the massage was being performed, and talk at length with the patient about anything and everything. For me her attitude was irritating but temporary, one wonders however what impact a person such as this would have on a patient's stress levels when they are exposed to it on a regular basis. In one of the massage sessions this particular nurse was responsible for the majority of the *nine* interruptions the patient endured during her time in the study (Wendy).

5.3.4 Disruptions to the protocol

As well as external disturbances influencing the sessions, it was evident right from the start of the study that certain specifications in the protocol were too stringent and not going to work. Wanting the patients to remain on bed rest for 20 minutes prior to having their baseline bloods taken for example, often during this time the doctors were performing the ward round and wanting to talk to the subject. Equally the patients would decide they wanted a shower before the session - or someone came in to make the bed thus 'getting it out of the way.' However, these disruptions occurred for patients in all arms of the study and as such should not have influenced the results in any respect.

In the same manner it proved impossible to anticipate patients' actions following a massage. It was always explained to them prior to starting a session that it was not compulsory for them to rest after the therapy had finished, but that they might like to make use of any sense of calm by relaxing for a while. Below is a description taken from my diary of how one patient reacted following his massage and my response. It was chosen as it sums up the issues in question. Once again the entry has been transcribed almost exactly as it was originally written:

'I finished the massage and left the room to return as usual in 10 minutes time for the first post-session blood. When I entered the room the patient shot upright from the prone position. I hastily encouraged him to lie back down. Although he responded to my request the first time he kept repeating this behaviour - followed by dramatically whipping off his tee-shirt (for me to reach his central line). In the end I gave up worrying but remained rather concerned that he was probably undoing all my hard work! To add insult to injury he followed this behaviour by going into the very dramatic details of the day of his daughter's birth - if there were any positive effects left from the massage after the jumping up scenario it was challenging to believe there would be by the end of the assessment period (Frank). (Note, this patient did respond initially with a drop in cortisol levels but by the end of the two hours it was back at baseline levels). Every time something like this happened I would mentally calm myself down and reiterate to myself that this was what it was like working on the unit. I would remind myself that if the benefits of massage were not robust enough to withstand such responses then I could not expect there to be any physiological changes.'

Disruptions to the sessions such as those illustrated may lead to what have been described as 'intervening events,' which both Cassileth and Vickers (2004), and De-Valois (2001), discovered can have a major impact on the length or depth of a patient's response to massage. A ward round discussion for example with the doctors, could lead to the medical team deciding to take a bone marrow aspiration from the patient, which is a very uncomfortable procedure. Awareness that they will have to endure the procedure at some point in the day is likely to hamper the patient's ability to relax. Equally, bad news may be given by the doctors regarding a patient's disease status. Under these circumstances it is impossible to buffer a patient from the consequences of such consultations or protect them completely from the associated stress reaction. However, whilst the event may impact on the length of a patient's physiological response to massage, it may be possible for interventions such as massage to minimise the length and depth of such negative encounters through diffusion of the emotional impact.

5.3.5 Clinical Trial Management

The final topic related to complications encountered whilst performing the trial, revolves around the general difficulties associated with management of trials in the clinical area. In a laboratory setting the majority of variables can be controlled, making it easy for the researcher to interpret results from data. Unfortunately, this is not the case for research undertaken in the clinical setting. Humans are unpredictable, as a researcher it is not possible to control their responses. It might be necessary to ask a group of people to stop doing something (in this case, the doctors were asked to stop prescribing a certain drug), however they forget. Equally doctors unfamiliar with the study might cover the unit at night and not know of the request – if the nursing staff didn't tell him or her of the appeal, then the drug was prescribed. There were many examples of such problems, such as the nursing staff being asked if they would mind taking a sample of blood from each study patient twenty-four hours after their session. The majority of the samples were not taken despite the request being written in the diary; therefore that part of the analysis had to be abandoned. It may be the subjects are required to act in a certain way, this can only be requested it cannot be enforced. Individual differences in the way patients react to a situation whilst adding to difficulties in interpretation of data help provide understanding as to how people deal with a set of circumstances as Lutgendorf (2003) pointed out in her paper. Segerstrom (2003) also reinforced the importance of understanding how individual differences impact on complex issues such as immunity and cancer; studies such as the one presented here can help to enhance such understanding.

The lesson to learn from this study is that clinical trials of this nature, which aim to look at a complex intervention, need to be flexible, not fixed. They must be designed to be adaptable, to be able to absorb the inconsistencies of the clinical environment and any data have to be understood to be the result of a particular context; if a different set of patients or intervening events had occurred the results would have been different: 'Reality is multi-faceted and changing, not objective and waiting for measurement' (Temple et al, 1996). Therefore any conclusions from work such as this are always going to be context dependant and whilst they are important for helping our understanding of how patients, for example, respond to a particular therapy, they cannot be held up as absolute.

5.4 Implications for Clinical Practice

5.4.1 Integration of massage

The major implication for clinical practice to come out of this study was that the results indicate massage – even single sessions of massage, are both safe and beneficial to patients being nursed in isolation.

The focus of this thesis was to provide evidence showing it was possible to enhance the supportive care of patients with haematological cancers being treated in isolation with massage. Apart from the statistically significant drop in cortisol and prolactin levels following massage, the fact that none of the subjects made a negative comment specifically relating to the impact of massage and the unanimous comment used by patients to describe their massage was 'relaxing' (see section 4.6.2.a), suggests enhancement of their sense of wellbeing. The results also suggest that massage had an impact on poor sleep (see section 5.2.3), and feelings of isolation - through the patient's relationship with me as the therapist. Both poor sleep and isolation have been shown to impact in a negative way on a person's immune function (see section 2.5) therefore it is possible for the use of regular massage to have a profound effect on the lives of isolated haematology patients. Cacioppo et al (2000) for example highlighted that chronically lonely students were characterised by cortisol levels, which were elevated throughout the day. It is possible therefore that the change in cortisol levels seen within this study were either due to a primary reduction in stress or a reduction in loneliness leading to a reduction in stress. It is proposed therefore that professionals working in this setting ought to consider integration of massage therapy (as defined by Avis, 2002) performed by appropriately trained therapists, into the routine treatment of the patient. Currently, technology and pharmacology is at the heart of the clinical care of the haematology patient. Nurses and doctors accept and agree that it must be so for the patient's own survival and protection. I suggest that the results presented in this thesis open up other avenues of care – other worldviews on which to centre care (Rankin-Box, 1997), which embrace the concept of holism. It is also proposed that such visions are just as valid and just as necessary to the patient if they are to heal successfully from their experiences as the pharmacologically focused attention they receive now.

Accordingly I propose similar services could and should be offered in other such units.

5.4.2 Staff Relationships

The results of this study clearly showed that massage measured as a single session, was of benefit to haematology patients undergoing high-dose therapy. What the research also brought to light however was that in order for such a service to run efficiently it was important that it be based on mutual understanding of the roles and responsibilities of the staff involved. As such it is imperative that any move to integrate massage into the clinical care of the patient be done sensitively with respect for the views of others Rankin-Box (2002).

To be in the position of looking at a situation from three different perspectives, that of nurse, therapist & researcher at the same time, as I was whilst running the study, is very powerful with relation to development of clinical practice, but also very challenging. The experience threw up many practical problems the majority of which have been discussed previously. However, it also opened my eyes and mind to the importance of several factors, particularly those relating to relationships between professionals:

Nursing: From the nursing perspective, the lesson learnt was that it was important to understand what a massage therapist could offer to a unit and how best to utilise her skills. A therapist if employed appropriately could be seen as an extension to the caring, nurturing aspect of nursing. Someone to offer specialised but integral care appropriate to the needs of the individual patient. However, in order for a nurse to triage that and other therapies appropriately he or she must understand the service a therapist is offering and embrace it as an additional benefit, not something to compete with their own care. Liaison based on mutual respect is paramount if this potentially powerful relationship between nurse and therapist is to work effectively. Garnett (2003) described the use of complementary therapies as: 'an exceptional system' evolved to deal with the 'exceptional existential anxieties' faced by patients nursed in the palliative care setting. It is suggested here that it is not just in the palliative care setting that such a system is necessary but all the way through a patient's cancer journey as there are always new anxieties to be faced. Garnett also

focused on the issue of trust; this is something endorsed by the present author. When working with such a vulnerable client group it is essential that the therapeutic environment be pervaded by an atmosphere of trust. There needs to be trust shown between nurse, therapist and patient in order to ensure a high level of security for the patient. Feelings of trust and respect enhance the caring environment in a way necessary to ensure the development of rewarding therapeutic relationships (Ernst & Fugh-Berman, 2002).

Therapists: From the therapist's perspective it is essential that he or she recognise and respect a nurse's unique and often intimate relationship with any one patient and not try to encroach on that. A nurse's responsibility is for the whole care of the patient – to be the patient's advocate in all things, therefore it is essential that the therapist liase with the nurse caring for a particular patient. Nurses can and do provide valuable information to the therapist about the clinical, emotional and psychological state of patients in their care. By appropriate liaison the therapist ensures they know what is happening for the patient before they enter the room and have a good understanding of potentially important matters that may require reporting back to the nurse following the massage session. Appropriate liaison also ensures that a time for massage is chosen which is not going to interfere with the routine care of the patient and will help to cut down on level of disturbance through for example the administration of chemotherapy.

Researchers: If research is to be carried out in the clinical setting then from the researcher's point of view, it is important for him or her to understand the relationship each of the other two professionals has with the patients. The nurse for example is the patient's advocate therefore it is imperative that the nurse understand any research project so that she feels comfortable with it and can help the patient to also feel secure. Equally, it is important that the nurse does not feel she is having her relationship with the patient compromised through research, owing to, for example being asked to do something she does not feel comfortable with. The therapist however may not have an intimate knowledge of the clinical care of the patient. It would therefore be inappropriate to involve them in research projects except within the remit of their role. Again, it is important that the researcher ensures the therapist

has full understanding of any research they are to be involved in so that they feel comfortable, as any discomfort is likely to be picked up by the patient.

The multiple roles I took on during the process of this study helped to emphasis for me that close, trusting and respectful relationships between nurse, therapist and patient are both vital and fundamental requirements of a massage service if it is going to run successfully. However, there are other important clinical issues to be addressed:

5.4.3 Service Provision

Another clinical issue to be addressed was the frequency with which any massage service should be offered to patients in this environment. The qualitative results from this study (see section 4.6.2) would suggest that once per week is not enough. Some patients requested regular, even daily massages. To have a daily massage service would help to deal with the issue of intervening events reducing the benefits of massage (see section 5.2) by allowing the patient to fortify the effects of therapy on a regular basis. Equally a daily service would give patients more choice and subsequently more control over when they decided to have a massage. It would also provide a safety net to ensure that even if a patient were unavailable to take up the offer of a massage on one day, it would not be a full week before they had the option again.

5.4.4 Visualisation

There has been a clinical issue highlighted by this work, which relates to findings associated with visualisation. Visualisation was offered to some of the patients in the control arm and proved to be a tool, which could quickly and easily be taught to patients. Comments made by patients in this subgroup (see section 5.2) intimated the technique enhanced their feeling of control and in some cases was shown to reduce physiological stress levels as measured through drop in cortisol levels. Because patients cope with distressing situations in a number of ways some actively, some passively, visualisation could be seen as a useful alternative or addition to massage for patients wanting a more active method of coping with stress.

5.4.5 Use of Essential Oils

One of the original aims of this work was to assess whether essential oils blended into the base massage oil inferred any extra benefit on the patient or whether they were a dangerous placebo in that they required metabolism by an already over-worked body. The results of this work suggest that whilst the experimental hypothesis postulating that aromatherapy massage would be more effective than massage using base oil at reducing symptoms of stress could not be accepted, essential oils do add benefit to the massage. This conclusion is based on several factors; firstly all patients enjoyed the oils. Secondly, the results of the study, including evidence of improved sleep patterns (see section 5.2.3), suggest a trend to signify that the presence of essential oils may enhance and prolong the effects of the massage. Finally the parallel laboratory work on the oils showed very clearly that several oils would usefully enhance a patient's defence against pathological micro-organisms such as Methicillin Resistant *Staphylococcus Aureus*, (see paper, appendix XV, page 326). Consequently, (as proposed in section 3.14.4) in view of the high level of immunosuppression experienced by the patients in the study, because the oils were shown to potentially enhance the body's level of protection against pathogens this was seen as a valid reason to use them in any massage service.

5.5 Recommendations for Future Studies

This work, as well as answering several research questions and as such, making a valuable contribution to nursing research, has also highlighted other areas for investigation:

5.5.1 Assessment of Sleep Patterns

There is further work, to be completed on the data all ready available. The timing of both the study sessions and the blood sampling for example, were standardised because of the diurnal variation of cortisol levels. However, very recent research (Hucklebridge et al, 2005; Federenko et al, 2004) has recognised that cortisol levels maybe a product of time of wakening and/or poor sleep; therefore standardisation of session times may not have been helpful. For that reason it is suggested that the baseline levels of hormones and change in levels following intervention for patients in this trial could be correlated with time of wakening or number of minutes / hours the patient was awake prior to study session - particularly as Williams et al (2005) suggest cortisol to be a product of stress levels and waking times. Because sleep appears to be an influence on cortisol levels and immune function (Irwin et al, 1994) it would be profitable to explore the effects of intervention in cases of sleep deprivation / disruption and to measure the change in sleep quality following massage in a more structured way than was done here, especially in light of the finding that patients in the experimental arms of the study showed significantly less need for rest ($P = 0.009$) in the 24 hours following massage. Soden et al (2004) used similar experimental conditions to those used in this work within the format of a randomised trial in an attempt to look at longer-term effects of massage in a hospice setting. They showed substantial improvements in sleep scores and reductions in depression scores but also struggled with a small sample size therefore were unable to demonstrate anything other than large treatment effects.

5.5.2 Assessment of Loneliness

Whilst it is recognised that the EORTC QLQ C-30 did not quantify the benefits of massage on quality of life in the manner anticipated, it did throw up some useful insights into the main difficulties the patients had to contend with. Understandably one of the major issues highlighted by patients at baseline was the influence their

situation was perceived as having on them socially. The median standardised score for impact on social activity was 0.00; this confirmed that patients saw their situation as causing them an exceptionally high level of social impediment. It is possible therefore that the patients are not only isolated but also lonely. In view of the potential impact loneliness has been seen to have on cortisol levels (Cacioppo et al, 2000) and immune function (Glaser et al, 1985; Hawkley and Cacioppo, 2003) it would seem appropriate to include a measure of loneliness into future studies in order to look for a relationship between baseline scores and patterns of cortisol production as well as correlating any change in values for the two measures following intervention.

5.5.3 Cumulative Effects of Massage

It was initially anticipated that some subjects would be kept in the study for more than one week in order to look at the cumulative effects of massage as a secondary analysis (with only the first week's results going into the primary analysis). This was seen as important because subjects' anxiety levels may be falsely high prior to their first massage session, given that they may not know what to expect. Equally on sequential weeks the memory of previous massage sessions may lead to deeper relaxation. Unfortunately, because of the major problems encountered around recruitment it was felt to be more important to recruit new patients than to continue with existing subjects and the plan was abandoned. However, it is still seen as valuable to look at the cumulative effects of massage. One way of monitoring this cumulative effect would be to use subjects as their own controls; to take a series of cortisol measurements one week before the study day, again on the day of the first study session then sequentially for as many weeks as they are in the study. This design would allow the researcher to identify the individual pattern of cortisol production for each patient prior to the trial and document on a within-subject basis, change in cortisol levels due to massage. Current work has validated such an approach by showing the circadian rhythm of cortisol to be highly reproducible. Selmaoui and Touitou (2003), in a recent study took 31 young adult males and measured the stability of cortisol and melatonin levels over three, twenty-four hour periods spread over six weeks. They were able to show stability of circadian rhythms for both hormones with the majority of subjects showing very little intra-individual or group variability over the three measurement periods. It has to be

noted however, that as the study was conducted in laboratory surroundings with subjects chosen for factors including stability of sleep patterns, it was not designed to accommodate changes in cortisol levels through reasons such as psychological stress or disturbance of sleep. In spite of the issues raised by the laboratory setting, the study by Selmaoui and Touitou (2003) confirmed the basic stability of diurnal patterns of cortisol secretion, therefore corroborating the validity of a study design such as the one outlined above. To work in this way would also allow the researcher to account for the individual differences known to exist in patterns of cortisol secretion. Smyth and co-workers (1997) in a more naturalistic setting, monitored salivary cortisol levels in 109 healthy subjects over two days. Interestingly, they discovered that only 51% of subjects showed the classic drop in cortisol levels throughout the day; 17% demonstrated no consistent pattern and 31% showed different diurnal patterns each day. It is suggested by recent research that rather than reducing cortisol secretion per-se, it may be more important to normalise the diurnal slope characteristic of cortisol secretion. Sephton and colleagues (2000) for example demonstrated in patients with metastatic breast cancer, that those ladies showing flat or abnormal cortisol rhythms had significantly earlier mortality ($P = 0.0036$). Equally, Peeters et al, (2004) observed, in a naturalistic setting, comparing cortisol secretory patterns of healthy subjects with those of patients suffering from major depressive disorder, that secretory patterns were erratic, particularly in patients with more severe or recurrent episodes. It is possible therefore that abnormal diurnal rhythm maybe indicative of underlying problems often associated with cancer patients such as fatigue and negative affect. Bower et al (2005) in a small study of patients who had survived breast cancer, showed not only that fatigued survivors ($N = 13$) had significantly flatter cortisol slopes ($P < 0.018$) than non-fatigued survivors ($N = 16$), but that fatigue severity showed a linear association with cortisol slope in that the flatter the slope, the more fatigued the person ($P = 0.022$). Polk et al (2005), in a much larger study of healthy adults (334) showed an association between trait affect and diurnal patterns of cortisol secretion. By first assessing a patient's regular cortisol secretory pattern therefore, it should be possible to identify whether massage is able to normalise the slope. This is seen as being especially important for those patients with high or flat cortisol rhythms, as these seem to be the ones particularly associated with underlying pathology (Bower et al, 2005; Sephton et al, 2000). That massage may have the capacity to influence

relevant factors is hinted at in this work as patients in the experimental arms showed statistically significant reductions in the amount of rest they perceived themselves as requiring compared to patients in the control arm (P = 0.009).

5.5.4 Correlation of Reduction of Stress with Immune Function

There are many factors, which in isolated patients undergoing intensive chemotherapy have the potential to alter cortisol levels from what is generally accepted as the normal diurnal slope. Some of these factors such as drugs and variation in waking time have been discussed previously. However, there are other factors such as fasting that have not yet been discussed but appear to have the capacity to alter cortisol release. Vance and Thorner (1989) for example showed that a five day fast in ten healthy men increased their 24 hour serum cortisol concentration 1.7 fold (P = 0.0006). The influence of fasting is of great relevance to patients with haematological malignancies as for various reasons they find it hard to maintain adequate food intake. All the issues highlighted make it hard to quantify or evaluate the clinical significance of any change in cortisol or prolactin levels seen in this or similar studies when taken in isolation. Nevertheless the results presented here are a useful indicator to show massage can influence stress levels as evidenced by the drop in cortisol and prolactin levels. One way in which to prove clinical significance would be to correlate any drop in cortisol levels with alteration in immune function. Stress may influence recovery of immune function in immunosuppressed patients following chemotherapy. More precisely, the make-up of the regenerating marrow maybe influenced in that T-helper cells developing in the presence of high levels of cortisol maybe predisposed to develop a line of Th_2 cells as described in a paper looking at glucocorticoids and immune function by Rook (1999). With this in mind, one line of research would be to look at regeneration of lymphocytes following chemotherapy with and without massage and document what happens to naïve $CD4^+$ cells. These are cells which have not yet acquired a 'memory' and are known as Th_0 cells; they have the potential to become Th_1 or Th_2 depending on a complex system of influences of which cortisol is a part (Elenkov, 2002) (see section 2.4.4). It would be necessary for any change in regenerating marrow to be correlated with change in cortisol secretion and other psychological measures of stress in order that a link might be identified between reduction of stress

through massage and improvement in immune function recovery as would be proposed by psychoneuroimmunology.

There is another way in which reduction of stress through massage may be able to influence immune cell populations, it is extremely relevant to patients with leukaemia and measurable in a research setting; apoptosis. Apoptosis is an active cell death process, which is used to eliminate excess cells during development, and has been particularly well characterised in immature T-lymphocytes. (Shi et al, 2003). Unfortunately when it goes wrong it can lead to immunodeficiency such as in AIDS. There is now evidence to suggest that chronic stress through the influence of cortisol is instrumental in increasing the rate of B and T-cell apoptosis, especially in the immature cells. In a synopsis of the available literature Shi et al (2003) suggest that stress-induced apoptosis in immature T-cells occurs through the HPA axis. Lill-Elghanian et al (2002), provide in-vitro data showing that immature B-cell lymphocytes are also particularly sensitive to cortisol-induced apoptosis. Papathanassoglou et al (2003), looked at the influence of cortisol and other factors on the up regulation of apoptosis in adult patients with multiple organ dysfunction (MOD). They looked at 35 critically ill patients and compared their cortisol levels to those of 35 age / gender matched controls. Cortisol levels were found in within subject comparisons to be significantly higher in the MOD patients at the point of maximum severity than in matched controls (MOD patients: 28.1 ± 7.46ng/ml; Controls: 7.5 ± 3.6ng/ml; $P < 0.03$), plus levels correlated with MOD severity ($P = 0.03$). Cortisol involvement in apoptotic regulation was assessed through correlation of cortisol with apoptotic markers and was found to be statistically significant ($P < 0.05$) on both the first and last days of the study, thus suggesting cortisol as a probable factor in apoptotic accentuation in patients with MOD. These results suggest it is possible that the prolonged regeneration of marrow, documented in some patients with haematological malignancies following chemotherapy, may be due in part to chronically high levels of cortisol leading to increased apoptosis of precursor cells. Because massage can reduce cortisol levels, it might be possible to influence the rate of apoptosis in such cases and therefore reduce the length of neutropenia observed. These thoughts have been corroborated by suggestions from Keicolt-Glaser et al (2002) in their appraisal of PNI and cancer, that therapeutic

interventions aimed at reducing stress levels may be able to influence apoptotic rate. Yang and Glaser (2003), in their very powerful paper effectively review and tie together all the current theories of how stress might influence the development and spread of cancer and include apoptosis in these reflections. Such findings all suggest it would be appropriate to design a future study to document and compare the apoptotic rate and time taken to regenerate white cells following chemotherapy of patients receiving massage compared with controls.

5.5.5 Essential Oils

Finally, in light of the fact that patients found the aroma of the oils appealing without any indication of adverse side effects, it is suggested that the role of essential oils in this setting deserves further attention. Equally the anti-microbiological effects of the essential oils identified in the laboratory work (see appendix XV, page 326), hint at potential uses for essential oils in their own right, as well as in a role of adjunct to massage. It is recommended that the first line of enquiry to be followed in relation to essential oils is to validate the preliminary findings presented here that oils are safe to be used in this setting. Whilst the reports from this cohort of patients indicated no problems in relation to the oils, that is they reported no adverse effects (such as skin irritation), data is urgently required relating to the biochemical effects of the oils – do they interact with chemotherapy; influence the patients blood biochemistry or vary the dosage of drugs received by a patient through binding to specific proteins? The other strand of this work to require further attention is the corroboration of the laboratory anti-microbial data with results of clinical studies. That is, do the oils still act as efficient antimicrobial agents when used in the clinical setting?

5.6 Summary

The discussion chapter of the thesis is split into sections, which follow a logical sequence and focus on the results of the study and reflections relating to those results, a section looking at problems encountered during the trial and a section offering implications for clinical practice. The chapter finishes with suggestions for future research.

The results section started by reiterating the fact that there was a statistically significant drop in cortisol and prolactin levels immediately following the massage for patients in both experimental arms as opposed to those in the control arm but there were no differences between the experimental arms. It went on to suggest a number of reasons for why that drop was short lived in many of the subjects and why there were no more correlations between the four physiological measures then would have been expected by change. From the psychological perspective the section reinforces and reflects on the fact that all patients who received a massage found it relaxing. There were many issues to be contemplated in relation to this study, however it is the ones thought to have greatest bearing on the results of the study, which have been highlighted here and they include issues relating to the patients' ways of coping. Likewise only the problems, which had the greatest impact on the running of the study, have been discussed here in detail. These include: the multiple roles of the researcher, recruitment, external disturbances and disruptions to the session.

In relation to implications for clinical practice, the results from this study confirm single sessions of massage as being both safe and beneficial to patients nursed in isolation. This fact is considered from the perspective of integrating massage into the clinical care of the patient. The importance of respectful and understanding relationships between professionals when developing such a service is discussed, as is the regularity with which massage could appropriately be offered to patients.

Finally several avenues of potentially stimulating work have been suggested as an expansion of the work presented here including looking at reduction of stress in parallel with regeneration of immune function following chemotherapy.

Chapter 6:

Conclusion

6.1 Introduction

In this chapter key points within the thesis have been summarised, conclusions drawn from the results of the research in relation to the original aims of the study and directions for future clinical and research-based work have been re-iterated.

Massage, with and without the use of essential oils is accepted as being of benefit to patients in many settings (Cassileth and Vickers, 2004; Hayes and Cox, 2000). Currently however, in the field of haematological oncology there is still major concern regarding the safety of such therapies as the patients are prone to infections and are at high risk of haemorrhage. With the focus of enhancing the quality of patient care, the aims of this study were to evaluate whether massage both with and without essential oils could be given safely to isolated haematology patients and to document whether physiological and psychological benefits were evident following therapy. It was also the aim to identify whether any benefits were manifest following single sessions of massage. Such work had never before been undertaken in this cohort of patients. Consequently, prior to this research there was no evidence relating to the safety and efficacy of using massage with or without essential oils in isolated patients suffering from of haematological malignancies. Equally there were no studies looking specifically at the efficacy of single sessions of massage. In other words, because of the amalgamation of patient population, detection and documentation of physiological and psychological benefits of massage; evaluation of single sessions of massage and the use of essential oils blended individually for the needs of each patient (see chapter 2, section 2.7), this work is unique in the appraisal of touch therapies.

6.2 Study Design

The safety and efficacy of massage therapy with and without the use of essential oils in this environment was determined in a clinically relevant way by utilising a mixed methods design. The study took the format of a randomised controlled trial but incorporated a substantial element of qualitative assessment; it took place on a high dose therapy isolation unit. Computer-generated randomisation was employed and 39 patients over a 2 year period were randomised into one of the three arms of the study: aromatherapy massage, massage with base oil or rest. The primary outcome measure was reduction in cortisol and prolactin levels as recognised physiological indicators of stress; however equal importance was placed on the results of the qualitative evaluation of the massage sessions. Alteration in hormone levels for patients who had received a 20-minute massage either with or without the use of essential oils was contrasted with change over the same time period for patients in a control arm who received 20 minutes of rest. Qualitative assessment of the therapy focused on a semi-structured questionnaire, therapist's diary entries and repeated quality of life and pain measurements. The findings from the quantitative and qualitative appraisals were combined for all patients into case files. A sample of three case studies was included in the main body of the thesis as well as the individually presented quantitative and qualitative results.

6.3 Results and Clinical Implications

From the perspective of safety, the crucial result from this trial was negative; none of the patients showed any indication of physiological side effects from the massage - bruising or skin reactions for instance. Similarly at no point during any of the sessions - including the SSI, did any of the patients' observations suggest they suffered any detrimental consequences following the massage, such as heightened anxiety. With regard to efficacy, inferential statistical analysis of the physiological data demonstrated a statistically significant drop in cortisol and prolactin levels in the first 30-minutes following therapy (cortisol, $P = 0.007$, following logarithmic transformation; prolactin, $P = 0.012$), suggesting a substantial decrease in the primary physiological indicators of stress. This was not correlated with consistent change in either HR or MAP; however, it was accompanied by a universal feeling of relaxation for patients in the experimental arms of the study suggesting a reduction in subjective appraisal of stress and possible clinical significance. By presenting a sample of case studies it proved possible to show how the various facets of a patient's response to massage married together.

This work has considerable ramifications for the supportive care of the isolated patient undergoing active treatment for haematological malignancies. To date the focus of care for such patients is based on a combination of technology and pharmacology. However, despite the difficulties in recruiting people to the study, (due mainly to the medical use of certain drugs which influence cortisol and prolactin levels) and thus a relatively small sample size, it has been shown that a marked fall in physiological indicators of stress can be achieved through massage. Therefore, the results of this research are compatible with the notion that massage performed by appropriately trained therapists would be a beneficial addition to the treatment of neutropenic patients and one which can be safely integrated into their clinical care. Equally, based on the comments made by patients during interview, essential oils appear to enhance the effects of massage without any negative side effects. Parallel in-vitro work on the essential oils also showed them to have anti-microbial properties, which may be valuable in the clinical setting. Clearly, further work is required to validate and corroborate the results presented here; nevertheless, in line with the original aims and experimental hypotheses of the study this

preliminary data has shown even single sessions of massage to be safe and beneficial additions to the clinical care of the patient in isolation. Equally, whilst it was not possible to accept the experimental hypothesis that aromatherapy massage would be significantly more effective than massage using base oil in reducing symptoms of stress, it was seen that essential oils could enhance the effects of the massage in a number of ways.

6.4 Future Studies

Whilst it was never appropriate to continue the aromatherapy massage service on the ALU without empirical evidence of its safety and efficacy, in the same way it is now appropriate to identify how massage can be of greatest benefit to patients prior to expansion of the service in order to best enhance patient care. Recent work for example has intimated patterns of sleep (Williams et al, 2005), and levels of loneliness (Cacioppo et al, 2000) may impact on the diurnal secretion of cortisol, consequently measurement of change in these variables in relation to change in cortisol levels following massage requires attention. Equally, the change in cortisol levels for many of the patients in this cohort was short lived; yet the patients on the ALU will continue to be under high levels of stress whilst ever they are inpatients. Therefore it is necessary to look at the cumulative effects of massage to see whether regular massage has a more prolonged impression on the signs and symptoms of stress.

Tied in with the ideas put forward here for future work, is the notion that cortisol impacts on the immune system in several ways, including influence over T-cell formation and apoptosis (see section 5.5.4). In view of the fundamental importance of immune function to patients with haematological malignancies, it is suggested that work looking at the impact of massage on stress should also monitor changes in immune status in patients receiving massage throughout their treatment compared to controls.

Finally, the role of essential oils needs much more attention. The results presented in this thesis have gone some way to provide evidence for their safety in this setting and to signify patients find them agreeable. Equally the parallel laboratory work indicated they are potentially useful as anti-microbial agents in the clinical setting. However, these notions require further consideration and clarification if clinicians are to be convinced as to the benefits of using such therapies on such a vulnerable population of patients.

6.5 Summary

The intention of this work was to validate the use of massage therapy in the support package of patients with haematological malignancies undergoing treatment in isolation. This thesis has provided evidence to suggest that massage is a therapy, which can be offered safely in such a setting, due to the absence of physiological side effects and negative comments in relation to the therapy sessions. Moreover, positive physiological and psychological responses to massage by this cohort of patients have substantiated the proposal that integration of massage into the clinical care of these patients would enhance their sense of wellbeing and reduce some of the stress-related effects of treatment. In short, this thesis demonstrates that massage with and without the addition of essential oils can be of considerable benefit to patients undergoing high dose therapy in isolation.

Before this study there was a widely held belief that haematology patients were too vulnerable to haemorrhage and cross infection to benefit from massage. It is recognised that such a deeply entrenched assumption will take a long time to change, especially among many of the senior haematologists in this country. However, this thesis will help to influence such change. There are now a small number of units in the UK where massage is being offered, it is to be hoped that the evidence provided by this and future research will increase the speed of this revolution in care.

Appendices

Appendix I

Audit

Jacqui Stringer
Nurse Aromatherapist (ALU)

AUDIT OF MASSAGE/AROMOTHERAPY SERVICE ON THE ALU 1997 – 1998

Introduction:

The ALU massage/aromatherapy service was set up in March 1997 on a temporary basis – funded by ALUPALS and available to patients and relatives. It was suggested that the service be evaluation after 2-4 months with a view to making it permanent if it was seen as an asset to the unit.

Following a meeting of staff during which feedback was given from ALU staff and patients in the form of verbal response and basic questionnaires, it was decided that the service was of benefit to the patients and was to continue – with regular evaluation, on a permanent basis. Funding would remain as before, through monies from ALUPALS.

In the months following that meeting uptake of the service has been good, with approximately 80 patients requesting massage. It is felt to be necessary therefore to audit it formally prior to possible/expansion/development of the treatments offered.

Method:

In order to monitor whether a massage service was in fact desired by the patients they were offered a short questionnaire (see appendix 1), on which they could indicate whether or not they would be interested in taking up the offer of a massage. The forms could be filled in anonymously so there was no pressure to answer in the affirmative.

To assess whether the therapy was appropriate to their needs, whenever a patient had been massaged for the first time, they were given another copy of the questionnaire to fill in with their thoughts of the service. Once again, these could be filled in anonymously and were handed into the secretary's office by a member of staff. A sample of one of the forms can be seen below:

ALU MASSAGE SERVICE

(With optional Aromatherapy oils)

Name/Anon

Date:

1) Would/have you taken up the offer of this service Yes ☐ No ☐

If yes, please answer question 2

If no, please answer question 3

2a) If your answer to question 1 was 'YES' but you have not yet been seen by Jacqui,
please let your team know and they will give her your name.

2b) If your answer to question 1 was 'YES' and you have received a massage, were you happy with this service? Yes ☐ No ☐

3) Any further comments would be gratefully received

Thank you for your help

The questionnaires have been collected over approximately the past 18 months and the results below show the patients responses.

Results:

1) <u>Pre-treatment responses.</u>

Unfortunately, due to time away by the therapist, not as many forms were handed out by the staff as was hoped. However, of the 17 responses, 16 forms were affirmative, only one person felt they would not find the therapy beneficial.

2) <u>Post treatment responses</u>.

Feedback following therapy was better. 35 forms have been returned up to October 1998. All of them responding in the affirmative, that is they found the treatment beneficial.

There is a comments box on the form and it is interesting to note the variety of different aspects of the therapy that the patients commented on:

Therapy		**Therapists**
Relaxing	(15)	Professional (3)
Soothing	(4)	Friendly
Excellent/Wonderful	(3)	Therapy well explained
Good to talk	(3)	Reassuring
Beneficial	(3)	Humanitarian
Very good	(3)	Gentle
Pleasant	(2)	Knowledgeable
Eased pain	(2)	Good listener
Reduces stress		Welcoming
Non-intrusive		
Helps with general well being		
Tailored to needs		
Time to talk		
A blessing		
First class		
Invigorating		
Felt better afterwards		

There were in fact only two 'negative' comments made:

More frequent sessions please (5)
A longer session would be nice

Conclusion:

It appears that judging by the returned forms, the massage service has made a positive contribution to the services offered on the ALU. For example 19 patients commented that the therapy was relaxing/soothing. In a time of high stress and anxiety, to be able to relax somebody is an important contribution to their treatment

and will improve their sense of well-being. Two patients noted specifically that massage eased their physical pain – without the aid of drugs, again a positive step. It is interesting that four people commented on being able to talk to the therapist and how that alone helped them, suggesting that it is the therapy as a whole, which is beneficial.

At present the service is only available one day a week. As can be seen by the above comments some patients felt that for their needs this was not enough. It must be noted that there is the possibility some patients may not have enjoyed the therapy but not felt inclined to return the form. However, it was never the case that once massaged a patient declined to be seen by the therapist on subsequent occasions, so one can only assume that the therapy was generally appreciated.

Summary:

It will always be the case that some people do not feel comfortable with this type of therapy. However, I think what this audit shows is that a relatively large number of the patients passing through the ALU do in fact receive a great deal of comfort from the treatment offered – consequently, it is suggested that the development of the service would now be appropriate.

Appendix II

Guidelines for Massage and Aromatherapy on the ALU

This document relates specifically to the practice of massage and aromatherapy for patients of the Adult Leukaemia Unit (ALU) at the Christie Hospital and needs to be read in conjunction with the Christie Hospital policies;

- **"Policy and practice for complementary therapies".**
- **"Appendix 1. Policy and practice for Massage and Aromatherapy".**

1.0 Introduction

The main body of information relating to massage and aromatherapy can be found in the Christie Hospital policy for Massage and Aromatherapy. However, due to the extra problems encountered by patients on the ALU it was felt necessary to expand on some safety issues relating to these patients within this document.

2.0 Evidence for massage and aromatherapy in haematological malignancies

Unfortunately, to press there is very little evidence looking at the benefits of massage and aromatherapy in this field (Tiffany et al 2001, Stringer 2000), it is assumed this is in part due to the minimal number of units on which such work is being carried out. However, workers in related fields (see main policy for massage and aromatherapy) have shown positive responses to such therapies.

3.0 Competent Practitioners

For a therapist to be able to practice on the ALU they must have undertaken training in a para-medical field (e.g. nursing or physiotherapy) and have been assessed as being of ***primary therapist*** level of competence. The levels of competence can be found in the general policy document. However, unless they have prior experience of working as a complementary therapist within a high dose therapy, isolation unit they will work with the responsibility level of a ***qualified therapist*** until they are felt to have obtained a suitable level of experience.

4.0 Concerns and Contra-indications for Massage

- Concerns listed in these guidelines are additional to those in the policy for massage and aromatherapy.
- Avoid patients with an undiagnosed rash. Once it has been diagnosed as none infective then the patient can be treated.
- Do not massage any patient with MRSA (check with the infection control team for confirmation of when a person is clear of the infection).
- Avoid massaging a patient who is actively bleeding.

- Show great caution if massaging an area with signs of prior bruising (it is possible to massage over a mild petechial rash for example if it is known to the medical team and the patient has since been given platelets). ALWAYS BE AWARE OF A PATIENTS PLATELET COUNT PRIOR TO MASSAGE.
- Whilst it is possible to massage a patient showing signs of sepsis, treat only peripheral areas of the body such as hands and feet.
- If the patient has had / is having TBI, be aware of potential side effects such as sore, irritated skin. If in doubt ask a senior therapist prior to starting a massage.

5.0 Safety and essential oils

Please use the following guidelines in conjunction with the hospital policy for massage and aromatherapy.

- Essential oils should not be used on any patients whose LFT's or U&E's are greater than or equal to 3 times the normal range.
- Store any carrier oils and essential oils in the fridge on the ALU.
- Any new oils require 'dampdusting' with an Alcowipe before using.
- All blends to be made up in the clinical room and labelled with the patient's name, the date and 'aromatherapy' (the actual prescription will be logged in the patients file).
- **Maximum** concentration of oils = 1.5%, for specific problems only (eg. Peripheral neuropathy).
- For general relaxation, or massage of larger areas (eg. Back) a maximum dilution of 1% is appropriate.
- Use an appropriately labelled, **sterile** container with lid for each patient prescription (eg. Urine sample pot!).
- Only take the patients own made up prescription into their room. The oils will have been chosen based on a prior conversation with the patient regarding needs / preferences etc. but if the blend is not acceptable to the patient then the blend is wasted and a new blend prepared.
- Dispose of any remaining prescription and container after use.
- If requested, only use an electric diffuser for essential oils in a patient's room – never candles. Always remove after approximately 30 minutes.

6.0 Hygiene

- Wear clean clothes and adhere to the ALU hygiene policy for nurses.
- Wear shoes for designated use only in the ALU.
- Ensure work surface is clean and dry in the treatment room prior to making up oil prescription.
- Oils (carrier and essential) to be stored in a clean fridge on the ALU and not to be removed from the treatment room during work hours.
- Wash and dry hands before mixing a prescription.

- Prescriptions to be made up in a sterile container (eg. A sputum sample bottle).
- Ensure oil bottles do not touch the sterile container.
- Ensure hands do not touch the apertures of bottles of carrier or essential oils when open.
- Wash and dry hands and put on a clean plastic apron prior to entering a patient's room.
- On exit from a patient's room, discard the remaining oil and container then wash hands immediately.
- Use clean towels for each patient.
- If used, clean electric diffuser thoroughly with an alcohol wipe prior to and immediately after use.

7.0 Consent

See overall policy document for basic guidelines regarding consent for therapy.

- Due to the unpredictability of the patients' condition when undergoing high dose chemotherapy, medical consent (written prior to the initial session) must be sought prior to each massage session.
- Prior to any consultation, liaison with the nurse responsible for that patient is necessary in order to familiarize the therapist with what is happening for them on that day (medically and personally).
- Ensure that the patient (and carers if appropriate) understands the therapy before they agree to the treatment.

Appendix III

Essential Oils Used in the Study

Name of Oil	Name of Oil
Angelica Root	Lemon
Basil (sweet)	Mandarin
Benzoin Resinoid	Marjoram (sweet)
Bergamot	Melissa True
Black Pepper	Myrrh
Cardamom	Neroli
Carrot Seed	Nutmeg
Cedarwood	Palma Rosa
Chamomile (German)	Patchouli
Chamomile (Roman)	Peppermint
Clary Sage	Rosemary
Cubeb Seed	Rose Otto
Cypress	Rosewood
Eucalyptus	Sandalwood
Frankincense	Spikenard
Geranium	Tea tree
Ginger	Valerian
Grapefruit	Vetiver
Jasmine Absolute	Yarrow
Juniper Berry	Ylang ylang
Lavender	

Appendix IV

Excluded Drugs List

Drugs used on the ALU, which are likely to affect prolactin levels:

- Dopamine blockers, e.g.: Nozinan
  Metaclopramide
  Domperidone

- Oestrogens

- Opiates

- Antidepressants, e.g.: Imipramine
  Amitriptyline
  Prozac

Drugs used on the ALU, which are likely to effect cortisol levels:

- High dose / long term Steroids

Appendix V

Introduction, Information and Consent for Study

Christie Hospital NHS
NHS Trust

Wilmslow Road
Withington
Manchester
M20 4BX

Hospital Tel: 0161 446 3000
Direct Tel: 0161 446 3524
Email: jacqui.stringer@christie-tr.nwest.nhs.uk
Internet: www.christie.nhs.uk

LETTER OF INTRODUCTION:

To Whom It May Concern:

On the Adult Leukaemia Unit there is a free aromatherapy service available to all patients. We are currently carrying out a study looking at the effects of this service and would appreciate your help in this matter. If you think you might be interested in participating in this project, there is an information sheet attached to this letter, which you may find useful to read.

If you are still interested please would you inform a member of staff and they will arrange for someone to come and discuss the study thoroughly with you.

Thank you for your time.

Jacqui Stringer
Nurse Aromatherapist (ALU)

Christie Hospital NHS
NHS Trust

Wilmslow Road
Withington
Manchester
M20 4BX

Hospital Tel: 0161 446 3000
Direct Tel: 0161 446 3524
Email: jacqui.stringer@christie-tr.nwest.nhs.uk
Internet: www.christie.nhs.uk

AN INVITATION TO TAKE PART IN A RESEARCH STUDY

TITLE OF STUDY: **EVALUATION OF AN AROMATHERAPY SERVICE ON A LEUKAEMIA UNIT**

INFORMATION SHEET

Introduction

The massage/aromatherapy service on the Adult Leukaemia Unit has been ongoing since March 1997. A previous audit has shown that the overall response to the therapy from the patients who made use of the service was positive. However, it is time for a formal evaluation of the service in order to determine whether there are any benefits to the patients.

What does the study involve?

The study involves you being randomised to one of these groups. Those randomised to two of the groups will receive a part body massage for a Monday or Thursday during the time that they are an inpatient on the ALU (with or without essentials oils, depending on which group), those in the third group will rest on their beds for an equivalent length of time for one week only).

Despite only two groups of patients receiving a massage, everyone in the trial will rest on their beds for twenty minutes prior to the treatment period. This will be followed by someone coming in to help you complete a short questionnaire (before and after the study period). Small blood samples will be taken from your central line before (and 4 times after) the same period. A therapist will then come and give those of you in the appropriate groups a 20-minute massage.

What if I consent to be in the study but change my mind?

If you want to pull out but still wish to take advantage of the weekly massage service offered on the ALU then that can be arranged for you.

Will what I say during any interviews be treated as confidential?

Anything you say during conversations with the therapist or anyone else connected with the trial will be confidential. All patients taking part in the trial will be identified by number only

Do any of my family/friends need to be involved?

Your family and friends do not have to be involved, but if you would like to discuss it with them that is understandable.

Is there any information regarding the study I need to consider?

There is nothing specific to tell you at this stage but if you have any further questions or concerns please do not hesitate to ask and we will do our best to answer the points fully.

Do I have to take part?

No. However, if you do decide to participate it will help us to evaluate whether the message service offered to the patients on the ALU is actually addressed

If I decide to take part, what do I do?

If you decide to take part, you will need to sign the consent sheet attached. It would be helpful if you could avoid visitors coming to see you on Thursday mornings and the early part of Thursday afternoons, as too much stimulation could alter the hormone levels in your blood.

Thank you for taking the time to read this information sheet.

Christie Hospital NHS
NHS Trust

Wilmslow Road
Withington
Manchester
M20 4BX

Hospital Tel: 0161 446 3000
Direct Tel: 0161 446 3524
Email: jacqui.stringer@christie-tr.nwest.nhs.uk

AROMATHERAPY ON A LEUKAEMIA UNIT

If you are interested in taking part in this study and have no further questions, please could you read and answer the questions below.

Thank you, Jacqui Stringer

CONSENT SHEET

I have read and understood the contents of the information sheet.

Yes ☐ No ☐

I have had the opportunity to read and ask questions about the study and received satisfactory answers.

Yes ☐ No ☐

I understand that everything I say will be treated with the strictest confidence.

Yes ☐ No ☐

I agree to take part in the study and understand that I may withdraw my consent at any time.

Yes ☐ No ☐

I agree to my GP being informed about my participation in the study.

Yes ☐ No ☐

Signed: .....

Appendix VI

Letter of Ethical Approval

your partners
in health

Manchester Health Authority
Gateway House • Piccadilly South
Manchester M60 7LP

Tel: 0161 236 9456

E-mail: enq@mchester-ha.nwest.nhs.uk
www.ManchesterHealth.co.uk

SOUTH MANCHESTER LOCAL RESEARCH ETHICS COMMITTEE

Phone: 0161-237 2392 **Fax: 0161-237 2383**
E-mail: christina.ireland@mchester-ha.nwest.nhs.uk

Mrs J Stringer
Nurse Aromatherapist
Adult Leukaemia Unit
Christie Hospital
Wilmslow Road
Manchester M20 4BX

19 January 2000

Dear Mrs Stringer,

Evaluation of an aromatherapy service on a leukaemia unit
Ethics Committee reference no SOU/99/238

Thank you for your letter of 30 December together with the amended information sheet and guidelines (Christie Hospital 'Policy and practice for complementary therapies' and 'Policy and practice for massage and aromatherapy'). I have considered the amendments and/or documentation submitted in response to the Ethics Committee's earlier review of your application on 2 December 1999. Acting on behalf of the Committee I am now able to confirm final ethical approval for the study.

Could you please send a copy of the separate guidelines for massage and aromatherapy on the Adult Leukaemia Ward, and also clarify whether there are any extra exclusion criteria arising out of any of the guidelines.

I have noted that Dr Morganstern has replaced Professor Scarffe as co-investigator.

The following items have been reviewed in connection with the study: ethical application form, protocol, amended information sheet, consent form, questionnaires.

The study should be started within three years of the date on which LREC approval is given. Would you please note that granting of ethical clearance does not confer management approval for the study. This can only be given by your employing authority. If you are employed by (or the study uses the facilities of) the Christie Hospital NHS Trust or the South Manchester University Hospitals NHS Trust, would you please contact either:

INVESTOR IN PEOPLE

Chief Executive: Neil Goodwin

- Christie Hospital R&D Database Administrator (446 3965), *or*
- South Manchester University Hospitals NHS Trust R&D Office (291 3914)

Insurance cover is required for any investigator who holds a substantive or honorary appointment with the University of Manchester and who is involved in a research study on volunteers or patients. If a project has been approved by an NHS LREC, it is only required to be reported to the Senate Ethics Committee in order that insurance cover can be provided. (If this applies to you or any co-investigator, please send two copies of the ethical application form and final approval letter to Dr T Stibbs, Secretary of the Committee on the Ethics of Research on Human Beings, Turner Dental School, Higher Cambridge Street, Manchester, M15 6FH, 0161-275 6689.)

You must notify any serious unexpected adverse events to the Ethics Committee. If any significant protocol amendments are proposed you must obtain prior approval from the Ethics Committee.

The Ethics Committee is required to monitor the progress of research studies and I will therefore be writing in about a year's time to ask you to complete a short review form.

Finally, please ensure that you quote the Ethics Committee reference number given at the top of this letter in any future correspondence.

Yours sincerely,

Dr W J Pettit
Chair

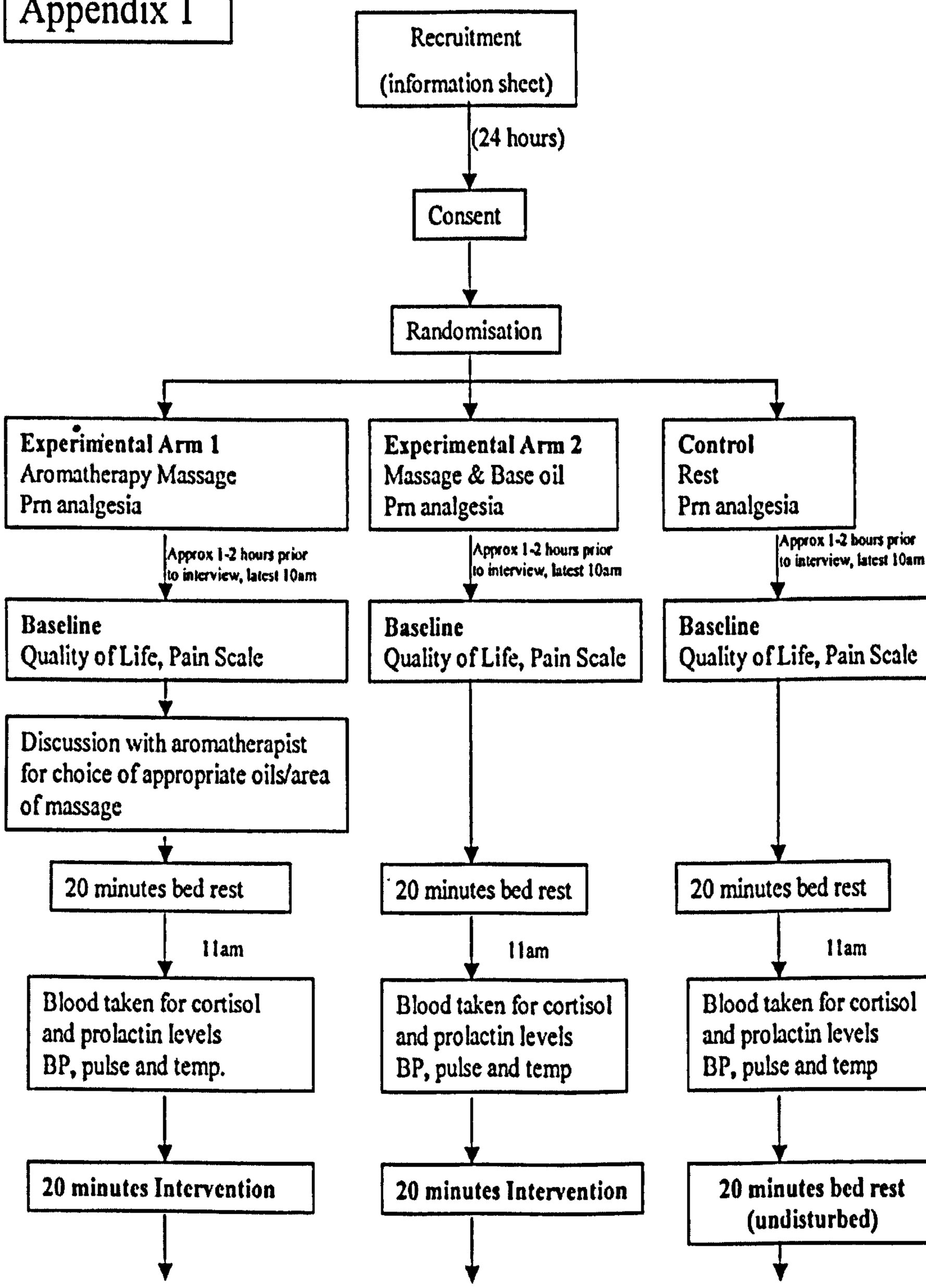
Appendix VII

Sessional Protocol Flow-Diagram

Evaluation of an aromatherapy service on a leukaemia unit

Appendix 1

Study Design



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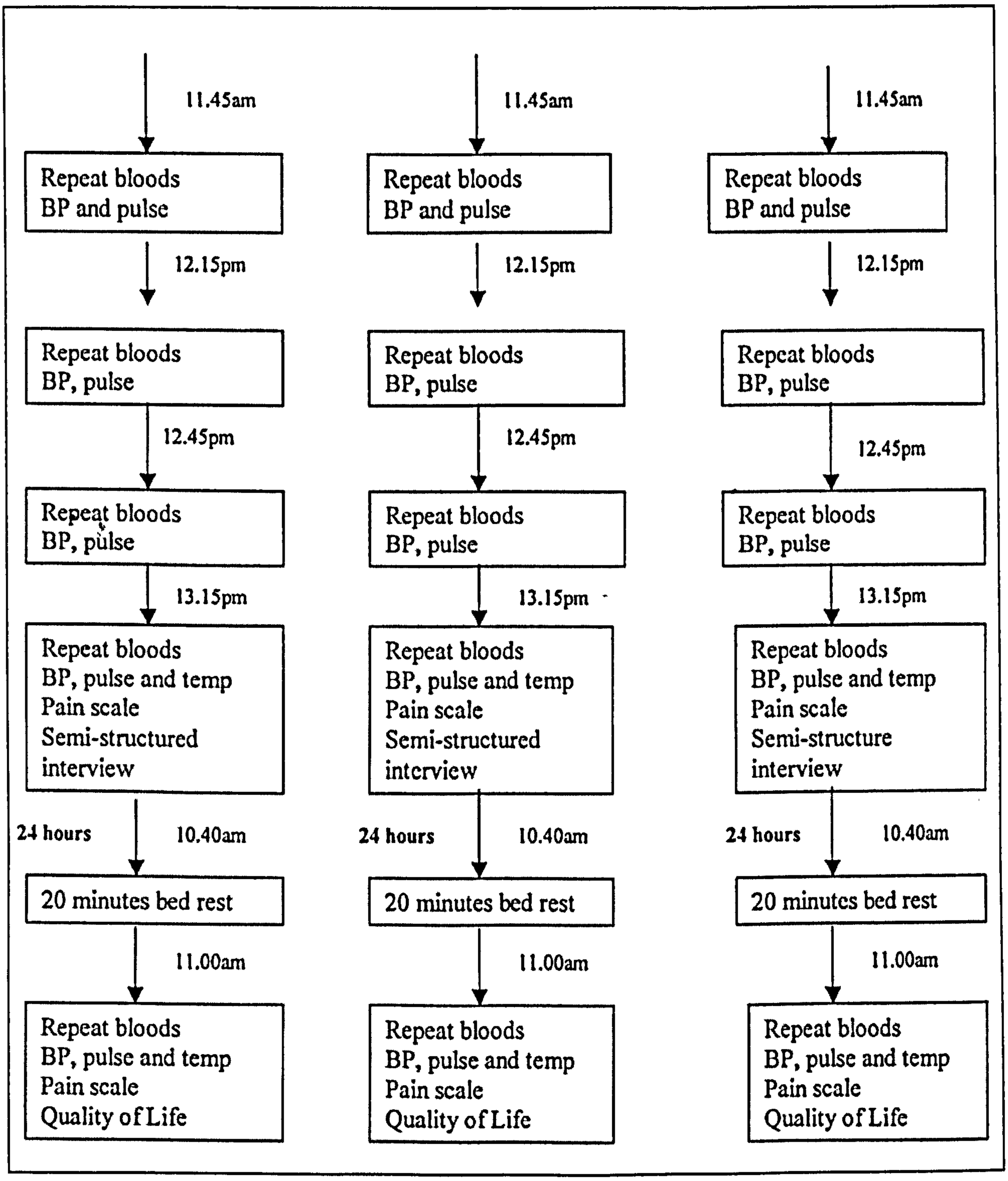
11.45am
Repeat bloods
BP and pulse
12.15pm
Repeat bloods
BP, pulse
12.45pm
Repeat bloods
BP, pulse
13.15pm
Repeat bloods
BP, pulse and temp
Pain scale
Semi-structured
interview
24 hours
10.40am
20 minutes bed rest
11.00am
Repeat bloods
BP, pulse and temp
Pain scale
Quality of Life
11.45am
Repeat bloods
BP and pulse
12.15pm
Repeat bloods
BP, pulse
12.45pm
Repeat bloods
BP, pulse
13.15pm
Repeat bloods
BP, pulse and temp
Pain scale
Semi-structured
interview
24 hours
10.40am
20 minutes bed rest
11.00am
Repeat bloods
BP, pulse and temp
Pain scale
Quality of Life
11.45am
Repeat bloods
BP and pulse
12.15pm
Repeat bloods
BP, pulse
12.45pm
Repeat bloods
BP, pulse
13.15pm
Repeat bloods
BP, pulse and temp
Pain scale
Semi-structure
interview
24 hours
10.40am
20 minutes bed rest
11.00am
Repeat bloods
BP, pulse and temp
Pain scale
Quality of Life

Appendix VIII

Study Proforma

AROMATHERAPY TRIAL

0220-JS
Mise 16/6/00

Table 1 - Registration

Hospital Number

Date of Birth (ddmmyyyy)

Gender — 1=Male, 2=Female

Eligible? — 1=No, 2=Yes

Exclusion Criteria (See Instruction Sheet) — 1=No, 2=Yes

Considered Unfit by Medical Staff

Past History of Psychiatric Illness (see notes P4)

Had Aromatherapy massage in the last 6 months

Past history of arthritic problems (see notes P4)

Aversion to massage therapy

LFT's and/or U & E'S >3 times normal limits

On Maxalon, Domperidone, Nozinan, High Dose Steroids in last week (see notes P4)

On Tricyclic/SSRI antidepressants (see notes P4)

- -

Consent given? — 1=No, 2=Yes

If no reason given?

AROMATHERAPY TRIAL

8220-AT
Rlse 16/6/98

Hospital Number |_|_|_|_|_|_|_|

Any alternative 'therapy' before now? Specify:
1=No, 2=Yes _____ |_|

y y m m

Any Aromatherapy/massage before now? Enter the appropriate date |_|_|_|_|

Date Randomised (ddmmyyyy) |_|_|_|_|_|_|_|_|

Randomised Arm |_|
1=Rest (control)
2=Massage with base oil
3=Aromatherapy Massage

Diagnosis: _____ |_|_|_|_| office use

y y m m

Date of Diagnosis |_|_|_|_|

Sites of Massage 1=No, 2=Yes

Head	Neck	Shoulders	Hands	Upper Back	Lower Back
|_|	|_|	|_|	|_|	|_|	|_|

Chest	Abdomen	Upper Legs	Lower Legs	Feet	Other
|_|	|_|	|_|	|_|	|_|	|_|

_____

Oils Used (See Appendix 1 for codes)

Oil 1	Oil 2	Oil 3
|_|_|	|_|_|	|_|_|

Criteria for choice of oil: |_|_|_| office use

Oil 1 _____

Oil 2 _____

Oil 3 _____

NB If information is not known or not applicable fill boxes with 9's

AROMATHERAPY TRIAL

0328-J0
Rlse 16/5/00

Table 2 - Baseline And Weekly Measurements

Hospital Number |_|_|_|_|_|_|_|

Date of Assessment (ddmmyyyy) |_|_|_|_|_|_|_|_|

Reason for Admission |_|
1=CT
2=CT + Transplant
3=Neutropoenic support
4=Septic episode
5=Other: _____

Karnofsky Performance Score (see notes P5) |_|_|_|

Room Number |_|_|

Baseline Full Blood Count (Normative data in appendix)

Hb |_|_|.|_| WCC |_|_|.|_| Platelets |_|_|_| Neutrophils |_|_|.|_|

Baseline LFT & U+E's (Normative data in appendix)

Na |_|_|_| K |_|.|_| Urea |_|.|_| Serum Creatinine |_|_|_|

Total Protein |_|_| Albumin |_|_| Globulin |_|_| Bilirubin |_|_|

Alk Phos |_|_|_| AST |_|_| ALT |_|_|_|

Baseline Microbiology in Last Week (see notes P5) d d m m y y y y

Date of Bacterial Infection |_| |_|_|_|_|_|_|_|_|

Date of Viral Infection |_| |_|_|_|_|_|_|_|_|

Date of Fungal Infection |_| |_|_|_|_|_|_|_|_|

Date of PUO |_| |_|_|_|_|_|_|_|_|

1=No Infection
2=Ongoing from previous date
3=Ongoing from new date
4=Resolved

Other Measurements

Prolactin |_|_|_|_| Cortisol |_|_|_|_| BP Systolic |_|_|_| / Diastolic |_|_|_| Pulse |_|_|_|

Sleep 1=No, 2=Yes

Well	Difficulty getting to Sleep	Kept Waking	Noises woke me	Felt poorly it kept me awake
|_|	|_|	|_|	|_|	|_|

Other reason specify: _____ |_|

NB If information is not known or not applicable fill boxes with 9's

AROMATHERAPY TRIAL

0330-JS
Mod 16/6/94

Table 2 - Baseline And Weekly Measurement cont'd

Hospital Number |_|_|_|_|_|_|_|

Temperature prior to message/rest (c) |_|_|.|_|

What time did patient wakeup? (HH:MM) |_|_|:|_|_|

Time Massage Started note time taken (HH:MM) |_|_|:|_|_|

Time Massage Started note time taken (HH:MM) |_|_|:|_|_|

Is the patient on any of these medications? (see notes P5)

1=No, 2=Yes

Maxalon |_| *

Domperidone |_| *

Nozinan |_|

Other Dopamine Antagonists |_|

Oestrogens |_|

Opiates |_|

Antidepressant (Tricyclic + SSRI's eg: Imipramine, Amitriptylne, Prozac) |_| *

Steroids |_| *

* Must be NO for initial trial entry, record details on Table 3

AROMATHERAPY TRIAL

0320-08
Mimo 16/6/98

Table 3 - ANALGAESIA AND PROLACTIN OR CORTISOL AFFECTING DRUGS FOR 1 WEEK PRIOR TO MASSAGE/REST

Hospital Number |_|_|_|_|_|_|_|

Date	Time	Drug Name	Office Use	Dose/Units	Type 1=Regular 2=Extra
d d m m y y y y	H H : M M				
d d m m y y y y	H H : M M				
d d m m y y y y	H H : M M				
d d m m y y y y	H H : M M				
d d m m y y y y	H H : M M				
d d m m y y y y	H H : M M				
d d m m y y y y	H H : M M				
d d m m y y y y	H H : M M				
d d m m y y y y	H H : M M				

NB If information is not known or not applicable fill boxes with 9's

AROMATHERAPY TRIAL

0220-JS
Misc 16/6/00

Table 4 - Likert Scale - Modified Brief Pain Inventory (Short Form)

- EORTC QLQ-C30

See Printed Forms

Baseline (pre trt)	LIKERT + EORTC QLQ-C30
2 hour set (imm. post trt)	LIKERT only
24 hour set of each (next day)	LIKERT + EORTC QLQ-C30

Repeat following week if patient returns

AROMATHERAPY TRIAL

0220-JH
Misc 16/6/00

Table 5 - After Start of Intervention

Hospital Number |_|_|_|_|_|_|_|

Date of Intervention (ddmmyyyy) |_|_|_|_|_|_|_|_|

Measurements at 30 mins note time taken (HH:MM) |_|_|:|_|_|

Prolactin |_|_|_|_| Cortisol |_|_|_|_| BP Systolic |_|_|_| / Diastolic |_|_|_| Pulse |_|_|_|

Measurements at 1 hour note time taken (HH:MM) |_|_|:|_|_|

Prolactin |_|_|_|_| Cortisol |_|_|_|_| BP Systolic |_|_|_| / Diastolic |_|_|_| Pulse |_|_|_|

Measurements at 1 hour 30 mins note time taken (HH:MM) |_|_|:|_|_|

Prolactin |_|_|_|_| Cortisol |_|_|_|_| BP Systolic |_|_|_| / Diastolic |_|_|_| Pulse |_|_|_|

Measurements at 2 hours
See notes P5 note time taken (HH:MM) |_|_|:|_|_|

Prolactin |_|_|_|_| Cortisol |_|_|_|_| BP Systolic |_|_|_| / Diastolic |_|_|_| Pulse |_|_|_|

Measurements at 24 hours
See notes P5 note time taken (HH:MM) |_|_|:|_|_|

Prolactin |_|_|_|_| Cortisol |_|_|_|_| BP Systolic |_|_|_| / Diastolic |_|_|_| Pulse |_|_|_|

NB If information is not known or not applicable fill boxes with 9's

AROMATHERAPY TRIAL

0220-JH
Misc 16/6/98

Table 5 continued - Interview

Semi-structured Interview at 2 hours

Hospital Number |_|_|_|_|_|_|_|

Time started (HH:MM) |_|_|:|_|_|

Introductory Statement:

1) Could you tell me about the things that you liked and disliked about the session you received?

Prompts: First the things you liked:

And the dislikes:

How do you feel now:

NB If information is not known or not applicable fill boxes with 9's

Appendix IX

Karnofsky Performance Status Scale

Reporting Clinical Condition of Bone Marrow Recipients in Terms of Activity Status:

Able to Carry on Normal Activity; No Special Care is Needed	**100%**	Normal: no complaints: no evidence of disease
	90%	Able to carry on normal activity
	80%	Normal activity with effort
Unable to Work; Able to Live at Home; Care for Most Personal Needs; a Varying Amount of Assistance is Needed	**70%**	Cares for self; unable to carry on normal activity or do active work
	60%	Requires occasional assistance but is able to care for most needs
	50%	Requires considerable assistance and frequent medical care
Unable to Care for Self; Requires Equivalent of Institutional or Hospital Care; Disease may be Progressing Rapidly	**40%**	Disabled; requires special care and assistance
	30%	Severely disabled; hospitalisation indicated, although death not imminent
	20%	Very sick; hospitalisation necessary
	10%	Moribund; fatal process progressing rapidly
	0%	Deceased

Appendix X

EORTC QLQ C-30 (Adapted) and Letter Giving Permission for Adaptation

EORTC QLQ-C30 (version 3, with modification)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

HOSPITAL NUMBER :

DATE:

		Not at All	A Little	Quite a Bit	Very Much
1.	Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2.	Do you have any trouble taking a long walk?	1	2	3	4
3.	Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4.	Do you need to stay in bed or a chair during the day?	1	2	3	4
5.	Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

During the past 24 hours:		Not at All	A Little	Quite a Bit	Very Much
6.	Were you limited in doing either your work or other daily activities?	1	2	3	4
7.	Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8.	Were you short of breath?	1	2	3	4
9.	Have you had pain?	1	2	3	4
10.	Did you need to rest?	1	2	3	4
11.	Have you had trouble sleeping?	1	2	3	4
12.	Have you felt weak?	1	2	3	4
13.	Have you lacked appetite?	1	2	3	4
14.	Have you felt nauseated?	1	2	3	4
15.	Have you vomited?	1	2	3	4

Please go on to the next page

During the past 24 hours:	Not at All	A Little	Quite a Bit	Very Much
16. Have you been constipated?	1	2	3	4
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21: Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall health during the past 24 hours?

1	2	3	4	5	6	7
Very poor						Excellent

30. How would you rate your overall quality of life during the past 24 hours?

1	2	3	4	5	6	7
Very poor						Excellent

(Note: This is not a standard version of the QLQ-C30, but has with permission been modified specifically for this study).

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Letter Giving Permission for Adaptation of EORTC QLQ C-30

EORTC
European Organization for Research and Treatment of Cancer

International Association under Belgian Law

EORTC QLQ-C30 USER'S AGREEMENT

The EORTC Quality of Life Study Group grants permission to Ms. Jacqui Stringer to employ **a modified version** of the EORTC QLQ-C30 in an academic quality of life study entitled: "*Evaluation of an Aromatherapy Service on a Leukaemia Unit*".

The Study Group will supply Ms. Jacqui Stringer, with: (1) the QLQ-C30 in the currently available languages; and (2) the standard algorithms for scoring the QLQ-C30. Use of the EORTC QLQ-C30 in the above-mentioned investigation is subject to the following conditions:

1. Ms. Jacqui Stringer confirms that this study is being conducted without direct or indirect sponsorship or support from pharmaceutical, medical appliance or related, for-profit health care industries.

2. Ms. Jacqui Stringer will not modify, abridge, condense, translate, adapt or transform the QLQ-C30 or the basic scoring algorithms in any manner or form, including but not limited to any minor or significant change in wording or organization of the QLQ-C30. **Except for the agreed upon change of text from "During the past week" to "During the past 24 hours", to be used solely for the above-mentioned study.**

3. Ms. Jacqui Stringer will not reproduce the QLQ-C30 or the basic scoring algorithms except for the limited purpose of generating sufficient copies for its own use and shall in no event distribute copies of the QLQ-C30 to third parties by sale, rental, lease, lending, or any other means. Reproduction of the QLQ-C30 as part of any publication is strictly prohibited. **Any copies made for its own use shall clearly state: "We are grateful to the EORTC Quality of Life Study Group for granting us permission to use a modified version of the EORTC QLQ-C30 in this study".**

4. Analysis and reporting of QLQ-C30 data by Ms. Jacqui Stringer should follow the written guidelines for scoring of the QLQ-C30 as provided by the EORTC Study Group on Quality of Life.

5. This agreement holds for the above-mentioned study only. Use of the QLQ-C30 in any additional studies of Ms. Jacqui Stringer will require a separate agreement.

Signed and dated by:

Karen West

4 August, 1999
Karen West
EORTC Quality of Life Group

Signed and dated by:

Ms. Jacqui Stringer

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E-mail: eortc@eortc.be

Appendix XI

Brief Pain Inventory (Modified)

MODIFIED BRIEF PAIN INVENTORY (SHORT FORM)

Hospital number:_____ Date:_____/_____/_____

Time filled in (HH:MM):_____ Pre/Post:_____

1) Do you think your pain is **Better / Worse / The same as last week?**
Please circle your choice.

2) How often have you had pain in the last week?
Constantly / Most of the time / Some of the time / I have had no pain
Please circle your choice.

3) Please rate your pain by circling the one number that best describes your pain at its **worst** in the past 24hrs

0 1 2 3 4 5 6 7 8 9 10
No pain — Pain as bad as you can imagine

4) Please rate your pain by circling the one number that best describes your pain at its **least** in the past 24hrs

0 1 2 3 4 5 6 7 8 9 10
No pain — Pain as bad as you can imagine

5) Please rate your pain by circling the one number that best describes your pain on **average** in the past week

0 1 2 3 4 5 6 7 8 9 10
No pain — Pain as bad as you can imagine

6) Please rate your pain by circling the one number that tells how much pain you have **right now**

0 1 2 3 4 5 6 7 8 9 10
No pain — Pain as bad as you can imagine

7) Please rate your pain by circling the one number that tells how **distressed** you have been by your pain in the past 2rhrs

0 1 2 3 4 5 6 7 8 9 10
No distress — Completely distressed

8) In the past 24hrs, how much relief have pain treatments or medications provided? Please circle the one percentage that shows how much relief you have received.

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%
No relief — Complete relief

9 a) Circle the number that describes how during the past 24hrs, pain has interfered with your: **General activity**

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

b) **Mood**

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

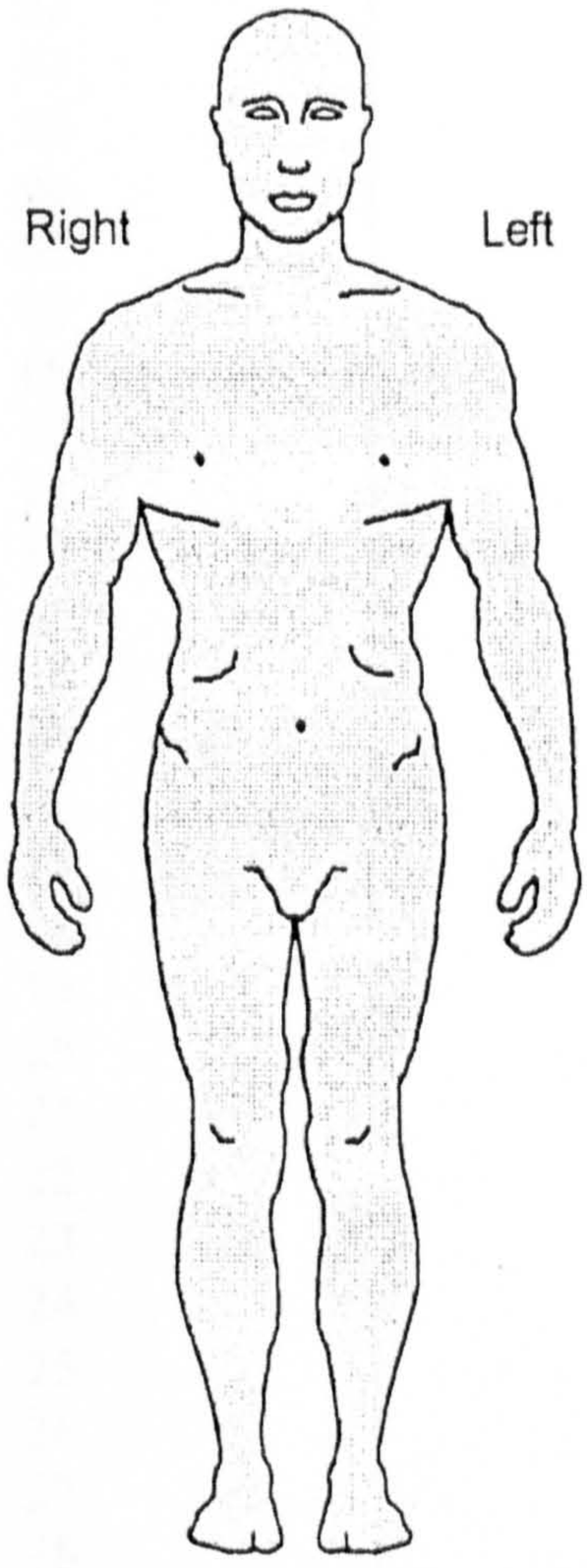
c) **Relations with other people**

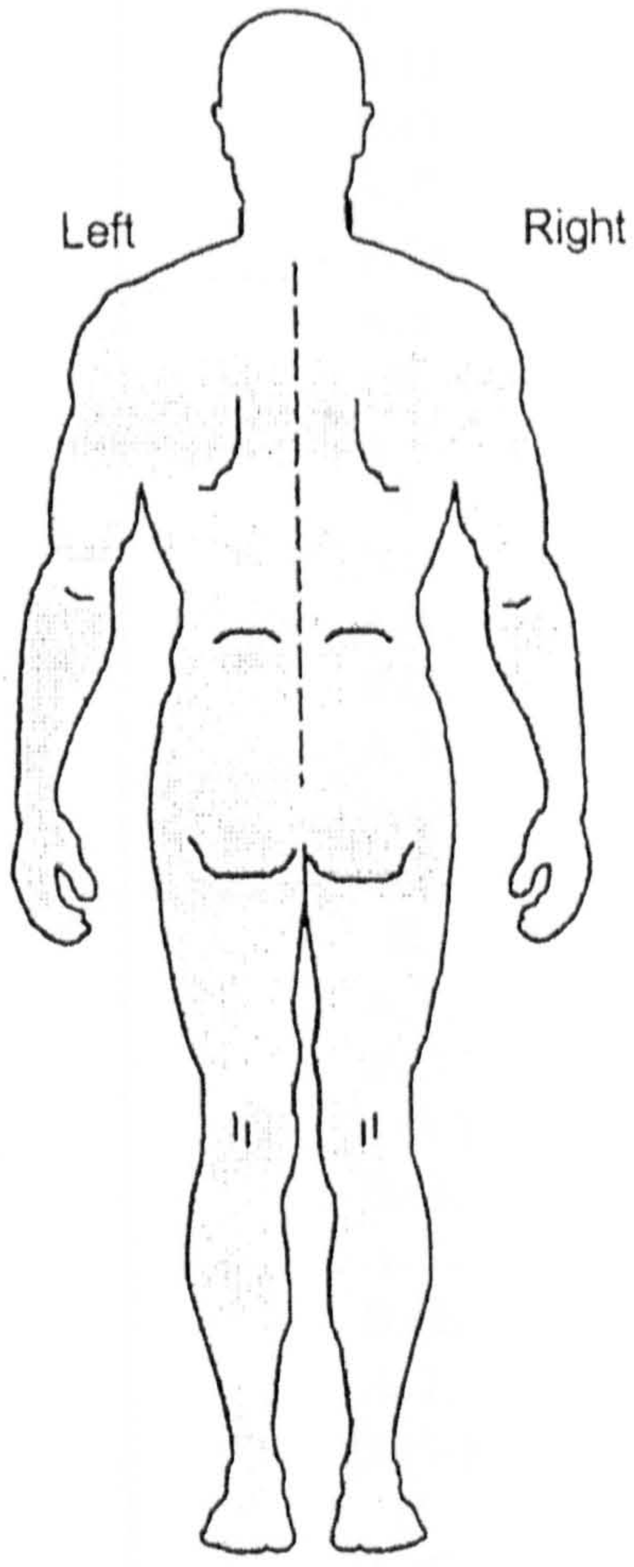
0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

d) **Sleep**

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

On the diagram, shade in the areas where you feel pain. Put an **X** on the area that hurts the most





Appendix XII

Pseudonyms with Corresponding Trial Number and Arm

Trial Number	Pseudonym	Trial Arm
01	Penny	R
02	Nocl	R (V)
03	Lucy	R (V)
04	John	B.O.
05	Gary	B.O.
06	Carol	A.T.
07	Frank	B.O.
08	Ann	A.T.
09	Cyril	R
10	Ian	A.T.
11	Alan	R
12	Nancy	B.O.
13	Diane	A.T.
14	Tom	B.O.
15	Paula	A.T.
16	Brian	B.O.
17	Wendy	A.T.
18	Roger	R
19	Jean	A.T.
20	Isabel	B.O.
21	Beryl	R (V)
22	Molly	B.O.
23	Norma	A.T.
24	Alice	B.O.
25	Fiona	A.T.
26	Colin	R (V)
27	Jill	R
28	Helen	A.T.
29	Paul	B.O.
30	Mike	A.T.
31	Megan	B.O.
32	Teresa	R (V)
33	Emma	R (V)
34	David	B.O.
35	Stuart	R
36	Ken	A.T.
37	Enid	A.T.
38	Olga	B.O.
39	Betty	R

Appendix XIII

Thematic Analysis, Raw Data

1. Psychological issues

- Positive emotions

Peace & quiet (Penny)
Calming, peaceful, felt better in myself, helped motivate me, relaxing, helped with emotional stress (Noel)
Great, fine, relaxing, the massage was very gentle and it was just what he needed, it was softer then other massages he's had. (John)
Yes. ...I really enjoyed it. I felt it was very relaxing, extremely gentle. I was surprised about that. It was just a nice experience ... (Gary)
It was very nice, gentle and it was very, very relaxing and pleasant, it was lovely, "that was wonderful, it allows you to completely forget everything for a while"(Carol).
It was very gentle. I was comfortable. It was pleasant, soothing. I suppose you could say it was relaxing as well. It was my first real experience, like I said, so I didn't really have a baseline for it. So altogether it was a nice experience.// I feel fine, although with the situation I'm in at the moment I do a lot of relaxing and sleeping, so it's something else that, if I'd have been bustling around I would have probably felt more benefit from it, whereas, as it is I spend most of the day relaxing, so it has not had a great impact. But like I say, it was very pleasant. (NB. Cortisol levels dropped).
(Frank)
I didn't dislike anything. I liked the calm, the peace, the feeling, the smell, everything, everything about it. There was nothing I disliked, it was blissful, I'm feeling really relaxed, really good. (Ann).
There might be value in actually having a period every day where you did actually get no disturbance, because you do feel people are always coming in demanding things of you, especially in the mornings, mornings are very bad (Cyril).
Well I found it very relaxing; I was amazed at how relaxing it was. 'You said you were amazed, did you not expect it to be?' No, I didn't expect it to be, no. I thought it would be a strange experience really, but it wasn't. I would have certainly had it before if I had known about it, what it was, I've had trouble for the past 18 months with pain in my legs and I think it would have been a great help. 'You said it was relaxing, do you still feel relaxed?' Yes. (Ian).
I did find it very, very relaxing, yes, it was a very nice sensation, it was very relaxing and I checked it out with Jacqui, I said 'is it okay if I talk or you know?' because I'm one of these people who doesn't like sitting in silence, and she said 'no, if you want to talk you talk' I felt comfortable talking through it, but no, I enjoyed the whole experience, I liked it very much so. Yes, it was good, good, good, good. (Nancy).
Well, it was so relaxing, really relaxing; I fell asleep (Diane).
Apart from the fact that I nearly fell asleep which is always nice, I felt quite relaxed, I must admit. I quite liked the quiet because it was pretty quiet at the time (Tom).

I enjoyed all of it; it was just really relaxing. Just lying here being pampered I suppose. I love having my feet and legs massaged anyway (Paula).
It was so relaxing. Brilliant, just a nice feeling, just a brilliant feeling – especially being a woman, if it had been a man I don't think I would have taken it on. That's all I can say really – excellent (Brian)
Just made me feel good, very, very relaxed with a sense of well-being. I left her looking very peaceful and relaxed. At the end of the final bloods M was still (miraculously) looking drowsy and said that after Kay had finished with her she was going to have a snooze - I hope she managed it. (Wendy).
It felt relaxing – not too intrusive, just nice really. I like my feet being tickled anyway. I feel it has been beneficial, it passed time as well in a pleasant way; it is very soothing. (Jean)
I liked it when she sort of fingered your spine. That was quite nice, then she did my head and that was quite nice as well. I'm just very relaxed. (Isabel)
Well I didn't dislike anything about it, I found it quite beneficial, and I found it quite positive. As it happened I was quite weary before she came in anyway. I did visualize the chemo working; it's not quite such a traumatic thing – more a Friendly thing, working on my behalf assisting the bone marrow going round absorbing all the bad cells. Relaxed, quite a bit better, it's given me something to focus on and the fact that she's taught me, instead of just lying there she said try and visualize, I found quite constructive. It's something that if I feel a bit worked up and panicky which I do do, I can lie there and visualize it doing me good. So I'm probably better for it, before I was a bit down in the dumps, a bit negative. (Beryl)
It was very relaxing right from the start because I fell asleep while she was doing it. At the beginning I was aware and I was just drowsy and then I went fast asleep. I'm normally not very relaxed. I'm a bit of a stiff person, usually jumpy, she told me what to do to relax my legs and I stayed like that for a long time. (Molly)
I liked everything about it. I liked touching your feet, I liked the fact that the room was really calm; I liked the fact that I was calm as well. I wanted to tell you. One of the good things was – can I just see if I can do it now? While she was doing it and the relaxation period afterwards, I went like that [sounds of breathing] it was like really dark and peaceful. I'm not saying it's not happening now – it could be because you're in the room and I'm conscious of trying to ? bring you. Did you used to breast-feed your children – I mean everybody's different but when I used to breast-feed – not the let-down reflex with the milk. I used to put ???? on [big sigh] – and it was so peaceful. And I think that's what I've been trying to do since I came here so it'll be interesting to see if it continues won't it? Because I was doing it while she was massaging me and when she laid me down and each time I breathed it happened but I don't think it's happening now. (Norma)
It's nice and relaxing because sometimes when you're in a situation like this you can't really get in to a book, you don't really sometimes want to concentrate on something, whereas when you're just being massaged you don't have to concentrate on anything, you know mentally it's just relaxing, you can just let go and relax. (Alice)
I liked it all, how relaxing it was and I couldn't believe how sleepy I was after and when it was happening, it was lovely. The whole thing was lovely. It felt so relaxing, the whole thing, smells beautiful, it was lovely. You were able to put aside your anxiety about being touched? Yes, it was super, it would never stop me doing it again, it was lovely. The whole thing was lovely and it's so nice to be offered something like that when you're here. The experience was lovely. (Fiona)

Well, nice to just rest up for an hour, can't think of anything I disliked about it. No, well I suppose there's not a lot to dislike really; I do a lot of resting up anyway. (Colin)
Liked the touch and smoothness on feet and skin. Gentle like ripples. 2. Found it relaxing and calming. "Feel relaxed. Noticed when went to bathroom, noticed how relaxed she was (less tension in shoulders), 'I hadn't realised how tense I'd been before.' (Helen).
Liked everything about it. Very soothing, could have nodded off, closed eyes, didn't actually sleep. Liked sensation of having oil put on. (Paul)
Very relaxing, relaxed my mind it was hypnotic, went into my own world. Took my mind off my nausea, sickness disappeared for a while. Now he feels 'emotionally stable, fine, no worries'. (Mike).
You enjoyed having your feet massaged? 'Oh yes!' Feels; at ease, relaxed. (Megan)
She gave me something to focus on which I did and err, I just liked the thought of the ……?…….. 'Clearly explained. You just had the rest? Can you think of any think of anything else you liked?' All of it really, it was a good conversation as well after that…..(explained the visualization process to the Research Assistant; chemotherapy clearing out leukaemic cells & watching good cells grow – like trees/fields of wheat. Mini discussion about that between the two of them, RA confirming that that was good). 'And the smiles, I can tell you seemed to find that good…' Yep. (Blood levels went down and continue to go down). (Emma)
She enjoyed doing the visualisation – she gave herself a challenge as she has one big prickly weed in her garden, which she hasn't been able to remove, and she saw herself getting rid of it. I encouraged her to use the technique whenever she felt like it as it obviously worked for her. – Bloods went down and stayed down. (Emma)
I certainly feel more invigorated. I like that invigorated feeling, it's a pleasant feeling. 'Describe how you feel now'. I feel, let me think how I feel, I feel very relaxed. (Nb. Bloods very erratic as he was on 50mg Prednisolone! ? given during post session bloods)(David)
I enjoyed the aromatherapy on my feet etc. it was very relaxing and very soothing I had no dislikes at all. I thought it was first class, very relaxing, and that was it. No, it was quite relaxing but I wasn't stressed before hand so ... I quite enjoyed it. I think it makes a difference if you need it……?….. I haven't had any particular problems ….?…….many people do. The massage was very, very gentle. You can't improve on excellent. (Interestingly this gentleman's blood levels went up ? case study) (Ken).
Obviously the massage, the relaxation of it, that's about it really, it's just calming, relaxing and it felt nice. Things were well explained (oh yeh,) that was something you liked about it (yeh, yeh), I knew exactly what was going to happen. (Enid)
I found that extremely relaxing, it was lovely, really excellent. Extremely relaxing, it was a lovely experience. I felt extremely chilled out afterwards, it was just that extra little special feeling. (Olga)

- <u>Negative emotions</u>

Boring (Penny),
It's not much different to what I do each day anyway so… Was foetal and quiet by the end of blood taking sessions (Lucy)
Honestly, I don't feel that much different (Gary)
The only thing I didn't like was it finishing (Ann).

I would say that you are doing it at a set time and it is better to be doing it just whenever you are in the mood. I sat and read poetry but then I do that when I am in the mood, but this time as we were doing it at this period and as I said, that's not as good as doing it when you would have done it spontaneously. That's right. Too regimented. 'Anything positive about it at all?' Not really, because the trouble is, I mean, you're doing it all the time in here anyway, and that's the only thing you can do in here, is rest. You haven't got anything to do, so I spend most of my time reading books as it is, so I would have been probably reading the newspaper If I hadn't have been doing what I was doing. Well I feel probably more agitated than normal and that's not the resting bit at all, it's the bloods and the fact that people are continuously in and out. What is it about having the blood taken that you don't like? I just don't like it. I don't like seeing my blood pouring out. It feels like it's being wasted, it's precious. I think that's probably what it is. Especially when your life's in a bit of a poor show anyway (Cyril).

From a personal point of view, the rest period wasn't significant. I think I would rather, under the circumstances, have gone straight into the aromatherapy. 'You said the rest period wasn't significant, what did you mean by that?' Well, I'd just had some bad news before we started, so it was very difficult to relax, it was difficult to sort of get my head together. 'And you were told to relax at a certain time? Were you told like, this is your rest period now or did you decide when you were having your rest?' No, I was just told I'll be back in half an hour, did I want any advice on relaxation technique, I said I'll just go to sleep. 'Did you manage to get to sleep?' Yes. (Alan).

It took a little time to get her ready as (quite understandably) she felt self conscious about stripping off (which she did behind a blanket screen). Once she was settled we commenced - or at least I gently put my hands on her back, and she screamed! Apparently she does not like oil..... I was becoming aware that despite her enthusiasm for my work and obvious love of essential oils she was in fact extremely ill at ease with the massage and she chattered all the way through it telling me how all her friends would be amazed if they could see her now - disbelieving almost (she mentioned in passing during a subsequent session that she had a problem with touch!!!) (Nancy).

There's nothing I can say that I haven't liked. I was a little bit light-headed after; I think it was that I was so relaxed (Diane).

I had that machine on whilst I was having it and that was right next to my head and I could hear it and I don't like that machine very much. Apart from that everything was wonderful, Oh the Alcowipes, they are horrible, yes that was the worst bit It just makes me feel ('It does actually make you feel ill') not very well, yeh. Something needs to be done about that (Tom).

The blood taking went all right - just one little one at the 12.15 collection when she commented that she soon would not have any left - a real concern or a joke I wonder? We'll see (Paula).

Towards the end of the massage she did start talking about how angry all her family were about her illness - especially her husband as they are regular church goers and he seems to see it as some divine punishment. (Wendy)

'Didn't like all them blood tests.' This has to be the most remarkably event free session so far - mainly due to A's quiet acceptance of what was happening to him (despite hating the smell of the Alcowipes!) (Roger)

It wasn't long enough. I thought it could have gone on a bit longer and have other parts of your body done as well. It takes you about five minutes to relax. Next time I

have a massage maybe I'll relax earlier, knowing what to expect. It's slightly uncomfortable to have the blood tests, a bit more of a nuisance really, just the smell of the Alco-wipes. (Short lived relaxation – friend started asking about why Jean couldn't have more Chemotherapy!)(Jean)

She'd gone and come back, she was doing my blood. I said have you finished "Oh Yes" she just caught me with the Alco-wipe and it woke me up. * Note associated rise in cortisol – dropped again straight away. I heard her asking him (the staff nurse when he was taking her blood for me) how long it would take to regenerate the blood. I take it that although she had not mentioned it to me this was an issue for her. Anyway, Steve reassured her that the small amounts we taken would not be "noticed" by her body. (Molly)

I'm not so calm as I was when it was going on. I suppose because there is so much going on it's like out of your mind again now, busy and bustling again. (Norma)

I know because of my circumstances it couldn't have been any deeper. I do like a deeper massage normally but that was perfect for my situation now. I've got all my tubes in my top shoulder so I couldn't have had it any deeper. Alice appeared quite calm and didn't get too wound up when some blood dropped on her (white) trousers... although as I came back in for the third time she did make the comment that she thought all 4 post session bloods were going to be taken at once – I give up, I think that this trial is turning into the newest comedy; 'Carry on Research! (Nb. Alice's levels dropped and stayed down despite this and the disturbances in her session) (Alice)

The only thing which caused her difficulties were the smell of the Alcowipes (nothing new there) but she made a very good point – she said that it was taking away the lovely smells of the oils, how much of an affect is the I wonder? (Cortisol dropped but not prolactin) (Fiona)

Couldn't smell oils - if I went out of room and came in I would smell it. The only time I could smell it was when I bent over my feet - knew it was in the air, but not very long. Noise outside (people talking and walking about), hard to concentrate on relaxing the body. In a quieter situation, could have relaxed more - soothing music might have helped too. (Helen).

Alchohol Wipes when doing blood makes me a bit heady, something seems to build up in my head. *Commented that Alco-wipes gave him a headache – more sensitive to it the more I used it. (Paul)

During QOL complained of big problems sleeping and I noticed he acknowledged lots of problems usually associated with stress e.g. tense, lack of memory/concentration, poor sleep etc. also still having problems with nausea and vomiting [just vomited before I came in the room but still wants to go on with it]. *During second and third post bloods started talking about lack of control, e.g. not wanting to buzz for cups of tea but frustrated because he couldn't go and get one. Not having a choice re when BP etc done/drugs brought into room – making him feel niggly. Said he felt better after talking about it. *?? Raised his cortisol levels talking about frustrations (Mike)

I guess that's the Alco swabs, the smell of them absolutely turns me over! And there have been rather a lot of them in the last few minutes! (Teresa)

'Can you describe where, how you feel relaxed?' Just am really, not like I was yesterday. I've not been allowed to go out of this place; I get stressed out just sitting in here. When we filled in the QLQ, she acknowledged feeling tense and unable to concentrate on things – although appears able to sleep. She has burning of her hands and feet through the Cytosine, so I suggested making up a lotion for her to reduce the

inflammation. Prior to me taking the blood she had a 'phone call from her family which appeared to be about "family hassles" – kids. Enid recognised that she also felt frustrated because normally she smokes and she didn't want to use patches – also because of the beautiful weather she would normally be outside. She also explained that she wasn't getting many visitors [next one is Saturday] although she only lives in Oldham, because they said they get bored – again Enid pointed out that she wishes she could go for a walk in the conservatory with her visitors. (Enid)
It's usually people poking and prodding you, taking blood and, unpleasant things happen. (Olga)
She also told me how her nephew has been held up at knifepoint for his car! [Which they took]. Her daughter is dyslexic [21yrs] and has post viral syndrome – so we talked about that and her youngest son [9yrs] gets bullied at school. (Olga)
Anything you disliked? What things did you not like about it? The smell of the things that ....?..... The smell of wipes? Yes. When you were having your blood taken you mean? Is there anything else that you disliked? (Betty)

- <u>Attitude of the patient</u>

Bored and counting the days, Interesting that when she was asked about her pain on QLQ she said she had none, yet when filling out the pain scale she acknowledged having some pain. Also at the beginning of the interview she said that her knees were the problem, yet when asked to pinpoint the pain she identified her stomach. Quite reticent/lethargic. Doesn't want to be here and didn't want to talk, therefore not easy to speak to. Penny tended to answer the QLQ questions in a somewhat contradictory manner, for example she graded herself as having no pain on the QLQ but then when we filled in the pain scale she graded herself as having some pain. Equally, with the SSI, there was nothing she disliked about the session and she would have a rest session again because of the peace, but then she said she wouldn't because it was boring! (Penny).
As a complete contrast to previous patients, Noel's attitude towards his situation was far more in the victim role and he appeared to need far more nurturing then any other up to press, interestingly, he has been 'abandoned' by his wife and has no dependents relying on him at home. Nb. He also expressed anger at situation, consultant, banging doors etc. (Noel).
Claustrophobia. John evaluated himself as having no pain and yet he had been complaining of very painful shoulders (John)
Patient very well and reassures me he's very food at relaxing and has decided to chill rather than climb the walls! – Does cross-stitch and writes poetry. 'This man certainly appeared very chilled'. (Frank).
QLQ – Interesting session, very open – amazed we were asking about her overall health "I've got cancer" she responded in between guffaws of laughter (Ann).
You would have more control then wouldn't you, if you had a chance to put the 'do not disturb' out. Obviously it has got to be within reason, but you do feel you are at the mercy of everybody who wants to come and do something at you all the time. Even if it's just giving you your lunch or whatever, it's not quite the same as you going down getting your lunch at home whenever you get hungry. The worse thing about being in these rooms is actually the fact that you have got so little control. I mean you can't do anything without asking somebody to do it, you know you really are so dependent on other people all the time. Talking about having bloods taken;

Then again, it's the control thing, I like to feel in control and again when they are doing that you are a passive thing aren't you. You just have to sit there while this is all done to you. The whole thing of being in these rooms is that you have no control, or not enough control. I mean, I know it's going to be like that but, it makes you feel like I'm just sitting here, I'm just the patient, it's still done to you, isn't it. It's not - major stress or anything like that, it's just another we're coming to take bloods, it's just on and on and on isn't it. 'Do you think you are talking lots now about not being in control and being passive and having things done to you, do you think that is a result since you have been ill or is that how you are as a person?' Oh no I'm like that inside as a person, yes. That type of person generally, but obviously it's intensified by being in here, yes. Cyril stoically battled his way through the qolq much of which he (quite reasonably) thought to be somewhat redundant - interestingly he took charge of this procedure himself unlike all the other subjects who were happy to let me do the writing (Cyril).

Alan, despite having a positive attitude appears to be encountering lots of problems and is now finding it hard to maintain his positivity, during the blood taking sessions Alan reiterated time and time again how hard it was for him to accept having to tolerate another chest drain and how difficult it was to remain positive in the face of adversity (Alan).

Proactive in helping herself; 'Well, the only oils that I actually use at the moment are lavender and tea tree, and I don't put them on my skin, I put them on my blanket, so that they are in the atmosphere, and the tea tree, that's a natural antiseptic. See, I'm very low at the moment and I'm more susceptible to infection, so to try and combat that I'm using the tea tree and I also soak my toothbrush in water and 2 drops of tea tree oil'. Nancy sees her leukaemia as a message to change. One other interesting point was that although Nancy was not yet fully comfortable with the blood taking aspect of her stay in the unit (though was at the same time at pains to reassure me that she didn't mind me taking it) she always took her own blood pressure (with an automated BP machine), perhaps this, and her choice to be in the trial were signs of her trying to maintain some control over her life. I was coming to realize the Nancy was in many ways a wise person - especially in the way she was dealing with her disease. She is also very open in expressing her emotions, if something worries or upsets her she will shed tears (though this did not happen on the day of the trial), which makes her appear very emotionally labile and her reactions to things can be slightly bewildering. (Nancy).

Diane has been battling with lymphoma for 17 years. To say she was in denial would be to put it too strongly but during the qolq session her focus was definitely on how she felt, her disease was not mentioned - even in passing and her health & qol she rated at 6 & 7 respectively (excellent). I also noticed she was very chatty but that if something happened which concerned her then she had a nervous laugh which would 'pop out' - this would happen quite often, as a contrast to which she was insistent that she felt no tension or worry in the hospital - a lady who was perhaps not acknowledging her own feelings - a good barrier in order to maintain sanity or a dangerous compression chamber in the making? Hopefully we will get some indication from the blood results (This turned out to be perceptive – her blood levels rose despite her positive comments – check drugs though) (Diane).

Jane seems very calm and sensible. She filled out the qolq with minimum fuss, then settled down to the massage with no chatter, she just closed her eyes and drifted (Paula).

It was difficult to know what Brian's primary motivation for a massage was as he

made a few (not so subtle) hints of a sexual nature but not blunt enough to be offensive. Having said that I'm not sure what affect that will have on his blood results (arousal vs. relaxation!). His answering of the QLQ was straight forward though he did seem to have a heightened expectation of what he was physically capable of (this would fit with other conversations in which it became obvious that physical strength was important to him). I left him awake at the end of the massage and when I came back in to take his bloods he jumped up in the bed and heaved up the backrest whilst still on the bed without any request for help from me! I tend to feel he is a very independent man with a need to maintain as much of that independence as possible. I also feel it would come hard for him to ask a woman for help out of 'chivalry' more than anything! Brian seemed quite unperturbed about the amount of blood I was taking - in fact I would say he enjoy the time to chat - in a very general way. Two interesting facts were unearthed however, firstly that his wife's father died of a haematological cancer at a similar age to Brian and that he thought of himself as a none-worrier 'worry is interest paid on trouble which may never happen' - so very true (Brian).

I just feel that whatever you can do to help yourself get better you should take Advantage of. I think these trials are excellent things; if you don't try them you never make any progress. 'Do you feel as if you are contributing to something?' Yes I do. Which isn't any bad thing is it? ('No') I don't feel as though I'm just lying here and everyone's doing so much for me, you know, I feel I'm right at the figure head and all this team of people working madly to get me better, all family and friends and everyone that I want to give something back. Wendy, today's subject has very generously agreed to participate in the trial because she wants to give something back, she went through the whole session assuming that she would have to have bloods taken every time she had a massage (I only found this out after the final blood had been taken) - and thinking that she was still looking forward to her Monday massage! I suggested that rather than punishment might it not be a lesson from God to help her and the family grow, that their experiences could be used to help others? She said that that was how she saw it and that she felt sad that her husband was so angry because she herself was not. (Wendy)

Andy, the patient I was left with is a quiet man who was busy reading his Bible when I went in and didn't say much but smiled a lot. This has to be the most remarkably event free session so far - mainly due to Roger's quiet acceptance of what was happening to him (Roger)

Isabel was quite a reserved person and difficult to "read" but genuinely interested in helping me and seemed to get great pleasure from the massage. (Isabel)

Beryl was very accepting of being put into the Rest arm. Then we continued to have a very long conversation about her PMH. Relapsed 1 week after her husband died of newly diagnosed lymphoma 2 years ago during school holidays – now she has relapsed again during school holidays. Has a partner [known since February] Bob, who she has moved in with – he is looking after her. Her three children [girls] are being looked after by friends. Beryl has a determined attitude regarding her illness and is trying to be positive but has insight into the fact that she does have negative thoughts +++. Trying to encourage her not to force herself too hard [another problem – pushing herself too hard] but is totally aware of the problem and is very open to the idea of trying to focus her mind through visualization/yoga etc.

Did QOL very openly and qualified answers. Unfortunately the drip started bleeping half way through but she says she still managed to focus.

Whilst I was taking her first post bloods she told me how she and her husband [Gordon] had lost their house [the council were knocking it down for a dual carriageway] and it took them 4 years to get compensation. They ended up living in a barn with a baby when R was pregnant over one winter then as they got the compensation Gordon became ill. NB: the husband was related to Princess Diana and had inherited wealth +++ which they put into antiques which they lost through repeated break-ins before they got the compensation money for the house.
Impression: Beryl is very talkative and perhaps uses this as a defence mechanism. She is prepared to be separated from her 3 girls for as long as it takes but is obviously concerned about potential financial implications of living long term with her partner until she gets somewhere for the girls and her. Other than the life story she was very accepting of me taking all her bloods etc and seemed very relaxed throughout the morning. (Beryl)
Very pleasant lady, keen to help but also keen to do anything, which may help her. (Molly)
She confessed that she has a generally anxious nature, which has been heightened due to recent events. I get the feeling it will be quite a challenge to get Norma to "chill out". I'm also aware that she is keen to do everything properly (including relaxing), which I think was making her a bit anxious in itself! (Norma)
I still feel very relaxed and I'm not a person who does relax easy. Fiona is a very easy person to talk to and appears to be coping very well. Unfortunately, I know from talking to her primary nurse that she's having problems at home as her ex-husband is very cruel to her regarding their 3 children (who normally live with her). Although she seemed very calm and 'together' when I saw her she had apparently had a blazing row with him on the phone the previous evening about the children visiting (he didn't want them to!). Little things she said hinted that she was finding her stay/treatment a greater ordeal then she was letting on. (Fiona)
Very difficult to tell whether he has any concerns about what we are doing – was very matter-of-fact re QOL, no apparent concerns about anything; just accepting of everything [on the surface] (Colin).
"Glad to be helping - breaks my day up. If it helps someone else, quite happy to do it. Blood being taken? Not a problem at all." Jill seems a chilled person and certainly didn't talk about feeling stressed when we did the QLQ, in fact she whipped through it in a very efficient way. (Jill)
My main impression was that Paul was still heavily influenced by his wife Joyce's death; although he wasn't maudlin he did mention it on various occasions. (Paul).
During QLQ complained of big problems sleeping and I noticed he acknowledged lots of problems usually associated with stress e.g. tense, lack of memory/concentration, poor sleep etc. also still having problems with nausea and vomiting [just vomited before I came in the room but still wants to go on with it]. (Mike)
She told me she likes to know everything that's going on and whilst I was taking the bloods [over the four sessions] she was asking what I was doing/what would happen to the blood etc.etc. It was as if it was another procedure happening to her and another opportunity to tell someone about all the problems she has had and of the misfortunes of those close to her. [She did the same thing to June when she massaged her the next week]. (Perhaps this strategy isn't very helpful for coping, as her relaxation didn't last very long – erratic blood results, nb. She was pyrexia @ 37.2 at the end of the 2 hour session) (Megan).

We filled in the QLQ when she explained that she felt a complete fraud for being here, also that although she did not feel stressed/tense about the illness [which she was dealing with "head on"] her son and husband were tense about her being in hospital and that was her main problem. (Emma)
Newly diagnosed ALL. Seems quite accepting of his situation (David).
Very interesting gentleman. Very active social life; talked a lot about wine and golf [including trips abroad]. Was in management and whilst he obviously finds his situation frustrating, his way of coping he said was to keep positive, get his head around what was happening and focus on getting out in 4 weeks. Emphasised that he has never been in hospital or been ill. Much talking and joking as we went through QOL stuff – determined not to acknowledge weakness and although had jokingly referred to frustration – didn't acknowledge it on the form. Seems to spend a lot of time pacing the floor – mentioned a few times [? Joking] that the nurses stopped him doing press-ups as the line might be pulled out. From a massage point of view his feet were showing signs of complete rigidity and was also tensing up his feet/legs constantly. I got the feeling that if he relaxed/let go at all he would completely crumble. I would be amazed if I managed to make a change to his Cortisol and if I did, what would happen? He's not in a place where he feels he can reflect on his position and get support to get through it – it has to be got through by positive thought and no acknowledgement of what MIGHT happen on a negative point of view. If I try to hint at anything that may concern him or give him too much detail about what is happening/what I am doing re bloods etc, he would drop his gaze and look away. My guess is that despite the charm he tends not to drop his guard or the act of being positive, which I guess could be quite a strain and stressful. (Not surprisingly, his bloods went up). (Ken)
She also told me how her nephew has been held up at knifepoint for his car! [Which they took]. Her daughter is dyslexic [21yrs] and has post viral syndrome – so we talked about that and her youngest son [9yrs] gets bullied at school. I noticed when we talked she did tend to wring her hands – a sign of anxiety I guess? However, this talk was balanced by talk of travel to USA to visit family and her budding creative card business [cards by post?] and we discussed her current position as being time out to think about where she wanted to go and her "hobby" without having to worry about going into work [Inland Revenue]. Christie experience in a positive fashion – a way to move her dream forward. (Olga).
Betty told me whilst we were completing the QOL how shocked she had been re diagnosis – now feels as if she's "in prison" and by the amount of times she mentioned being locked in her room, I guess she is having a hard time dealing with it and in fact commented that she felt alone despite her husband being with her most of the time. This appears to be making her irritable [I guess – mainly with him, as she sent him off one day after he kept telling her what a lovely day it was outside!] She was very active; gym, walking etc – likes being outside, hence the frustration now. Her husband came back as I did the first post blood – it's interesting to see how she has lightened up a bit and has started bantering with me rather than describing her weariness. Maybe that's how their relationship works – she has to be strong but whatever, they certainly bounce off each other. Husband [Jim] went off to get a sandwich and Betty visibly flattened once he'd gone she seems to keep up a strong front when he is there only. My impression is that she seems to spend a lot of her time reminiscing and remembering how hard life has been. (Betty)
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- Comments about therapist

Jacqui has a nice calming, soothing influence on people. She has got an aura about her. (Noel)
'Thought that you would feel uncomfortable with having to take your clothes off, but you didn't?' Yes, but I didn't. No and she was very sensitive with it. (Nancy)
Warm hands (Tom).
Gentle hands – the most gentle hands you've ever felt really (Brian).
She made me feel very relaxed and comfortable, she's so gentle and looked as though she's enjoying what she was doing and that she firmly believes that what she is doing is right, she communicated that to me (Wendy).
She was very nice, she was lovely. (Molly)
I could tell she was very good because she used different massage techniques and because I've done massage myself so I know that she is very good and I like the use of different massage techniques because obviously the different techniques makes you feel different to how it's pressurizing or not pressurizing on your different muscles and your bones and which part of your body it's on. It was adapting, using different massage techniques on to different parts of the body and even on the same parts she used different techniques. She is very pleasant. (Alice)
I think Jacqui is lovely (Fiona)
Jacqui was very nice, very pleasant. (Paul)
Jacqui, I likes Jacqui……?…… very informative,…….?…… (Megan)
Pleasant operator, very nice person Teresa)
She was very nice. Calming. 'That was good, so you found her helpful?' Mmmm. Betty)

- Comments about oils

I couldn't smell the oil as much as I thought I would be able to and I would have preferred that (Carol).
I liked the smell. I don't want to get rid of the smell, when that's wafting over it's really nice. (Ann)
Very pleasant, the smell of the oil and all that sort of thing, citrus. I didn't get the, they said there was a cedar smell as well, but I didn't get that. I got the citrus one definitely (Ian).
I liked the smell (Norma)
I liked the smell it was beautiful (Fiona)
Couldn't smell oils - if I went out of room and came in I would smell it. The only time I could smell it was when I bent over my feet - knew it was in the air, but not very long. (Helen)
Destressing……?…….. Just the smells and it felt nice. (Enid)

- General comments about the session

I just think it should be a regular thing for anybody that wants it. It can only be beneficial can't it if you are relaxed and accepting a nice, calm atmosphere. Yes, I think it's brilliant. I think it is a very necessary service really, I think it's time people saw that side of medicine as being important, you know, holistic or whatever approach (Ann).

I just felt the whole idea was very good, it was a really good idea, and I'm glad I can help with what she's doing (Diane).
I can see the benefits of it, it's probably better to have it than not have anything at all (Tom).
If you've enjoyed something there is not a lot you can really say is there? I was almost asleep, I knew when she went out of the room but I just didn't want to open my eyes (Paula).
I do think it's a good thing that they are doing clinical trials of these things because I'm a big believer in the whole body thing. You do get all the medical treatment there's no doubt about that, when it comes to the emotional you don't find anybody with time enough to deal with that and I think something like this does allow you to unload your feelings if you like, unwind yourself and if it's done in a proper clinical trial, if it's part of the whole treatment then I think it's a good thing for you, it's working along with the orthodox stuff, I can't see that it couldn't benefit somebody, if they're able to relax enough to allow it to do it. Because you get so much stuff going inside you that makes you feel rotten that you just want someone to make you feel better. (Beryl)
It was a good time to talk – with someone who was independent, not one of my nurses or doctors. (Mike).
I'd like a massage every day if I could have one! And I wouldn't mind if it was plain or aromatherapy, any massage I find very, very relaxing. It is, it's quite an incentive for coming in! Knowing that they have it on offer. (Teresa)
It was a lovely experience and it would be nice to just …?…, you know, when you wanted it not just when …every couple of days if you've got stuff on that day and you can't do it you're going to miss out, be nice to be able to say I'll have one tomorrow instead. Especially when you're stuck like this, you haven't got much else to look forward to as it were. (Olga)

- <u>Prior concerns / thoughts about future sessions</u>

Yes, as long as I got peace and quiet (Penny),
I would recommend it to everyone (therapist and session) (Noel)
No, don't want again, Wants a massage on Monday (Lucy)
Yes, to another session (John)
Oh yes, definitely (Gary)
If I offered you another massage session, would you like one? 'Please' (Carol)
And you would recommend it to other patients? 'Yes, definitely'. So if you were offered a massage again, you would take it? 'Oh yes'. (Frank)
(Would you have another m?) 'Oh yes, any time'. (Ann)
I probably wouldn't. I would have some rest sessions obviously, but I would do it when I wanted a rest session, you know. If they said, you know, I'm letting you go and have a rest session, I don't think it would be practical anyway, to be quite honest. (Cyril).
I would be keen to have one, yes - When asked on the Monday if he would be interested in participating in the trial Ian jokingly said that he had once been invited to a massage parlour but he was not brave enough to go – I'm not sure what he thinks I am going to do to him! I tend to feel he's quite cautious regarding the massage (Ian).
'So if you were offered a period of rest again with nobody coming in to disturb you, would you go for it?' Possibly, but I don't know how I'm going to get it because I

have a heavy schedule this afternoon (Nb. He went on to use the massage service +++) (Alan).
I didn't really know what to expect, I thought I might feel uncomfortable, because I didn't realise I had to take my top off and things, so I thought that I may feel uncomfortable, but I didn't feel uncomfortable with that at all. I really enjoyed it; yes I'd definitely have another one. I just really enjoyed it and because it was so new to me and it's something that I have not done before, I would definitely do it again, you know. Note also confessed she doesn't normally like being touched. (Nancy).
'Would you choose to have a massage session again?' Yes (Diane).
Oh yes, yes tomorrow! (Laughs) (Tom).
'Would you choose to have a massage session again?' I would. (Paula).
David had made his feelings clearly known to Peter in that he would only be happy if it was a female who performed the massage. Interestingly, one of our other patients (not on the trial) said the same thing - something to think about when employing future staff! Definitely, definitely – no question about it. I've never had one before in my life. If somebody's prepared to do that to you well I'm glad to accept it, willing to accept it I should say (Brian).
'So if you were offered a massage session again, would you have one?' Most definitely. She went through the whole session assuming that she would have to have bloods taken every time she had a massage (I only found this out after the final blood had been taken) - and thinking that she was still looking forward to her Monday massage! (Wendy).
So, if offered, would you have a rest session like this again? 'Yes'. So you're going to have a massage session on Monday are you? 'Yes.' (Roger)
Would you have a massage again? Yes – definitely, I'd have a back massage. Looking forward to the next time. I've had a massage before and I really enjoyed it and I knew I would enjoy it again, especially when you're like this it's especially nice. (Jean)
If offered this again would you have a massage again? PT: Yes, definitely. (Isabel)
I would always choose to have a rest session yes, but it would have been interesting to try one of the others certainly, I would like to try aromatherapy massage. (Beryl)
Yes – I want to access massage when discharged. (Molly)
So would you choose to have the session again? 'Mmm.' (Norma)
Yes, definitely because I enjoy massage, I think it suits me, I think everybody I know it suits. (Alice)
I was a bit nervous about it at first because I don't really like being touched. So if you were offered massage again you would take it? Without a shadow of a doubt, yes it was lovely. (Fiona)
I'd be quite happy to – no preference really (Colin).
If offered both, would go for the massage ('Oh God yeah!')" (Jill)
Would love full body massage. Get rid of some of them knots, tension, (Paul)
Never had one before, always been pessimistic thought it would be rub it and that's that (in fact it was hypnotic, went into my own world) – that's all changed feel very positive about massage. It was so relaxing, like to experience it again. (Mike)
Would you choose to have a massage session? 'Oh yes, yes.' (Megan)
Would you choose to have a rest session like that again, if that was offered? Well, I could do that any time couldn't I? That's really...you don't have to be offered, there's nothing else to do here. (Teresa)

If you were given the chance to have another rest session like that would you do so again? 'Yes, yes' (Emma)
So if you were offered to choose would you have the massage session again? I would yes, yes, definitely. (David).
Oh certainly, yes. Excellent, can we start again this afternoon? I think if one was ...?.... it would be quite beneficial (Ken)
Would you choose to have another aromatherapy session?' Oh yes, definitely. (Enid)
Would you choose to have a massage again? Yes. (Olga)

2. Physiological issues

- Physiological improvement

It took away some of the pain. An issue re pain? A lot of psychological pain, erratic grading of pain. Difficulty reinforcing the fact that he won't get massage today [to set up one with Tina over W/E?] Seems to respond to the attention as down graded his pain following talking to us (Noel).
Shoulder feels better (John)
I feel great, much better (Carol)
I wasn't looking forward to having my feet done, because I'm very sensitive with that, but it didn't affect me at all 'And did it include massaging your feet?' Yes, toes and everything, bottom of my feet and everything. Whereas I would have thought it would have got me going, but it was superb (Ian).
My legs feel nice and smooth as I get dry skin on my legs especially being in here they've gone quite dry (Paula).
My back feels more supple – easily moved – whether I'm just imagining it or it will be I don't know. Loosened up, say (Brian).
She was going to try beans on toast when we'd finished so perhaps her stomach was feeling better? (Isabel)
Well, to be honest with you my feet feel a lot better for it, they're usually very tender underneath. They feel lovely now; feel great, and my ankles feel better. I will tell you something, my foot – when I'm walking seems to pull into my big toe and I could feel it going away, eased the tension. (Molly)
I liked where I had it because I find I get a lot of tension in my shoulders usually so obviously I've not been doing a lot of work since I've been in here but it was very nice and soothing. It was an area that I enjoy a bit of relaxation there. I feel really good, I feel great, I don't know if it's because I've not had the radiotherapy today but I feel really like I could go shopping for twelve hours. (Alice)
I have a lot of tension in my neck and my back and I could just feel it going, it was lovely. (Fiona)
"Feel relaxed. Noticed when went to bathroom, noticed how relaxed she was (less tension in shoulders) (Helen).
'Feet are on fire, feel champion, fine.' N is due a knee replacement [R] and the other is aching due to overcompensating therefore, legs it is for massage, especially since he is also suffering from restless legs He commented after I'd finished the first leg that it felt a lot more relaxed. (Paul)
Took my mind off my nausea, sickness disappeared for a while. (Mike).
So it's helped your skin, so your skin feels softer ('softer'). (Enid)

3. Environmental issues

- Amount of the session spent in conversation

No conversation (John)
No conversation (Gary)
No conversation (Carol)
No conversation (Frank)
No conversation (Ann)
Rather than wanting to relax and drift off to sleep I sat watching me and making the odd comment (on general subjects) such as he fact that he had lost some muscle bulk on his legs but that he used an exercise bike and that helped maintain muscle tone. I estimate this light conversation took up approx 5 - 10 % of the session maximum (Ian).
100% of session = conversation (general) (Nancy).
No conversation (Diane).
No conversation, though wife asked him if he was asleep as I left the room and woke him up! (Tom).
No conversation (Paula)
B asked me questions about my work through a large part of the session (Brian).
Despite looking decidedly drowsy by this stage W seemed to feel the need to talk to me off and on through out the session. (Wendy)
No conversation (Jean)
Minimal lighthearted conversation (Isabel).
No conversation (Molly)
No conversation (Norma)
Minimal conversation (For about 5 minutes at the beginning – about my work) (Alice)
Chatted prior to the session but nothing during the session. (Fiona)
Most of the session – talking about potentially emotive subjects (e.g. wife's death). (Paul).
No conversation during session (Mike)
Conversation +++ (approx. 85% of the time) about very emotive subjects – including diagnosis Jean actually talked most of the way through the session about problems with G.P.'s lack of referral for treatment [said she would have been dead if left to him]* and about friend who also has Myeloma. In other words, not very relaxing stuff! *She also told the whole of her medical history re the Myeloma with all its traumas. (Very erratic blood results). (Megan).
Conversation 50% of the time, about wife who died of AML approx 6/12 ago. Interesting to note that D talked of his wife much of the time but in a way that made it seem she was either still alive or long dead. (David).
Conversation 100% of the time. During the massage there was a non-stop stream of conversation about anything and everything. If conversation was not going on then K instigated it, about his youth, food and wine [most stressful issue I think], past injuries [eg cut toe water ski-ing], the garden, my children etc – anything but his current position [the closest we got was when he was talking about food/meals etc and his wife said, stop torturing yourself]. (Ken).
No conversation (Enid).
Conversation most of the time about emotive, general & reflective topics. (Bloods still went down). (Olga)

- Impact of external disturbances to the sessions

Fiancé in room, I felt very uncomfortable with the idea of asking him to leave so he stayed even though, despite him being quiet throughout, it was less than ideal to have him there (Penny).
Doors banging (Noel)
Father in residence with mother, the phone kept ringing, Dad arrived back and started wondering if maybe they couldn't get enough Bone Marrow out of sister Sarah as she had been in theatre for a long time! (Lucy)
Just about to start massage when the phone rang, John didn't answer but it rang for ages – then we took the phone off the hook. (John)
Coughing bouts x 2 during massage (Gary)
It would have been a very serene session if I had not had to disconnect drips, give antibiotics and reconnect drips (the last was the worst as the machine kept playing up and making horrendous bleeping noises). The final disturbance came when her husband arrived to visit but he is a lovely soul and not very noisy! (Carol)
Example of a disturbance for me – not the patient! The massage itself went well and was conducted in silence, Frank being on his stomach whilst I massaged his shoulders; although I should add that radio5 was on in the background the whole time. He explained to me previously that at home there is a lot of noise and that room 9 on the ALU is very quiet compared to what he is used to so he uses the background noise of the radio as a type of sedative! Having finished the massage I left the room to return as usual in 10 minutes time. When I entered the room he pinged upright from the prone position, I hastily encouraged him to lie back down (although he responded to my request the first time he kept repeating this behaviour - followed by dramatically whipping of his tee-shirt, so in the end I gave up worrying!) Concerned that he was probably undoing all my hard work! (Frank)
Unfortunately her sister-in-law arrived and I had previously got the impression that she wasn't much relishing her visit so I'm not sure what that will do to her results as she stayed for the rest of the time! (Interestingly, this does not appear to have inflenced her blood results) (Ann).
***Biggest problem; he had a dose of maxalon 2 days ago [one only – 10mgs]. Decided to go ahead with study, as Cortisol seems to be the most consistent measure rather than Prolactin anyway. Wife present throughout session but didn't talk. [Did ask him if he was still awake just after I left the room!!] – Blood levels still went down despite all this. (Tom)
Today's session seemed to quite straightforwardly, except for Paula needing Oromorph 20 minutes before the massage (she had not had any overnight), and the fact that a visitor popped up unannounced 10 minutes before I started!! These things are sent to try us! (Paula).
** Yet again, I noticed that my remaining candidate had been given a daily dose of Maxalon up to 24.09.01 for the 3 days prior to that date. I decided to go for it on the expectation that any influence would be on the prolactin only ** No blood results (Brian).
As is usually the case when one is making a special effort to look efficient everything became very chaotic! Firstly Wendy was in the shower, then when I came back James was there with all the junior doctors, then the cleaner asked if she could wash the floor. Finally it was 10.55 when I got into the room to do the baseline interview -

just as Rita arrived to put up some chemo!!! I managed to make use of her though in that she took my baseline bloods for me thus recouping some of the lost time. Tina was still in the room when we were filling in the qolq but as I moved swiftly on to the massage (feet, using lemon and mandarin) she went out for a drink thus leaving her mother in peace - or so we thought until Jude came in with a message from some reverend so there was a slight pause whilst we negotiated when he should ring back. Then, surprise surprise, Rita comes banging back in to put a flush up. I quietly entered the room, Wendy soon opened her eyes but she still looked relaxed then guess what, yes, Rita banged in saying she didn't want me to lock off the flush - so I didn't! As I was finishing she came back in <u>again</u> to use the line. When it was time to go back in to take the next lot of bloods she was still in there - giving antibiotics I assumed, until I entered the room to find her sat on the chair peering at Tina's twin sisters wedding photos!! Needless to say I was pretty cheesed off but what could I do? I took my bloods and left, she followed soon after. Next time I entered it was hot on the tail of Tina, by then I had just resigned myself that it was going to be Piccadilly Circus in room 15 today - if the blood results show anything after this lot it will be nothing short of a miracle! There was definitely an issue here around 'ownership' of the patient. This particular nurse had a major problem with me spending the morning with 'her patient'. Unfortunately, rather than tackle me about it, her response was to keep herself well and truly in the frame during the session. Interestingly this didn't stop the drop in cortisol levels, but would they have been greater without the interruptions or did Wendy find such a large amount of attention (banging aside) supportive? (Wendy).

Bad start – 10.40am and she wants a shower – not done paperwork yet. The massage session went very well (feet) with C appearing very chilled afterwards – then the friend arrived… 12.15 Went for a shower [didn't have one before as Cath the cleaner was cleaning the room]. 12.45, friend started asking about why she couldn't have any other chemo (she's got relapsed NHL) who needs enemies…! 13.15 Mum arrived. (Jean)

Unfortunately this lady has been suffering with nausea and vomiting. Doctors have just written her up for Maxalon [she has had Cyclizine this am] but I'm allowed to use her before the Maxalon. [I kept checking she didn't feel nauseated throughout the session]. Next problem; central line wouldn't work for taking bloods!! She said she was happy for me to keep stabbing her but I felt that since Jane (nurse) needed some bloods perhaps she could put a canula in – she did. Although it worked I had to do some acrobatics with it i.e. hanging it over the side of the bed etc. but we did manage to get the blood and she didn't seem too fed up. (Isabel)

As I came back at 12.15 for the 2nd bloods her husband [?] turned up and didn't take the subtle hint that she was asleep, in fact seemed slightly irritated by the fact and despite Molly and I being quiet he kept asking questions. (Molly)

Unfortunately, just before I was due to start, the doctors' ward round appeared and it was the doctor who makes her anxious because he doesn't speak clearly and she has a hearing problem. The QLQ took quite a while to fill in but that was partly because her husband was still in at the time and the pair of them kept going off at a tangent. I was aware that there was a lot of noise outside on the Unit – I'm not sure how much that would have disturbed her. Plus, despite having a wee just prior to the massage, the first thing she said was "That was lovely and if I can just have a wee I'll be able to relax properly"!! One of the nurses also started talking to her about the life cycle of the nit (Norma is a health visitor) & she was getting visibly anxious about not being able to remember. Needless to say I reassured her this was not surprising

under the circumstances, but I ask (not for the last time I am sure) why can some nurses not pick when they are upsetting patients – they are supposed to be their advocates? ' I'm not so calm as I was when it was going on. I suppose because there is so much going on it's like out of your mind again now, busy and bustling again.'(Norma)

I found out she'd just rung a friend to come and visit her at 12.00 and it took me ages to get blood out of her line. When I finished the massage, despite me asking Alice to take her time getting up she was already leaping off the bed before I'd left the room – needless to say I'm not expecting miraculous results from this session! By the time I came back 10 minutes later to take the first bloods Alice's friend had arrived and spend part of the blood taking being emotional about Alice being in the position she was – if I get any decent results out of this blinking trial it will be a bl***y miracle!!!! (Alice)

Just before the session started her partner arrived. When I came back after the rest period [she had no particular needs with this] her partner was laid on the bed next to her. She also informed me that the cleaner had come in as I left [GREAT!] – still, that's life on the ALU I suppose. Then Brenda pitched up to make the bed while I was taking the 11.45 bloods but that was fun – good laugh. Then Paula pitched up as I was leaving after taking the 12.15 bloods to give a GCSF injection – I'm not sure what that will do to the stress levels – (it raised them). (Jill)

Noise outside (people talking and walking about), hard to concentrate on relaxing the body. In a quieter situation, could have relaxed more - soothing music might have helped too. Massage started well [soon drifted] – then brother barged in as I started the second foot! She carried on resting but I could see she was no longer deeply relaxed. I explained to her brother what was happening before he re-entered; if I can make a difference with all this going on it will be a miracle but definitely a real result! Dave did one of the bloods for me whilst he was putting up the campath. Then lunch appeared between the last two bloods and I am sure she felt rushed eating her lunch [guilt, guilt!!]. (Something certainly had a major impact on her 2-hour blood – either the rushed lunch or the campath) (Helen).

Someone arrived to take her for an X-ray approximately 12.45 when I was taking her bloods, we deferred it but I think it worried her, as she does not want to leave the room. NB2: there were 2 x mini earthquakes in the early post-session time – Teresa felt it and was a bit concerning! (Bloods shot up about this time) (Teresa).

Emma had a couple of 'phone calls from partner and father but actually worked that into the session by explaining to them over the 'phone what she was doing [someone also went in with a paper]. (Emma)

This quiet lady had her husband in attendance throughout the session – "He likes to look after me" was Enid's comment. Her husband decided to stay though I don't know whose choice that was – was it normality and comfortable, reassuring or was it irritating and she felt she couldn't relax properly? It will be interesting to correlate with the blood results. (Bloods went down initially but shot back up towards the end of the 2 hours) (Enid)

4. Therapist's reflections on the study process

It was evident right from the start that certain specifications in the protocol were too stringent and not going to work, for example, wanting the patients to remain on bed rest for 20 minutes prior to having the baseline bloods taken. If the doctors aren't doing the ward round and wanting to talk to the subject, then the person decides they

want a shower before the session - or someone comes in to make the bed thus 'getting it out of the way'. The other issue I hadn't foreseen was the telephone, it usually rings just as I'm about to start taking bloods or half way through a session. Some people are more than happy to take it off the hook - others are not so obliging, all I can do is to try and note all the times it happens. It once again struck us how extreme these people are - they have a life threatening illness yet they feel perfectly healthy a lot of the time.

Another interesting issue to come to light this week was how patients can 'pigeonhole' their problems. John evaluated himself as having no pain and yet he had been complaining of very painful shoulders, I could only suggest that because the pain was not related to his Hodgkin's disease he did not feel it would be relevant to me (John).

I just want to make a note of this ladies dramatic blood results (esp. Cortisol) there was a consistent and quite dramatic drop in cortisol levels as the blood sampling continued. Is this a real effect - given that she was on diamorphine, and if so did it happen because she was able to take advantage of the oblivion the diamorph. allowed in order that she continue the relaxation process started by me - in which case this sort of work has massive implications for patients in ITU. Or was it simply an effect of the diamorph.? (Carol)

Having finished the massage I left the room to return as usual in 10 minutes time. When I entered the room he pinged upright from the prone position, I hastily encouraged him to lie back down (although he responded to my request the first time he kept repeating this behaviour - followed by dramatically whipping of his tee-shirt, so in the end I gave up worrying!) Concerned that he was probably undoing all my hard work! He followed this by going into the very dramatic details of the day of his daughters birth - great, if there was any effect left from the massage after the jumping up scenario there certainly won't be now! – c'est la vie! (Frank)

I verbalized my concerns over whether just documenting drugs known to have an effect on prolactin was sufficient to account for the sometimes dramatic fluctuations in prolactin levels (even when a direct cause was not identifiable) and whether what I should in fact be doing is making a not of all the drugs the patients are on and looking retrospectively perhaps for any influences. This is a massive undertaking, which has been rejected once, but maybe it needs further discussion. (Frank)

Ann has coped well with her chemotherapy so far and was keen to be part of the study. She understood everything that was expected of her perfectly and when we filled in the QLQ with her there was no confusion in answering the questions, which she did very realistically. Interestingly however, whereas previous patients appeared to answer from a very subjective standpoint, Ann had an almost objective realism in her answers - to the point that she let out a guffaw of laughter when I asked her to grade her health and bluntly pointed out that she had cancer! A blatantly obvious statement, which no one so far had commented on - why? I suggest it is because she copes with things by facing them head on with full acknowledgement of their implications whilst most people we have encountered so far tend to cope in a more reactive way, that is by dealing with the symptoms they feel from the illness / treatment and suppressing or ignoring the cause of these symptoms - perhaps the enormity of the disease is too much to cope with for most people, or perhaps they can respond in a more positive manner towards what is happening if they suppress their knowledge. Either way, Ann was certainly one of the 'healthiest' patients in the trial so far but she has graded that health lower than any other subject - she graded it in a way one would expect an observer to grade it - objectively, not taking into account

how healthy & well she was actually *feeling* (a fact that she acknowledged to us on more than one occasion (Ann).

Although Cyril and I had nice little chats each time I went in to take his blood (including the financial effects of him being in hospital as he is self employed) it became fairly obvious by the 12.45 bloods that he was finding the procedure somewhat of an irritation as he muttered something to the effect of 'this is a bit of a con, I thought you'd take the blood in one job lot' (this is in spite of him insisting he'd read and understood the information sheet and me reinforcing the point that there would be several blood samples over a relatively short period of time). I can only assume that if one is getting a massage (even if you're not sure you will enjoy it) that is a reasonable payoff for having the bloods taken whereas with nothing in return the 'novelty' soon wears off and despite being prepared to take that gamble the reality is somewhat more irritation than was expected! (Cyril).

The QLQ was as usual filled in with the same level of amusement at certain questions – I'm beginning to wonder if we will get any useful data from that angle of the study but at least I can feel satisfied that I screened the alternative questionnaires thoroughly (Ian).

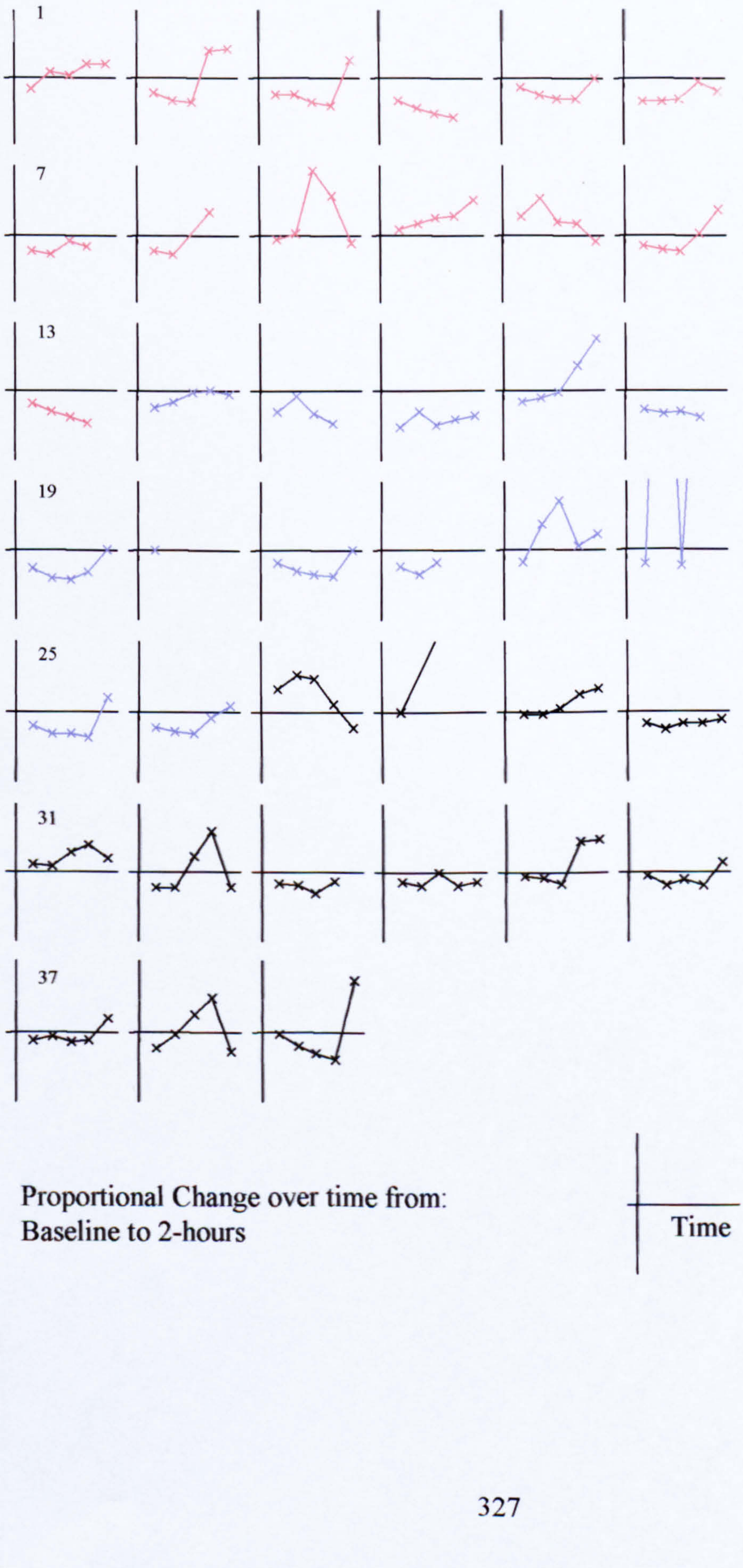
I found today's session very difficult. Alan, despite having a positive attitude appears to be encountering lots of problems and is now finding it hard to maintain his positivity. I found this hard because despite his reassurances on Monday that he had not had a massage before and didn't mind if he was in the control arm I felt as if I had also let him down and increased his catalogue of disasters. From a purely personal point of view, if someone is in pain (physical, psychological or spiritual) the instinct is to nurture him or her and protocol did not allow for this. Instead I found myself taking his precious blood (he is pancytopenic and getting no increments from blood or platelet transfusions) with no benefit to him - is this ethical? I was asked if I would take 30mls of blood for HLA antibody screening during the second session which didn't help my feelings of making his situation worse - especially when he asked if all the blood I was taking was for the trial - although it was not it made me acutely aware once more of how precious their blood is to them and generous is the spirit that would let me take so much under such circumstances. Finally, when I went in (after Kinta had done her stuff) to give him the repeat qolq for the next day he looked so sad that I sat down and listened properly. I desperately wanted to make it better for him and to give him a big hug but of course that is not appropriate except under the guise of a massage! When I talked to Kinta about how I was feeling and she pointed out that I was carrying out all the research (and maintaining a very busy service) by myself so it was bound to effect me at times I know she's right but I'm still not sure how I feel about continuing. (Alan)

Today should have been a study day but I couldn't, I didn't have the heart to make George (my only candidate) commit himself to the chance of not getting a massage when it was blatantly obvious that he both wanted and needed one (he was suffering from constipation due to part of the chemotherapy regimen). The memory of my misery at talking to Norman last week in his distress but not being able to treat him was still too raw and fresh in my mind, besides I don't think it would have been ethical - it certainly wasn't to me. Of course my experiences of the last two weeks throw up a major short - coming of the study; patients who <u>really</u> need the service can't by definition be included because one cannot take the risk that they are randomised to rest. So, the new patients with leukaemia who are finding it difficult to cope, those with physiological or psychological problems, those who have relapsed and are finding it hard to deal with the implications, these are the people the

service was set up to help yet they are by necessity being excluded from a trial aimed at evaluating the service. I'm not sure what the answer to this is - perhaps case studies at a later date? (Between sessions 11 & 12).
Before I start my journal about this session I just want to make a note about my thoughts regarding a potential confounding factor, Cyclosporin. I am going to have to ask Steve (pharmacist) for more information but my current knowledge is sufficient to know that despite not being flagged up in the main literature as a drug influencing hormone levels I am convinced that there is a high chance of it effecting one if not both the hormones currently under investigation - I just wish I'd thought about it earlier (Paula).
** Challenge – I have collected different types of information from each session, I didn't reflect on attitude, problems, amount of conversation etc. standardly for each patient, just what the salient points were for each session.
He is of short stature and it turns out that he failed to thrive as an infant as well as having renal problems. His medical notes suggested that there may be a degree of mental impairment but this was not greatly evident when talking to him - the only slight problem was keeping him to answering the qolq within the framework of the last 24 hours but other patients have shown similar problems. I was concerned as to whether he was able to give full informed consent but was somewhat reassured to see that the medical team had also consented him to enter one of their drug trials. (Roger)
What was horrid for me though was that she admitted to not sleeping well and to having bad constipation – things I could have helped with but couldn't. (Jill)
My assessment of this patient showed slight confusion/ bewilderment about the disease, treatment and going by the SSI, this trial. So, not a lot of information gained except for the questionability of informed consent! (Stuart).

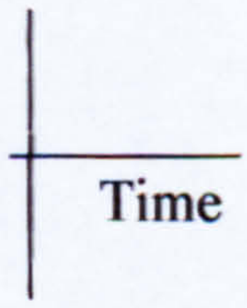
Appendix XIV

Graphs of Change in Individual Hormone Levels (Cortisol)

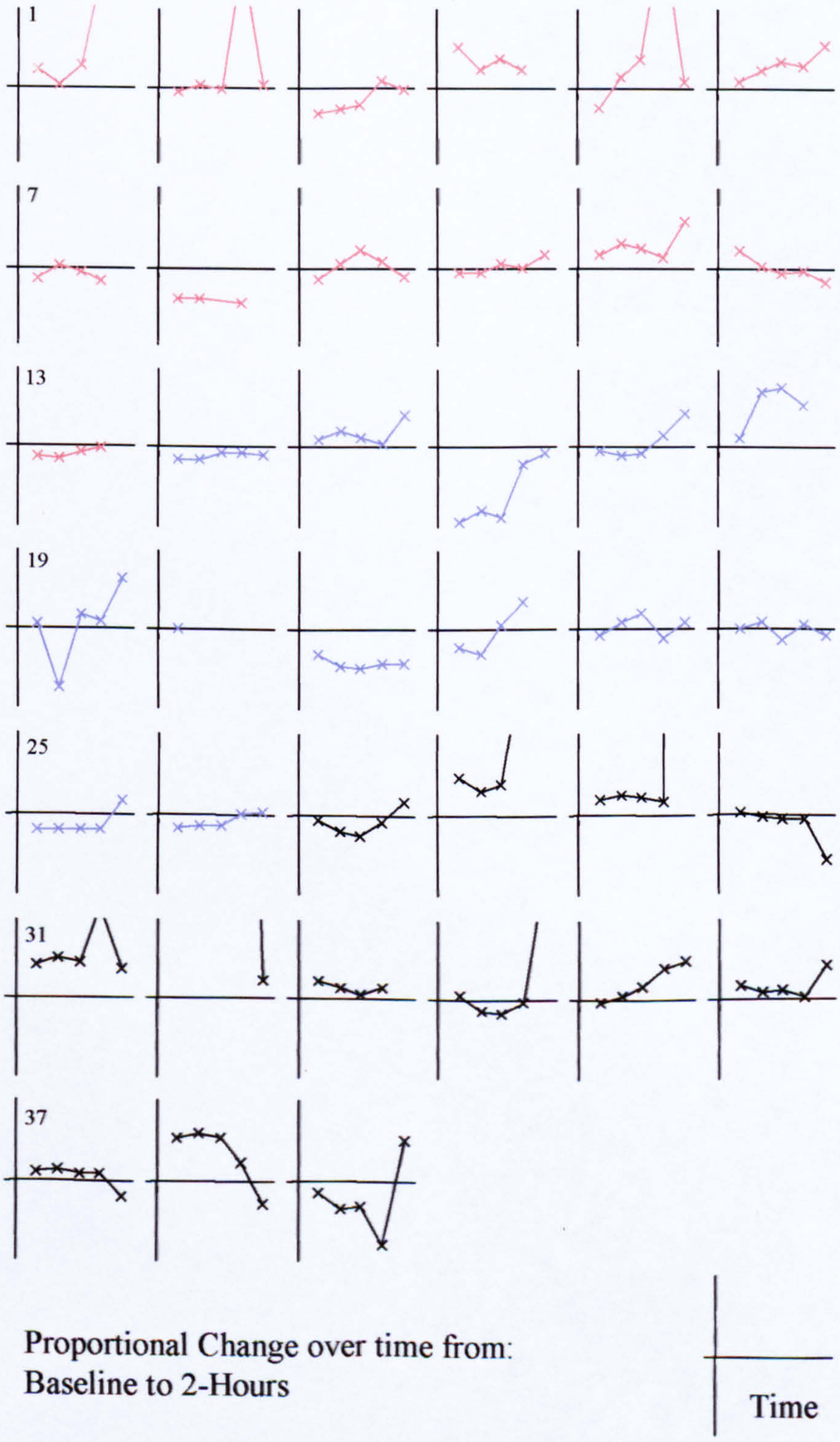


Graph No.	Trial No.
1	19
2	28
3	8
4	30
5	15
6	25
7	17
8	23
9	37
10	36
11	13
12	10
13	6
14	7
15	4
16	22
17	5
18	20
19	12
20	16
21	24
22	29
23	31
24	34
25	38
26	14
27	3
28	1
29	9
30	11
31	18
32	32
33	26
34	27
35	35
36	39
37	21
38	2
39	33

Proportional Change over time from:
Baseline to 2-hours



Graphs of Change in Individual Hormone Levels (Prolactin)



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18	20
19	12
20	16
21	24
22	29
23	31
24	34
25	38
26	14
27	3
28	1
29	9
30	11
31	18
32	32
33	26
34	27
35	35
36	39
37	21
38	2
39	33

Proportional Change over time from:
Baseline to 2-Hours

Appendix XV

Essential Oil Paper

A critical evaluation of the antibacterial and antifungal activity of essential oils

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Keywords: Essential Oils, *Candida*, *Aspergillus*, MRSA, VRE

Abstract

Objectives: The aim of this study was to investigate the inhibitory and cidal effects of a wide range of essential oils against fungi and bacteria commonly implicated in disease in immunocompromised patients.

Methods: The antimicrobial activity of 37 essential oils were tested against four species each of *Candida* and *Aspergillus* and bacteria including *S. aureus* (including MRSA) vancomycin resistant Enterococcus, *Bacillus cereus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *E. coli* and *Stenotrophomonas maltophilia*. Activity was assessed both in microdilution assays and disc diffusion assays. Oils demonstrating high levels of cidal activity were additionally examined using time-kill assays

Results: Palmarosa, peppermint and rosewood oils demonstrated broad spectrum inhibitory and cidal effects against all isolates other than *P. aeruginosa* at dilutions of up to 1:160. 14 other essential oils demonstrated broad-spectrum activity at slightly lower levels. 20 oils demonstrated either low or narrow spectrum activity. Individual oils and blends of oils demonstrated rapid cidal activity often within 2 minutes of contact.

Conclusions: The use of certain essential oils as skin disinfecting agents or in aromatherapy may be beneficial in terms of antimicrobial activity, and have potential for treatment of cutaneous infection or colonization. Bacteria with resistance to multiple antibiotics (MRSA and VRE) were effectively inhibited and killed by dilutions of 1:1280 of 7 essential oils.

Introduction

The use of plants and plant-products for their healing properties has been recognized since antiquity. Worldwide, vast numbers of plant products are used for medicinal therapy.[1,2] Historically, the antimicrobial properties of essential oils produced by aromatic plants have been used extensively in food preservatives, antiseptics and anti-infective agents.[3,1,4] "Unconventional" therapy is gaining increasing public acceptability, with 22% of respondents in a 1998 UK survey purchasing complementary or homoeopathic remedies within the previous year [5] and a growth in expenditure on unconventional therapy of 50% between1995–2000 in the UK.[5] Such increasing expenditure on herbal medicines is a worldwide phenomenon, with sales in the USA rising from US$1.6 billion in 1994 to US$4 billion in 1998. [6] The reasons for the growing trend for people to look to complementary therapies instead of, or as an adjunct to, orthodox medicine over the last few years are complex, but include anxiety about ever more powerful drugs and dissatisfaction with the perceived limitations of orthodox medicine.[7] The international move towards increasing use of a wide variety of therapies, including essential oils, has occurred despite the fact that up until recently there has been minimal scientific research demonstrating objective benefits for such remedies.

The burgeoning interest in the anti-infective properties of essential oils is highlighted by their increasing profile in the scientific literature; a 'PubMed' search of the term "essential oil AND antimicrobial" identified more than 200 publications, with 140 of these published in the last 5 years. Additionally, there is no shortage of anecdotal data collected over hundreds and

thousands of years, especially in relation to hygiene and healing. Price and Price have reviewed the traditional uses of essential oils and correlated these with the available evidence for such usage, and in some cases the corroborative evidence is very compelling.[8]

Essential oils are used in aromatherapy (the therapeutic use of essential oils) with the assumption that they have multiple effects resulting from the complex nature of the constituents of the oils. Many of the constituents such as polyphenols, [9] terpenoids [10,11,12] and flavonoids [11] have potent antimicrobial activity, but these and other components also have other physiological effects, such as the stimulation of phagocytic cells (tannins), inhibition of microbial adhesion (mannose-specific lectins) and enhanced wound healing. It is possible that the components of the essential oils act together against microbes (either synergistically or antagonistically). It is therefore important to examine the antimicrobial activity of the complete oils rather than their individual components, as in practice they are used as mixtures. Whilst more and more evidence of ways in which essential oils can potentially be used within the clinical setting is coming to light through scientific study,[13,14] the integration of such potentially useful therapies into traditional medical care requires a methodological approach. Specifically, a systematic strategy is required to qualify, quantify and justify how, why and when essential oils may be most effectively used.

Modern cancer and intensive care therapy is commonly associated with substantial immunosuppression. The consequences of such immunosuppression include sometimes life-threatening, acute and chronic

fungal and bacterial infection. As well as adversely affecting the clinical outcomes of patients receiving cancer therapy, such infection impacts substantially on the health economy through increased health resource utilization for management of infection. While the anxiolytic properties of essential oil aromatherapy have been evaluated in patients with cancer, [15,16] there has been little consideration of the anti-infective properties, and more generally their utility in reducing the incidence of cross infection through their use in skin disinfection. There are currently a broad range of products available both to cleanse the skin of medical practitioners to reduce the incidence of cross-infection and treat patients colonized with multi-resistant organisms such as MRSA before surgery. Unfortunately compliance within medical practitioners is often poor and patient compliance is less than ideal as treatment is prolonged and often perceived as unpleasant. The current study was undertaken to critically evaluate the anti-infective potential of essential oil aromatherapy as an adjunct to conventional therapy; the study reports the *in vitro* antimicrobial effects of 37 essential oils against fungi and bacteria commonly implicated in disease in immunocompromised patients. A subgroup of the oils was examined using time-kill assays to assess their suitability for use in skin disinfection products.

Methods and Materials

Essential oils

The essential oils (Natural Touch Aromatherapy, Hampshire, UK) are detailed in Table 1. The same batches of oils were used in all experiments (additional batches were tested and had similar results, data not shown). All oils were stored in sealed bottles in the dark at 4°C. The quality and purity of all oils was confirmed by gas chromatography by the suppliers.

Fungal and bacterial strains

Fungi were isolated from recent clinical samples obtained from patients with a range of invasive diseases including septicaemia, wound infections, urinary tract infections and pulmonary aspergillosis. The fungal strains tested comprised *Candida albicans* FA1936, *C. tropicalis* FA3099, *C. glabrata* FA8829, *C. krusei* FA3657, *Aspergillus fumigatus* AF293 (NCPF 7367), *A. terreus* AT7130, *A. niger* AN8 and *A. flavus* AFL128. The isolates were subcultured from frozen stock and were grown on Sabouraud dextrose agar (Difco, Surrey, UK) at 37°C in air for up to 10 days.

Bacteria were isolated from recent clinical samples obtained from patients with a range of invasive diseases or were obtained from reference strains used within the Microbiology Laboratory at Salford Royal Hospital, Manchester UK. The bacterial strains tested included methicillin resistant *Staphylococcus aureus* ATCC33591 (MRSA) (a strain recommended for testing hand wash solutions), Oxford *S. aureus* ATCC9144 (a strain recommended in susceptibility testing), Vancomycin resistant enterococcus (VRE) (clinical isolate), *Bacillus cereus* (clinical isolate), *Pseudomonas*

aeruginosa ATCC25668 (clinical isolate, *Klebsiella pneumoniae* (clinical strain), *E. coli* ATCC10536 and *Stenotrophomonas maltophilia* (clinical strain). The strains were subcultured from frozen stocks and grown on blood agar (Oxoid, Basingstoke UK) in air for up to 48 hours.

Media and inocula

Aspergillus conidia were harvested by washing the surface of the culture with 25mL of phosphate buffered saline (PBST; Life Technologies, Paisley, UK) containing 0.05% (v/v) Tween® 80 (Sigma, Poole, Dorset, UK). *Candida* blastoconidia were collected from 3 or 4 colonies and suspended in PBST. Colony-forming units (CFU) were counted using a haemocytometer and diluted as required in PBST. For determination of the minimal inhibitory concentration (MIC) using microdilution methods, a final inoculum of 0.5–2.5 x 10^5 CFU/mL of *Candida* spp. or 0.5–5x10^4 CFU/mL for *Aspergillus* spp. was prepared. For surface seeded plates used in disc diffusion assays, the inoculum was adjusted to provide confluent growth.

Four to five morphologically identical colonies of bacterial strains were harvested and suspended in sterile distilled water. The inoculum was adjusted to 1x10^6 CFU/mL for microdilution methods. For surface seeded plates in disc diffusion assays the inoculum was adjusted to provide confluent growth.

MIC determination using a microdilution assay

All MIC assays with fungi were determined in RPMI 1640 (Sigma) supplemented with 2% (w/v) glucose (Sigma) and buffered at pH 7.0 with

MOPS (Sigma). MIC assays with all bacteria except VRE were determined in Isosensitest broth (Oxoid,). VRE MIC assays were conducted in Brain Heart Infusion (BHI) broth (Oxoid).

The methods used were based on either NCCLS 38A[17] (*Aspergillus*), AFST-EUCAST [18](*Candida*) or NCCLS M7-A5 [19] (bacteria). In brief, the essential oils were diluted 1:4 in either RPMI 1640 (fungi), or 1:20 in Isosensitest broth (bacteria other than VRE) or BHI broth (VRE) and mixed using a vortex mixer for at least 10 seconds to form an emulsion of the oil in culture medium. The oil suspension was then double diluted in flat-bottomed microdilution assay plates from 1:5–1:10240 with a final control row consisting of medium only. Plates were sealed with a microdilution plate-sealing strip (Sigma) and incubated at 37°C in air for 24–48 hours.

The MICs of *Aspergillus* were determined visually and were defined as the concentration of the drug in the first well that showed no growth. Minimum fungicidal concentrations (MFC) were determined by culturing 100µL from each well in the microdilution plate that had no visible growth; the MFC was taken as the first well with less than 5 CFU (>99.99%).

The MICs of essential oils against *Candida* and bacteria were determined using a spectrophotometer (490nm filter) and a no growth endpoint. MFCs were determined by culturing 100µL from each well in the microdilution plate that had no determinable growth; the MFC was taken as the first well with less than 5 CFU (>99% kill for *Candida* or >99.99% kill for bacteria).

MIC determination using a disc diffusion assay

RPMI agar (RPMI 1640 medium containing 1.5% Bacto Agar [Becton Dickenson, Oxford, UK]), Isosensitest agar (Oxoid) or BHI agar (Oxoid) were surface seeded with organisms and allowed to dry at room temperature in a laminar flow hood. A 6mm sterile paper disc (Mast Bootle, Merseyside, UK) was placed onto the dried surface in the centre of the plate and 10μL of the essential oil were pipetted onto the disc. Plates were incubated for 24 hours at 37°C in a moist atmosphere. Zones of inhibition were calculated by measuring the zone of inhibition from the disc to the perimeter of growth.

All MIC and MBC assays were performed in duplicate on two separate occasions.

Time-Kill studies

All time-kill studies were performed in culture media and using inocula as described in the section MIC determination using a microdilution assay. Bacteria and fungi were preincubated in culture media at 37°C on an orbital shaker for 4 hours to ensure they were in logarithmic phase growth. In these studies palmarosa, rosewood or geranium oils were diluted 1:50 in culture medium and vortexed (for P. aeruginosa oils were diluted 1:16.7). Bacteria or fungi added to give a give a final suspension in 1:100 diluted essential oils (for P. aeruginosa the final concentration was 1:33). In all cases control suspensions were prepared without the addition of fungi or bacteria.

After further vortexing samples (100μL) were removed at time-points from 2 - 40 minutes post contact. Samples were immediately cultured onto solid medium ensuring the inoculum was spread beyond the initial contact area (to avoid inhibition by any essential oil carried over).

Results

The MICs and MBCs of 37 essential oils against *Candida* and *Aspergillus* spp are shown in Table 1. Geranium, palmarosa, peppermint and rosewood demonstrated inhibitory activity at dilutions of ≥1:1024 against both *Candida* and *Aspergillus*. Lavender, marjoram sweet French, may chang, neroli bigarde, melissa true and rose otto demonstrated slightly lower activity with inhibitory concentrations of ≥1:32. Fourteen of the oils had little activity (only effective at concentrations greater than >1:10 or were only effective against 2 strains).

Results of the disc diffusion assay are shown in Table 2. The overall pattern of inhibitory activity was similar to the microdilution assay with palmarosa, peppermint, rosewood and rose otto demonstrating the highest and most broad spectrum inhibitory activity. *P. aeruginosa* and *K. pneumoniae* were most resistant to essential oils by disc diffusion, demonstrating resistance to 22 oils. VRE were most susceptible to the oils under test demonstrating resistance to just 2 oils.

The MICs of 37 essential oils against gram-positive bacteria are shown in Table 3. Palmarosa and melissa true demonstrated cidal activity against all gram-positive isolates at dilutions of ≥1:160. Peppermint, neroli bigarde and rose otto were cidal against all gram-positive isolates at dilutions of ≥1:40. Patchouli and sandlewood were cidal at ≥1:160 against all gram-positive isolates other than *B. cereus*. Nineteen of the oils had little activity (only effective at concentrations greater than >1:20 or were only effective against 2 strains).

The MICs of 37 essential oils against gram-negative bacteria are shown in Table 4. In general the essential oils were less effective against gram-negative bacteria with *P. aeruginosa* being resistant to inhibitory and cidal effects of all oils other than neroli bigarde (1:320) and eucalyptus (1:20). Inhibitory and cidal effects against *S. maltophilia, E. coli* and *K. pneumoniae* were demonstrated with palmarosa, peppermint, rosewood neroli bigarde and melissa true (at concentrations ≥1:160). Twenty-three of the oils had little activity against gram-negative bacteria (only effective at concentrations ≥1:20 or were only effective against a single strain).

The results of the time-kill experiments are summarized in table 5. In general the essential oils demonstrated rapid cidal effects with the majority of inoculum killed in the first 2 minutes of contact. It was difficult to determine very low counts (<100/mL) due to the cidal activity of the essential oils that were carried-over during subculture (1μL).

Reproducibility

All MIC, MFCs and time-kill assays were repeated on at least two occasions. Replicate samples were within two dilution wells (in the microdilution assays) and time-kills gave broadly the same time-kill profile.

Discussion

The results of the present study clearly demonstrate that many essential oils, which are commonly used by aromatherapists and herbalists, have broad spectrum and rapid antibacterial and antifungal activity against a wide range of clinically relevant pathogens. It is also of interest that oils with the greatest activity against bacteria were also highly active against fungi. It is of note that activity against *P. aeruginosa* was almost totally absent with just neroli bigarde demonstrating activity in the microwell assay and lavender in the agar diffusion assay. Activity was retained against isolates with resistance to broad spectrum antibiotics. Specifically there was no obvious tendency to reduced activity of the oils between methicillin resistant *S. aureus* and a fully susceptible *S. aureus* with oils demonstrating bactericidal activity at dilutions of at least 1:1280 against both strains.

The pattern of the antimicrobial effects of the essential oils determined by microdilution assays and disc diffusion assays are not identical but demonstrate similar spectrums of activity. The differences are possibly due to variable solubility of the components in liquid medium and limited diffusion of large or highly charged molecules within agar. In both methods palmarosa, peppermint and rosewood oils demonstrate impressive antimicrobial activity. Other data obtained within the study (data not presented) indicate that all oils with antimicrobial activity were sterile and therefore should not in themselves be a source of infection.

Essential oils have been used for many years by aromatherapists and herbalists. In general the oils are diluted in a drop-wise fashion into a carrier

medium (often oil), which is then used either directly onto the skin or is inhaled as a vapour. It is important to realize that sensitive balances and scales are not available to practitioners and the oils are diluted directly using droppers attached to the stock bottles. In this manuscript we have therefore attempted to present the data in a manner (using ratios) which represents the most common way in which the oils are used in therapy and is therefore directly transferable to the clinic where ratios of >1:50 are regularly used. A ratio of 1:1280 translates to approximately 780mg/L.

In this study the oils have also been used directly as purchased from a wholesale supplier. The oils have been used in this form rather than as purified components because this is the form in which they are used by aromatherapists and herbalists in clinics and so again the findings of the study should be directly transferable to clinical use. Further essential oils are complex mixtures of compounds produced by plants and often have potential benefits unrelated to antimicrobial activity, such as enhanced wound healing [20] and anti-inflammatory or analgesic effects, [21,22] which might be degraded on purification or fractionation.

Essential oils and plant products have been used to treat infections for centuries but well designed randomized controlled clinical trials are scare [1,23] and it is therefore difficult to assess the efficacy of the agents in many clinical settings. Evidence of the efficacy of essential oils against onychomycosis and tinea pedis (tea tree oil *Melaleuca alternifolia*) seems clear with response rates similar to conventional therapies. [14,24] Further trials have also demonstrated the efficacy of oils in treating vaginal candidiasis, [25] dandruff, [26]

superficial fungal infections [27] and topical treatment for eradication of MRSA colonization. [28] Unfortunately, most clinical trials of essential oil preparations suffer from either poor design or very small patient group sizes.

This study has established both the range and antimicrobial activity for a number of essential oils, enabling well designed prospective clinical studies to be undertaken. The essential oils examined in this study demonstrate a broad range of rapid antimicrobial activity which appears unaffected by resistance to conventional antibiotics. In particular, these data have enabled us to predict concentrations of essential oils, which would be clinically effective for future clinical studies. Future *in vivo* studies and clinical trials are important to address any potential safety issues before these treatments can be routinely recommended as supplementary in the supportive care of immunocompromised patients colonized with bacteria or fungi.

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