Psychosocial Factors Influencing Adherence to Iron Chelation Therapy in Patients with Thalassaemia

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ABSTRACT

This study investigated a number of psychosocial factors and their relationship to non-adherence to iron chelation therapy in patients with thalassaemia. The quantitative component aimed to examine the relationship between non-adherence and psychological distress, well-being, social support, self efficacy, acceptance of illness, health locus of control and value of health. It employed both a correlational and between groups design. A patient, doctor and nurse estimate of non-adherence was collected and participants were also allocated to one of two groups on the basis of a biological marker of adherence. The qualitative component to the study involved the presentation of two case studies based on a semi-structured interview.

Participants were recruited from two inner city hospitals whilst receiving blood transfusions or waiting for a consultation. A total of fifty two subjects were recruited to the quantitative part of the study.

The correlational component revealed a weak association between several of the psychosocial variables and non-adherence. In addition, total psychological distress significantly contributed to the prediction of non-adherence as reported by the patients. Lower levels of self efficacy also significantly contributed to the prediction of non-adherence as measured by the doctor. No significant differences were found between the biological groups in relation to any of the psychosocial or demographic variables. In addition, the qualitative component of this study highlighted a number of themes which helped to elucidate the quantitative findings.

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CHAPTER 1: INTRODUCTION

1. Adherence and chronic illness

Having to live with a chronic illness and endure a strict medical regime can have a profound effect on an individual's psychological and social status. In the case of the diagnosis being made at birth it is the family of the infant who have to learn new skills and make adjustments. Then, as the individual matures, they themselves have to learn a set of illness related tasks. Moos and Schaefer (1984) comment that these tasks will involve adjusting to the symptoms and the incapacities brought by the illness, dealing with and learning any special treatment required and maintaining adequate relationships with health-care providers.

These illness related tasks can affect the individual's psychological and social status and when thinking about the effects of a chronic illness it is important to draw upon a biopsychosocial approach. This approach was first proposed by Engel (1977) who highlighted the limitations of a purely biomedical model of disease and stressed the importance of knowledge of the total context in which the individual is functioning. In order to consider the total context it is recommended that the social and psychological factors are considered alongside the medical factors. Green (1985) commented that the interaction between the biological, social and psychological components of an illness comprises an "illness dynamic". Green proposed that this concept can be usefully applied in understanding how the individual will respond to a medical regime. One such response will be the patient's level of adherence to the treatment.

Adherence is a serious and chronic problem and low rates of adherence are problematic in many chronic diseases. Such diseases include asthma (Yeung, O'Connor, Parry & Cochrane, 1994), heart disease (Horwitz *et al.*, 1990) and cancer (Lilleyman & Lennard, 1996). As a result, non-adherence is now well recognised as significantly contributing to treatment failures in medical interventions. It is also expensive, and in the USA the cost of non-adherence to ten drugs was estimated to be in the region of 400-800 million dollars (DOH & Human Services, 1980, cited in Myers & Midence, 1998).

Furthermore, non-adherence can interfere with an individual's quality of life and can constitute a potential threat to life. It is therefore not surprising that there has been considerable research into the factors influencing patient adherence in relation to a variety of treatment regimes. One such factor that has been examined as a potential threat to non-adherence is the psychosocial status of the individual. If the psychosocial factors that influence non-adherence to medical regimes can be identified then appropriate interventions can be introduced, thus improving quality of life and potentially saving lives. However, one chronic illness where the associated psychosocial factors and risks to adherence have not been examined much is a blood disorder called thalassaemia.

2. Thalassaemia

2.1 Definition

The term thalassaemia is applied to a group of diseases of varying severity which are a result of genetic defects in the globin (polypeptide) chains of haemoglobin. The type of thalassaemia is determined by the type and actual number of genes affected. Any of the globin genes can be affected, i.e. α, β, γ or δ, but only β and α defects are clinically relevant. The others are less common and less significant. The clinical features of the thalassaemias result from both the anaemia itself and from complications relating to the treatment.

Thalassaemia major is the severest form of β-thalassaemia and was first described in 1925 by Cooley. It is therefore also referred to as Cooley's anaemia. Patients with classical homozygous β-thalassaemia are healthy at birth without any obvious defects. However, after the switch of the foetal haemoglobin to adult haemoglobin, usually between the ages of 3-18 months, the children will present with signs of anaemia. The symptoms may be incessant crying, difficulty with feeding, frequent vomiting, difficulty with settling and frequent infections. If no diagnosis is made and no treatment provided the prognosis is extremely poor and patients will die from anaemia, infections or heart failure before the age of five (Fawdry, 1944; cited in Ratip, 1996).

Thalassaemia intermedia is the term applied to a form of β-thalassaemia which is less serious than thalassaemia major. It is similar to thalassaemia major in terms of its genetic, biochemical and morphological characteristics and the majority of children

present with moderate anaemia after the age of two. However, blood transfusions do not have to be given regularly because the anaemia remains within moderate limits. There is therefore a more favourable prognosis in thalassaemia intermedia but the syndrome does cover a range of clinical severity.

2.2 Incidence

The world-wide distribution of thalassaemia coincides with that of falciparum malaria and is therefore common in Mediterranean countries, the Middle East, Africa and South East Asia. It is extremely uncommon among the indigenous populations of Northern Europe where the carrier frequency for β thalassaemia is 0.7 to 2 per 1000 (WHO, 1988; cited in Ratip, 1996). It is also uncommon in the native British population where the carrier frequency of β thalassaemia is 1 in 1000 (Knox-MacAulay, Weatherall, Clegg & Pembry, 1973), a finding which is consistent with the Northern European data. The relative frequency of thalassaemia intermedia in different populations ranges from about 2-10%.

As a result of the migration of different populations, thalassaemia is now however found in Northern European countries as well as Great Britain, Australia and North and South American countries (Matthews & Malios, 1976). Affected ethnic groups include Pakistanis, Sikhs, Bangladeshis, East African Asians, Italians, Chinese, West Indians, Nigerians and Vietnamese. The carrier rate among Cypriots in the UK is high at 17% for thalassaemia major and 7% for thalassaemia intermedia.

In countries such as Great Britain where the ethnic population is increasing there has been an increase in racial mixing. This factor, when considered alongside prenatal diagnosis and the option to abort has resulted in an overall decrease in the incidence of thalassaemia. Improved patient survival does however mean that as a global disease thalassaemia is becoming increasingly more common.

2.3 Treatment

2.3.1 Blood transfusions

Patients with thalassaemia major need regular blood transfusions in order to maintain a level of circulating haemoglobin which is high enough to ensure an adequate supply of oxygen to the tissues (Porter, 1996). If they do not have regular transfusions they will feel run down and lethargic. In an examination of patient adherence to another part of the treatment regime for thalassaemia, Beratis (1989) notes that only one patient out of thirty one otherwise non-adherent patients did not follow the recommended schedule of blood transfusions. Beratis suggests that this is a result of the immediate experience of symptoms.

In a review of the current strategies and perspectives in thalassaemia treatment Porter (1996) notes that haemoglobin levels should be maintained above 12 g/dL in order to suppress the production of (defective) red cells and to avoid secondary bone changes, hypersplenism and hypervolaemia. Thalassaemia major patients are therefore transfused with red blood cell concentrates every two to four weeks in order to keep the mean haemoglobin in the range of 12-12.5 g/dL. If there are no complicating

factors, the rate of fall in the levels of haemoglobin will be about 1g per week and the volume of blood needed to be transfused will vary depending on the interval between transfusions. The main risks from transfusion include iron overload, infection and immunisation to transfused red cells. It is also important to ensure against HIV and hepatitis B. Other risks associated with blood transfusions are detailed in Table one.

Porter (1996) notes that patients with thalassaemia intermedia usually manage to grow and develop at lower levels of haemoglobin and as a result regular transfusion programmes are not started unless there are major problems such as a significant delay in growth and / or sexual development. It is more likely that thalassaemia intermedia patients will need blood sporadically when there is a sudden drop in haemoglobin as a result of acute infection.

2.3.2 Iron Chelation Therapy (Desferal)

Model (1976) reported that iron overload is an inevitable consequence of regular blood transfusions in thalassaemia major. This is because humans have no significant capability of excreting iron and it is consequently stored in body tissues. Desferal was first discovered in 1960 and is an iron chelating agent which has improved the survival of iron overloaded patients. It is in fact the only iron chelating agent to have been extensively used in clinical practice in the last thirty years. Prior to its introduction most patients died before the age of thirty from heart disease as a result of iron overload.

In a review of the literature Porter (1996) notes that desferal was initially established to increase urinary iron excretion following intramuscular injection in the 1960's. By the 1970's it was clear that if it was given by this route over a period of 7 years liver iron concentration would be reduced. Subsequently, continuous infusion was found to be more effective in excreting iron than intramuscular treatment and it was shown that subcutaneous infusion over 8-10 hours was sufficient to maintain negative iron balance.

Porter (1996) notes that evidence for improved survival in patients treated with desferal began to emerge in the 1980's and that higher dose treatments were then introduced for patients with massive iron overload or heart failure. It was however only in the late 1980's and early 1990's that the full impact of desferal was clearly documented (Zurlo *et al.*, 1989; Brittenham, 1994). Analyses indicate that adherent patients can have 100% survival at age 25 whereas survival in the poor adherent group is only 32% (Brittenham, 1994).

2.3.3 Desferal Treatment Regime

Desferal is dispensed in 500 mg vials as a white powder which is reconstituted into a solution by adding sterile water. The solution is acidic and the concentration should not be greater than 10%. Higher concentrations will increase the risk of local skin reactions at the sight of the injection. Desferal is poorly absorbed by the gut and is therefore not as effective if it is taken orally.

Porter (1996) notes that the route of administration of desferal depends on the nature of the individual's problem. If the patient has experienced significant cardiac dysfunction then continuous intravenous desferal is used. This is started in hospital but as the patient recovers an indwelling portacath can be inserted which is then accessed by inserting a needle through the skin and into the portacath. The needle can then stay in place for a week or more. An alternative to continuous intravenous treatment is continuous subcutaneous treatment. However, in this situation the needle usually causes soreness and the patient will need to insert a new needle daily.

There are a number of different modes of administration of desferal available to patients. Historically the most widely used delivery system has been the battery-operated syringe driver systems. More recently a number of other lighter or smaller systems have been used. Battery operated pumps can take larger volumes of solution allowing continuous intravenous treatment for up to one week. However, an alternative is to use the disposable balloon pumps which work by expelling fluid under the pressure produced by filling and by the expandable balloon. These devices are simple and light and are attractive to patients who need continuous infusions. They are also available with the solution already prepared.

Porter (1997) notes that an 8-12 hour subcutaneous infusion of desferal 5-6 nights per week is standard practice for thalassaemia patients. This will maintain iron loading at levels below those regarded as toxic. It is recommended that desferal should usually be started when the serum ferritin (iron loading) reaches 1000 μg/L or when a child with thalassaemia major reaches the age of 3 years. If treatment is started before these

stages then growth retardation may result. In addition, failure to start treatment at these points may also lead to growth retardation due to iron overload.

Iron overload can also occur in thalassaemia intermedia despite minimal blood transfusions. This results from excessive dietary iron absorption but the exact mechanism by which this occurs remains unclear. In patients with thalassaemia intermedia where the rate of iron loading might be slower the optimal time to start treatment has not yet been clearly established. However, if serum ferritin levels reach 1000 μg/L, treatment should be considered. Porter (1996) notes that treatment at standard doses subcutaneously two to three times a week will generally achieve a negative iron balance in these patients.

2.3.4 Efficacy Monitoring

The most convenient way to monitor iron loading is by the serum ferritin. In relation to this, Olivieri *et al.* (1990) reported that iron excretion correlates with serum ferritin as well as with desferal-induced urinary iron excretion. This is not however a perfect indictor of iron overload as serum ferritin reflects iron stores predominantly in the liver and can be falsely elevated with hepatic inflammation or damage. Serial measurements are therefore a more reliable measure of serum ferritin than single measurements and ideally these values should be measured monthly. A more reliable, but less convenient and extremely invasive way to monitor efficacy is by serial liver biopsies.

The target ferritin should be below 2000 μg/L as Olivieri *et al.* (1994) reported that the risk of complications from iron overload increases as the value rises above this.

However, when ferritin levels fall below 1000 μg/L the risk of desferal toxicity increases. It is therefore important to give doses of desferal appropriate to the degree of iron overload.

2.3.5 Side Effects of Desferal

Porter (1996) notes that there are a number of side effects associated with the use of desferal. High frequency sensorineural hearing loss has been seen in patients on high desferal regimes and problems with vision are also possible but again these are usually confined to high doses. Local mild reactions such as skin reddening and soreness at the sight of subcutaneous infusion may also be seen and are often caused by desferal being reconstituted above a concentration of 10%. Increasing the volume of water used to dilute the desferal can however reduce these reactions.

In addition, there is also an increased risk of Yersinia infection in iron overload which increases with desferal treatment. Patients who experience diarrhoea, abdominal pain or fever should stop desferal and if Yersinia is diagnosed then antibiotics should be prescribed. Finally, whilst the use of desferal usually improves growth in thalassaemia major by decreasing iron overload if too much is given growth retardation my result.

2.3.6 Complications of current or past iron overload

As a result of desferal treatment patients can now live longer without the complications of iron overload. However, the complications of current or past iron overload can still affect various aspects of the persons medical functioning. Regular monitoring for the

early signs of the complications of iron overload can help maximise both the quality of life of the individual as well as their life expectancy. Porter (1996) provides a review of some of the main medical complications resulting from current or past iron overload. These are outlined below.

As indicated earlier, regular monitoring of growth is particularly important as a change in the growth velocity can indicate under or over treatment. Before the introduction of desferal growth was usually poor as a result of iron overload. Growth is now however relatively normal and desferal has been shown to improve growth and pubertal development. However, over-treatment can cause growth retardation. If this is the case, reducing the dose of desferal can restore growth.

In addition, with optimal chelation therapy, the proportion of patients who develop secondary sexual characteristics has gradually risen, although Porter (1996) notes that this is still better achieved in females (70%) than in males (40%). Puberty may still be delayed in a variable proportion of patients and fertility is often relatively short lived. Indeed, some patients never become fertile without medical intervention.

Another serious late complication of iron overload is insulin-dependent diabetes. This affects about 6% of thalassaemia major patients on current standard treatment but is uncommon in thalassaemia intermedia. Porter (1996) notes that there is now convincing evidence that chelation prevents insulin dependent diabetes. In addition, osteoporosis, liver fibrosis and Hepatitis C add further risk factors. Infections can also

be frequent and severe in both thalassaemia major and thalassaemia intermedia and include pneumonia, meningitis, peritonitis, osteomylelitus and ear infections.

Finally, cardiac complications are the major cause of non-infective death in thalassaemia major. In a study examining survival and causes of death in 1087 Italian patients Zurlo *et al.* (1989) reported that heart disease was the most common form of death (63%) and that it was present in 76.8% of the patients who had died. The extent of the damage was directly related to the transfusional iron overload in the absence of, or poor adherence with chelation therapy.

Wolfe, Olivieri & Sallan (1985) have shown that regular chelation prevents heart impairment. In this study, only one out of the seventeen well chelated patients became cardiopathic, whereas heart failure or rhythm abnormalities appeared in twelve out of the nineteen poor adherers. Furthermore, in a 20 year study by Olivieri *et al.*, (1994) no cardiac complications occurred in those whose ferritin levels were kept below 2,500 µg/l or only exceeded this limit in less than 33% of the evaluations performed over the years.

A summary of all the complications seen in untreated thalassaemia major and complications due to iron overload and transfusions are presented in Table one.

2.4 Summary

Thalassaemia is a chronic illness that develops in the first few years of life and requires lifelong treatment. This treatment includes regular blood transfusions (every 2 to 4

weeks) and subcutaneous infusions of an iron chelating agent (desferal) for 8-12 hours per day, 5-6 times per week. If patients do not have regular blood transfusions then they will begin to feel run down and lethargic, and adherence to blood transfusions is not considered to be a problem. There are however no immediate effects of failure to adhere to iron chelation therapy which may lead to non-adherence given the intrusive nature of the regime. If desferal is taken as often as is recommended then patients can enjoy a long life with minimal clinical symptoms. There are however serious implications of not adhering to the desferal regime, the ultimate being death as a result of heart failure.

For an individual diagnosed with thalassaemia the treatment regime is lifelong and complex and requires major adjustments in lifestyle - initially for the parent who has to take responsibility for their child's treatment and then for the patients themselves as they learn the set of illness related tasks. Undoubtedly this will have profound effects on the patient's psychological and social status. It is therefore to the literature on the psychosocial effects of thalassaemia that we now turn.

Table 1. Complications of Thalassaemia Major (Canale, 1974)

(Modified by Berdoukas, 1998)

Haematological	1. Hyperbilirubinaemia[a] 2. Coagulation defects[a/b] 3. Immune and allergic reactions due to blood transfusions[c] 4. Lymphoid hyperplasia[a/c]	5.Pancytopenia[a] 6. Functional asplenia[a] 7.Extramedullary haemopoietic masses[a]
Cardiac	1 Arrhythmias[a/b] 2. Pericarditis[a/b]	3. Cardiac failure[a/b]
Hepatic	1. Pigment gallstones[a] 2 Hepatitis B and / or C[c]	3. Cirrhosis and decreased protein synthesis[a/b]
Renal (rare)	1. Interstitial nephritis[a] 2. Hyponatraemia[a]	3. Renal enlargement[a/b] 4.Hypochloraemic alkalosis[a]
Endocrine	1. Diabetes mellitus[b>a] 2. Hypopothyroidism[b>a] 3. Short stature/ failure to thrive[b>a]	4. Hypothyriodism[b>a] 5. Delayed sexual maturation[b>a]
Bone changes	1. Osteoporosis[a/b] 2. Craniofacial deformities[a]	3. Pathological fractures[a] 4. Synovitis &/or arthritis[b>a]
Dermatological	1. Hyperpigmentation[b] 2. Folliculitis (rare)[a]	3. Leg ulcers[a]
Other	1. Pulmonary complications[a/c] 2. Psychological problems[a/b/c]	3. Neuromyopathy[a/b]

(a) Various complications seen in untreated thalassaemia
(b) Complications due to iron overload
(c) Complications due to transfusions.

3. Psychosocial factors in Thalassaemia

Psychosocial problems are becoming increasingly important as the number of living thalassaemics is rising globally. Their prognosis is steadily improving as a result of regular blood transfusions and early introduction of regular iron chelation therapy. Ratip & Modell (1996) note that when modern treatment is provided and there is patient adherence, 80% of the patients live a minimum of 20 years. Considering the importance of the problem, there are only a limited number of studies examining the psychosocial impact of thalassaemia. Indeed, only one study (Ratip & Modell, 1996) to date has examined the psychosocial impact of thalassaemia intermedia.

Thalassaemia and the treatment it requires are responsible for a range of psychosocial burden. The quality and the quantity of this burden varies both within and across the developmental life cycle and as a result studies have examined this impact during childhood, adolescence and adult life. The studies on the psychosocial burden in childhood will now be examined alongside those in adulthood due to the evidence that childhood psychological disorders are associated with poor adjustment in adolescence and adult life (Target & Fonagy, 1996).

3.1 Psychosocial factors in childhood and adolescence

Studies examining the psychosocial impact of thalassaemia for children and adolescents have highlighted a number of different factors. These include education, sport, family adjustment, social isolation, self image and psychiatric illness.

With regard to education, Logothetis *et al.* (1971), examined 138 people between the ages of 2 and 28 and found that the intelligence of thalassaemia children is within the normal range. This finding has also been supported in more recent studies (Tsiantis, 1990; Beratis, 1993). In addition, a largely retrospective study by Ratip (1996) examined 64 thalassaemia patients aged between 6 and 34 years using a semi-structured interview. Ratip found that 62% of the thalassaemia major and 43% of the thalassaemia intermedia patients reported that their education was affected by having to take time off school because of their illness. The study did however include mainly adults whose comments would have referred to the situation between 10 and 20 years ago and modern management will have greatly reduced the number of absences from school.

There is little information in the literature on how the sporting lives of children with thalassaemia are affected. In Ratip's (1996) study sport activity was affected in 86% of the thalassaemia major patients with 38% not participating in any sports at all. In comparison, sports activity was affected in 62% of the thalassaemia intermedia patients and 33% could not participate in any sport at all. However, no data was provided in order to make comparisons between these results and those within the general population.

With regard to social support, Tsiantis (1990) examined 40 children between the ages of 7.5 and 12 years and reported that many children with thalassaemia had few friends. However, in a phenomenological study examining five adolescents between the ages of 14 and 19 and their parents, Georganda (1988) reported that the patients' relationships

were not affected. They did however worry that when friends found out about the illness they wouldn't be liked anymore. They also wanted to forget that they had the illness.

In relation to family support, Tsiantis (1990) reported that the children remained dependent on their parents who were in turn overprotective towards them. On the other hand, Tsiantis (1990) also noted that parents can exert excessive pressure on the thalassaemic child to achieve standards of academic work or sport. This was linked to parental denial of the problem. Furthermore, Ratip (1996) found that a lack of communication between the child and the parents about the illness can result in the child not being able to discuss their feelings and their worries about the illness and that this can result in emotional isolation. Some children can then become very secretive at school and not get involved in the normal activities.

Living with a chronic illness can also frequently have consequences on an individual's self image. In a presentation of two case studies, Georganda (1990) reported that chronic illness can represent being different, inferior and inadequate and that this can lead to a loss of self esteem and feelings of increased dependence. Tsiantis (1990) also found that thalassaemia children with facial deformities and other physical abnormalities tended to have negative self concepts with respect to popularity, happiness, satisfaction and anxiety.

In addition, the research indicates that there is a high incidence of psychiatric disorders in children with thalassaemia and that the most frequent are anxiety and then

depression. In Georganda's study (1988), whilst there was no evidence of major psychiatric illness, patients were afraid of early death, medical complications, loss of independence and failing to have a career or a family. They also reported feelings of sadness and depression. Sherman *et al.*(1985) also found poor psychiatric adaptation with dysphoric moods and low self esteem in 23% of the 23 children aged between 6 and 16.

Furthermore, Beratis, (1993) investigated psychiatric disorders and the social profile of 57 children with thalassaemia and reported that the number of psychiatric disorders was significantly greater in thalassaemia patients than in a general population control group. Oppositional defiant disorder was diagnosed in 23% of the thalassaemics compared to only 5% in the control group. In addition, the thalassaemia group demonstrated a significantly greater frequency of disturbed behaviours with relatives and friends than did the controls. Tsiantis (1990) also found that 42.2% of the thalassaemia children were diagnosed as having a psychiatric disorder as opposed to 31.2% in a control group of chronically sick children.

3.2 Psychosocial factors in adulthood

Studies examining the psychosocial burden for adults with thalassaemia have highlighted the areas of social integration, social isolation, family adjustment, self image and anxiety. There are however few studies of the psychosocial burden of thalassaemia in adulthood when compared to those in childhood and adolescence. The existing research will now be reviewed.

The clinical severity of the thalassaemia syndrome has been found to have a significant influence on social integration. Ratip (1996) reported that 48% of the thalassaemia major and 19% of the thalassaemia intermedia patients had problems with social integration in that they were either unemployed or unable to set up a family as a result of the illness. Additionally, only three thalassaemia major patients were married and only one of these had a child.

In addition, the Ratip (1996) study indicated that the social activities of 34% of the thalassaemia major patients and 28% of the thalassaemia intermedia patients were reduced to a severe degree. As a result, relationships with friends were affected adversely. The major reason given for this social isolation was because they were taking their desferal. Ratip also reported that denial was an important issue with 19% of the thalassaemia major and 24% of the thalassaemia intermedia patients telling no one about their illness except for their best friends.

Another issue that has been identified in the research is that of parental overprotection. Ratip (1996) found that 57% of the adult thalassaemia major patients and 43% of the thalassaemia intermedia patients felt that they were overprotected by their parents. This finding was supported by Woo, Giardina & Hilgartner (1985) who reported a 91% incidence of overprotection in 22 mostly adult thalassaemia patients.

Furthermore, with regard to self image, Woo *et al.* (1985) reported that 54% of the patients considered themselves different. Two thirds wanted to change the fact that they had thalassaemia and yet surprisingly, nearly half were content with their personal

circumstances and did not wish to be like anyone else. Ratip (1996) also found that 48% of the thalassaemia major and 62% of the thalassaemia intermedia patients felt some degree of difference when they compared themselves to their peers and their siblings. The reasons given included both physical and social factors. Furthermore, Politis *et al.* (1990) found that 70% of the Italian thalassaemics in the study considered themselves as normal whereas one quarter felt that they were sick but that they could handle their problems. This study concluded that patients can show a good level of integration and favourable self image.

Finally, the research indicates high levels of psychiatric symptomatology in thalassaemia patients and that anxiety is a common feature of this. Woo *et al.* (1985) reported that about two thirds were worried about pain, death and the unknown. Ratip (1996) also reported that 77% of the thalassaemia major patients and 57% of the thalassaemia intermedia patients had a degree of anxiety. Examples of worries were fear of early death, not being able to set up a family, or in the case of thalassaemia intermedia, having to start transfusions and desferal treatment. In addition, Georganda (1990) reported that the accurate perception of the implications of such an illness cannot but create feelings of anger and depression, fears and worries.

3.3 Summary

The research suggests that there is a range of psychosocial burden associated with living with thalassaemia. The main areas have concentrated on the psychosocial issues for children and adolescents although there is also some research on adult factors.

Across all age groups there would appear to be difficulties with social isolation / integration, self esteem / self image and psychiatric symptomatology.

It can therefore be seen that living with a chronic illness such as thalassaemia requires that the patient endures a strict lifelong medical regime. They also experience a range of psychosocial burden associated not only with the illness but also with the actual treatment. Given the enormity of this biopsychosocial burden, patients may in certain situations or at certain stages in their life feel that they cannot cope. It is possible that this may manifest itself in a failure or partial failure to take their treatment as often as is recommended. It is therefore to the literature examining adherence to medical regimes that we now turn.

4. Adherence to medical regimes

4.1 Terminology / conceptualisation

The terms compliance and adherence have both been used over the years in relation to medical regimes. The term 'compliance' has traditionally been used to refer to the extent to which patients are obedient and follow the instructions of health care providers. It could be argued however that the term 'non-compliance' carries a judgmental attitude and that it suggests deviant behaviour on the part of the patient. This is in contrast to the term 'adherence' which is thought to imply a voluntary collaborative involvement of the patient in the mutually accepted treatment regime (Meichenbaum & Turk, 1987). This new way of conceptualising adherence seeks to

empower patients and broadens the choices they can make about the way they react to and cope with illness.

Adherence is a difficult concept to define and should be viewed as a complex dynamic phenomenon that can change over time. For example, a patient's adherence to one feature of the treatment regime does not ensure adherence to other features or even to the same feature at a later time. Indeed, adherence to medication can be defined in a number of ways. Ley & Llewelyn (1995) report that these can include not taking enough medication or taking too much medication. They also suggest that it may be that patients are not observing the correct interval between doses or the correct duration of treatment.

Another difficulty relating to the definition of adherence is that there are many health related problems for which there is little agreement as to what level of adherence is required to achieve the desired effect. Indeed, in some medical conditions adherence is very complex. A recent report by the Royal Pharmaceutical Society (1997; cited in Myers & Midence, 1998) noted that there is no recognised or accepted definition of non-adherence. It suggests that apart from actually not having the medicines dispensed most departures from adherence are partial and not total. It also suggests that terms like 'poor' or 'incomplete' or 'inadequate' adherence are probably better descriptions of the problems than 'non-adherence'. Gordis (1976) has suggested that non-adherence can be conceptualised as "*the point below which the desired preventive or desired therapeutic result is unlikely to be achieved*" (p.52). However, the problem

with this criteria is that it assumes that the percentage of the performance of the recommended behaviour necessary to achieve the desired effect is known.

Examples of definitions of non-adherence criteria include Gordis, Markowitz, & Lillienfield, (1969) who defined adherence on a course of penicillin when 75% of the urine tested was positive for the drug. Furthermore, in a study of rheumatic patients Donovan & Blake (1992) identified different forms of non-adherence. Some of the participants were totally non-adherent, some took fewer tablets than prescribed and others actually took more. Finally, in the study by Beratis (1989) which examined adherence to iron chelation therapy, non-adherent participants were classified as those who obtained less than 60% of the recommended dose.

4.2 Incidence of non-adherence

The level of adherence in the general population varies depending on the patient population, medical condition, form of treatment and the definition of adherence. As a result, the precise level of treatment non-adherence is difficult to determine. Most estimates of non-adherence range from a low of 15% to a high of 93% (Kaplan & Simon, 1990). Meichenbaum & Turk (1987) note however that estimates converge at 30%-50% in chronic illness.

As noted above, the level of treatment adherence varies depending on a number of factors. In their review of the literature, Meichenbaum & Turk (1987) note that the highest rates of adherence occur for treatment with direct medication (injections, chemotherapy), high levels of supervision and monitoring, and acute onset. In

contrast, they also note that the lowest levels of adherence occur with patients who have chronic disorders, when no immediate risk or discomfort is evident, when life-style changes are required and when prevention rather than symptom palliation or cure is the desired outcome. Furthermore, non-adherence has been reported to be a serious problem for the chronically ill who do not see any immediate beneficial results from adhering to the treatment regime.

In addition, a number of studies have indicated that non-adherence can be a problem in conditions which are life threatening and that it is not just confined to less serious conditions. Studies of patients who have had organ transplants indicate that these patients are just as likely to be non-adherent even though non-adherence can lead to rejection of the organ or death of the patient. For example, Didlake, Dreyfus, Kerman, van Buren, & Kahan (1988) reported non-adherence to be the third leading cause of renal transplant rejection behind rejection and systemic infection. In addition, in a study by Kiley, Lam, & Pollak (1993), the incidence of non-adherence in kidney transplant patients was assessed. Twenty six percent of patients were classified as non-adherent to medication, 23% as non-adherent to diet and 28% as non-adherent to both diet and medication. Furthermore, Rovelli *et al.* (1989) examined 196 patients in a pre-transplant medicine regime and reported that 15% were considered non-adherent. Indeed, 30% of non-adherent patients either rejected the transplant organ or died compared to only 1% of the adherent patients.

4.3 Measurement of adherence

The assessment of adherence is a complex task and a number of different forms of assessment have been used. Each however has its own set of problems and would therefore indicate the need for multiple assessments rather than just one (Meichenbaum & Turk, 1987). Many measures are available and may include interview, self report, self monitoring, pill counts of unused tablets, tallies of refills of medication, behavioural measures, clinical rating, marked-sign techniques, biochemical indicators and clinical outcome. The methods chosen by the researcher will be dependent on the treatment regime and the available resources.

Myers and Midence (1998) note that pill counts are the most widely used objective measure of adherence and have been found to yield higher estimates of non-adherence when compared with self report measures. However, this method can be intrusive and does not actually indicate whether the medication was taken or whether it was thrown away. This also applies to the method of checking prescriptions in that the prescription may have been collected but this does not imply that the medication has been taken. In addition, whilst electronic measuring devices are becoming more widely used, some of them look obtrusive and patients may be aware that their medication usage is being monitored, thus affecting their behaviour.

Myers & Midence (1998) also note that patients are accurate when they say that they have not taken their medication. Self report measures have however been challenged because they may be inaccurate and are likely to be biased. Ley (1988) notes that the patient may want to deliberately deceive the researcher or that they may not

understand the treatment regime and therefore may not realise that they are not adhering. It may also be that they have simply forgotten that they did not take their treatment. It is also possible that the patient may want to be viewed positively by the health care provider and thus overestimate their levels of adherence. In addition, it is possible that the simple act of self monitoring may serve as a cue and thus alter behaviour.

Overall, whilst there are clear limitations to self report it has been suggested that certain simple self report measures can be used to assess and predict adherence. In an extensive review of the literature, Kaplan & Simon (1990) conclude that patients can be very accurate in predicting the likelihood that they will adhere to a treatment regime. This is if they are asked simply and directly.

Biochemical markers are another useful measure of adherence because they are less subject to bias than self reports. In the case of patients with thalassaemia the levels of serum ferritin can be useful biochemical markers. These results should however be met with caution as the actual iron loading can be distorted by liver inflammation and infection.

With regard to doctor reports the evidence suggests that they are particularly bad at determining whether patients have taken their medication correctly and that they tend to overestimate adherence (e.g. Brody, 1980). For this reason it has been suggested that it is worth considering other health professionals judgements of adherence.

Indeed, a recent study by Edelman *et al.* (1996) suggests that nurses may be less biased in their rating of patient adherence.

4.4 Summary

The shift from the term 'compliance' to 'adherence' represents an important step in emphasising the self regulatory activity of the patient and is therefore the term that will be used for the purposes of the present study. Previous research indicates that non-adherence is a difficult concept to define and that it may indeed be defined in a number of different ways. In fact it has been suggested that the terms 'poor', 'incomplete' or 'inadequate' adherence may constitute better ways of describing this concept. For simplicity however, the term non-adherence is used in this study to refer to greater levels of percentage of treatment missed along a continuum.

Adherence is a complex phenomenon that changes over time and is therefore a difficult concept to define. Furthermore, alongside the difficulties associated with its definition are the difficulties associated with its measurement. No one method of measuring adherence is foolproof and a number of measures of adherence should be employed in any one study. The measures employed will depend on the nature of the illness and the treatment regime.

Over the past thirty years many studies have examined the sorts of factors that influence adherence to treatment regimes in relation to a number of medical conditions. The existing research on adherence to iron chelation therapy will now be reviewed.

5. Adherence to iron chelation therapy

A number of studies have commented upon the difficulties associated with adherence to the desferal regime (e.g. Politis *et al.,* 1990; Massaglia & Carpignano, 1985; Georganda, 1990). There is however only one research study that has examined psychosocial influences on adherence to iron chelation therapy (Beratis, 1989). In this study, the adherence levels of 113 thalassaemia patients aged between 7 and 28 were assessed and 31 (23.7%) were found to be non-adherent. Thirty one adherent patients were then matched as a control group. Non-adherent participants were considered to be those who obtained less than 60% the recommended dose of subcutaneous infusions of desferal. The study does not however state a rational for this criteria.

Non-adherence was assessed by obtaining information about the medical treatment from the patients and their families, the haematologist, the nurse to which the patient was assigned and the psychiatrist who performed the psychiatric evaluation. The study does not indicate however what adherence information was obtained. In addition to these reports serum ferritin levels were also taken and indicated that the non-adherent participants had higher ferritin levels than the adherent participants.

A semi-structured interview was then conducted with the non-adherent group. The results indicated that excluding separation anxiety disorder and primary functional enuresis the frequency of psychiatric disorders in the non-adherent and adherent groups was 68% and 10% respectively. Oppositional disorder was the most frequent psychiatric disorder and was associated with the most profound deviation from adherence. However, in one third of the non-adherent patients no psychiatric disorder

was identified. For all patients the most frequently stated reason for non-adherence was pain. This was followed by local swelling, secrecy, boredom and denial.

It can therefore be seen that there is only one study examining non-adherence to iron chelation therapy and that this specifically examined the incidence of psychiatric disorder in a non-adherent group. Given the complexity of the concept of adherence, factors associated with non-adherence will vary between individuals, illnesses and treatment regimes. However, due to a lack of existing research regarding non-adherence to desferal it is to the literature regarding factors associated with non-adherence in chronic illness that we now turn. This serves to provide a framework for thinking about potential influences on adherence to the desferal regime.

6. Psychosocial factors in chronic illness and adherence

6.1 Overview

A great deal of research has been conducted into the determinants of, or factors related to adherence and many possible reasons for non-adherence have been identified. Some of the general issues in adherence to treatment include, doctor-patient communication (Noble, 1998), prospective memory (Ellis, 1998) and the influence of written information on patient knowledge (Raynor, 1998). Additional reasons for non-adherence which have been investigated include the characteristics of the patient, the physician and the treatment regime (Meichenbaum & Turk, 1987). The characteristics of the patient that have been examined include both social and psychological components.

The literature regarding a number of selected psychosocial factors associated with chronic illness will now be presented alongside the research examining the relationship between these factors and adherence. Demographic variables, psychological distress and well-being, social support, health locus of control, health value, self efficacy and acceptance of illness will all be examined in the context of the chronic illness and adherence research.

6.2 Demographic variables

Reviews by Haynes, Taylor & Sackett (1979), Kaplan & Simon, (1990) and Meichenbaum & Turk (1987) all indicate that the majority of studies fail to find an association between adherence and patients' socio-demographic variables. In addition, the idea that stable socio-demographic or dispositional characteristics are the sole determinants of adherence has been discredited by evidence that an individual's level of adherence may vary over time and between different aspects of the treatment regime (Cleary, Matzke, Alexander & Joy, 1995). These reviews therefore indicate that considerable research efforts have all failed to identify any stable personality traits or socio-demographic characteristics that predict which patients will or will not adhere.

6.3 Psychological distress/ well-being

It is well known that illness can result in a number of psychological difficulties and increased psychiatric symptomatology has been reported in a number of the studies investigating the psychosocial impact of thalassaemia (Tsiantis, 1990; Georganda, 1988; Sherman *et al.*, 1985; Woo *et al.*, 1985). Furthermore, the Beratis (1989) study

indicates that increased psychiatric symptomatology is associated with non-adherence in thalassaemia patients.

In the general adherence literature depression and anxiety in particular have been found to be associated with poor adherence. Higher scores on the MMPI depression scale have been associated with dropouts from cardiac rehabilitation exercise programs and from alcohol treatment (Blummenthal, Williams, Wallace, Williams, & Needles, 1982; O'Leary, Rohsenow, & Chaney, 1979). Anxiety has been also been associated with poor medication adherence amongst hypertensives (Nelson, Stason, Neutra, Soloman, & McArdle, 1978). In addition, Nagy & Wolfe (1984) found that adherence to self management procedures for adults with diabetes, hypertension and / or pulmonary disease was negatively associated with psychological symptomatology.

It is important to note however that the emotional consequences of chronic illness are not all negative. Just as negative psychiatric symptomatology is associated with non-adherence feelings of well-being may be associated with adherence. However, no study to date has examined this relationship.

The few studies that have investigated positive outcomes in chronic illness report that individuals have found an increased value in close relationships, greater meaning in day-to-day activities and greater compassion towards others with difficulties (Laerum, Johnson, Smith & Larsen, 1987). Georganda (1990) also notes that the presence of a chronic illness can be growth promoting and reminds us that in Chinese the word 'crisis' is written by two symbols; danger and opportunity. In addition, in a study of

adolescent thalassaemia patients, Zani, Di Palma & Vullo (1995) conclude that chronic illness does not imply psychopathologies and that it can actually strengthen resources. Ryff (1989) has reviewed various perspectives on positive psychological functioning and notes that previous perspectives can be integrated into one summary. These include self acceptance, positive relations with others, autonomy, environmental mastery, purpose in life and personal growth.

6.4 Social support

The concept of social support has also been examined in the chronic illness and adherence literature and a vast body of research supports the notion that people with partners, friends and family members who provide emotional and material support are in better health than are people with fewer social contacts. For example, Thompson, Gill, Abrams & Phillips, (1992) examined sickle cell disease and reported that good adjustment was associated with family functioning which was characterised by high support and low conflict and control.

However, as a construct, social support is multifaceted and the particular definition of social support has an important effect on the relationships found. There are many different definitions of social support. For example, Cohen & Wills (1985) distinguish four different functions, namely esteem support, informational support, instrumental support and social companionship. An emphasis on one or other of these aspects has resulted in a variety of measures that are not highly related to each other (Sarason, Sarason, Shearin & Pierce, 1987). In their development of a brief measure of social support Sarason *et al.* (1987) define two components. One is the number of available

others the individual feels they can turn to in times of need and the other is the individual's degree of satisfaction with the perceived support available.

This resource of social support can be mediated in a number of ways. It has been suggested that it can have both direct and indirect effects (Cohen, 1988). The direct effect of social support reduces or eliminates stress by modifying cognitive appraisal or by changing physiological responses. The indirect effect on the other hand operates by bringing about changes in health related behaviour. One such change in health related behaviour that has been associated with social support is adherence to the treatment regime.

For example, in a review of the literature examining social support and adherence in diabetes, Warren & Hixenbaugh (1998) note that it is the individual's 'perceptions' of the nature and function of relationships that is important. They comment that this information is a better indicator of non-adherence to a medical regime than more objective measures such as network size. In addition, Doherty, Schrott, Metcalf & Lasiollo-Vailas (1983) examined the relationship between instrumental spouse support (i.e. how to follow a medical regime), its determinants and husbands' adherence to behaviours that prevent coronary heart disease. They found that spouse support was significantly and positively correlated with patients' adherence to medication packet counts. Among highly supported patients the mean adherence score (96%) was significantly higher than among patients with low support (70%).

6.5 Health locus of control / value of health

Another concept which has been examined in relation to chronic illness and adherence is that of health locus of control. The notion of locus of control arose from Rotter's (1954) social learning theory and refers to the extent to which the person feels they have control over what happens in a situation (i.e. internal locus) or that the situation is being controlled by other factors, for example, other people, luck or chance (i.e. external locus).

The main prediction from this theory is that internals on the multidimensional health locus of control will be more likely to engage in health promoting activities although during an acute or chronic illness it may be advantageous to believe in powerful others (Norman & Bennett, 1996). In a review of the literature, Horne & Weinman (1998) note that empirical studies investigating the role of health locus of control beliefs in adherence are not conclusive. Some have found no association between control beliefs and adherence (Harvey, 1992; Harvey & Peet, 1991, cited in Horne & Weinman, 1998) and in studies where associations are found, there is little consistency in the type of control which is associated with adherence (Wilson, 1995; Bruhn, 1983, cited in Horne & Weinman, 1998). Horne and Weinman (1998) do note however that the use of disease-specific measures of assessing health locus of control improves the utility of this construct in explaining medication related behaviour (e.g. Georgiou & Bradley, 1992).

The validity of the concept of health locus of control in predicting health behaviour has however been challenged. Believing one can control ones health would not necessarily

be associated with actually taking steps to maintain good health if health is not particularly valued. Many instances can be found in which people's values guide their behaviour and the value that an individual places on their health has generally been assumed to be universally high. Indeed, in the context of a life threatening disease it has been considered a safe assumption that the salience of health and the value put on it is consistently high.

Lau, Hartman & Ware (1986) note that the concept of health value has not been applied in any systematic and theoretically sophisticated manner to health research with the exception of a limited number of studies that explore the health locus of control concept. They note that internal health locus of control beliefs should be associated with health behaviour among people who value health highly but that there is no reason to expect this association among people who do not have a particularly high value on health, particularly if some other conflicting behaviour is more highly valued.

6.6 Self efficacy

As one focuses attention on a specific behaviour, beliefs about the degree of control one has over the behaviour may be closely related to other expectancies such as beliefs about one's competency in being able to perform the behaviour. These are called self efficacy beliefs. In the health psychology literature the usefulness of the concept of self efficacy has been widely accepted. In relation to adherence at least two types of efficacy beliefs are thought to be important, namely outcome efficacy and self efficacy. Outcome efficacy refers to beliefs about whether the behaviour will result in an

effective outcome whereas self efficacy concerns the individual's beliefs as to whether they will be able to carry out the behaviour.

Bandura (1977) notes that individuals are thought to acquire their sense of self efficacy from their assessment of the outcome of their own behaviour, the behaviour of others and feedback about their behaviour that they receive from significant others. According to Bandura (1977), expectations of self efficacy are the most powerful determinants of behavioural change because self efficacy expectancies determine the initial decision to perform a behaviour, the effort expended and persistence in the face of adversity.

Experimental research strongly suggests that self-efficacy is a more powerful predictor of behaviour than either outcome expectancies or past performance (Bandura, 1977). Several studies have demonstrated a relationship between perceived self efficacy and adherence to recommended health-related behaviours. For example, in a study by Kaplan, Atkins and Reinsch (1984) patients with chronic obstructive airways disease who were given specific training to encourage adherence in a walking exercise prescription increased their walking compared to those in the control group. The authors noted that these changes were mediated by specific self efficacy for walking.

6.7 Acceptance of illness

Another psychological factor associated with chronic illness and one that may potentially be associated with non-adherence is an individual's difficulty accepting the fact that they have an illness. In a presentation of two case studies of thalassaemia

patients Georganda (1990) notes that when our body is ill it causes pain and frustration. When an individual has flu they may well ask themselves when they will get well again. However, when the individual has a chronic illness they will never be well again - the illness is part of them. This can be a very difficult idea to accept.

It is not easy to incorporate the presence of an illness in your self image and feel good about yourself. Georganda asks the question, *"Can it be that your body causes you pain and frustration and yet you take care of it?"*(p.466). In addition, Georganda notes that the single most important factor in the adaptation to thalassaemia is a persons attitude to what they have, how they view the illness and how it is incorporated into their self image. Is it that they are ill and therefore weak and fragile, or is it that they have an illness which implies that they are in control of the situation.

Existing research indicates that a persons acceptance of their illness can have implications for their psychological health. Hogg, Goldstein & Leigh (1994) examined acceptance of illness in patients with motor-neurone disease and found that greater physical impairment was accompanied by less acceptance of the illness. Their results also indicated that people who were more accepting of their illness showed less anxiety and depression beyond the influences of the severity of the illness. In addition, Revenson & Felton (1989) examined rheumatoid arthritis patients and found that increased disability was related to lowered acceptance of illness and increased negative mood. However, whilst this concept has been examined in the general health research no studies to date have specifically examined the relationship between acceptance of illness and adherence.

6.8 Summary

The literature indicates that there are many psychosocial factors associated with chronic illness and that some of these may influence adherence to a medical regime. Some psychosocial factors have been more extensively researched in relation to adherence than others. The research indicates that there is little evidence supporting the idea that demographic variables will influence adherence. The research does confirm however that people with a chronic illness are more prone to psychiatric symptomatology, particularly anxiety and depression and that this is associated with non-adherence. In addition, whilst there is evidence that the emotional consequences of chronic illness are not all negative, this concept has not been examined in the adherence literature to date.

Another possible barrier to adherence may be difficulty accepting the illness. Existing research has made connections between difficulties accepting one's illness and increased psychological symptomatology. There is however no available research to date on the direct relationship between acceptance of illness and adherence. This is in contrast to social support where there is a wealth of research linking this concept to adherence. In addition, health locus of control has also been extensively researched although its relationship to non-adherence is inconclusive. Using a disease specific measure and a value of health measure can however improve the validity of this construct in relation to adherence. Finally, the concept of self efficacy relates to the individual's assessment of their own behaviour and research suggests that it can be a powerful predictor of behaviour, including adherence.

7. Rationale

Cardiac complications are the major cause of non-infective death in thalassaemia major as a result of iron deposition the heart. The extent of the damage is directly related to the transfusional iron overload in the absence of, or poor adherence to, iron chelation therapy. Ratip (1996) acknowledges the need for more studies to analyse the psychosocial burden associated with thalassaemia and comments that *"the weight of the perceived burden is indicated by the fact that the main cause of death from thalassaemia in developed countries is non-compliance with treatment, when patients give up the treatment either partially or completely"* (p.42). Ratip & Modell (1996) also note that in Western countries today, the most common cause of death is psychosocial. In addition, Georganda (1990) notes that obtaining adherence with medical treatment is relatively easy when the child is young and the parents co-operate but that it is difficult when dealing with teenagers who do not want to adhere to anything and with adults who do it because they have to - although they do not care - and not because they want to live.

It is therefore surprising that only one study to date has specifically examined factors affecting adherence to iron chelation therapy and that this was with a mainly adolescent population. The present study aims to examine a number of psychosocial factors which may influence adherence to iron chelation therapy in an adult population of thalassaemia major and thalassaemia intermedia patients. The psychosocial factors identified for examination are based upon an examination of the literature regarding the psychosocial burden of patients with thalassaemia as well as the general literature on adherence to medical regimes in chronic illness.

As noted previously, increased psychiatric symptomatology in patients with thalassaemia has been reported in a number of studies (Tsiantis, 1990; Georganda, 1988; Sherman *et al.*, 1985; Woo *et al.*, 1985). This psychiatric symptomatology has also been linked to increased levels of non-adherence to iron chelation therapy in a study by Beratis (1989). In addition, connections have been made in the general literature between psychological distress and non-adherence. The relationship between psychological distress and adherence will therefore be examined. Furthermore, the literature indicates that the emotional consequences of chronic illness are not all negative. Just as psychological distress has been associated with non-adherence, well-being may be associated with adherence and this relationship will also be examined.

Existing research has indicated that social support is associated with adherence. Furthermore, research regarding the psychosocial burden associated with thalassaemia has highlighted the difficulties that the patients have in relation to social integration. Ratip (1996) reported that patients with thalassaemia can experience difficulties with social integration and that their social activities are reduced. Ratip & Modell (1996) in their review of the psychological and social aspects of thalassaemia intermedia also note that the effect of thalassaemia on patients' social life needs to be studied more fully as it is a major factor affecting their quality of life. The relationship between non-adherence and social support will therefore be investigated. Additionally, Georganda (1988) states that the single most important factor in the adaptation to thalassaemia is a persons attitude to what they have, how they view the illness and how it is incorporated into their self image. As a result the relationship between acceptance of illness and non-adherence will also be examined.

Furthermore, self efficacy, locus of control and value of health are all health related constructs that have been shown to be related to non-adherence. They have not been examined in a thalassaemic population in any previous research and will therefore be investigated in the present study.

Finally, only one study to date has examined non-adherence to iron chelation therapy and as a result the variables examined in the present study are based upon existing research regarding the psychosocial status of the thalassaemia patient and a review of the general adherence in chronic illness literature. It would however be interesting to gain a greater understanding regarding the sorts of factors that make it more or less difficult to take desferal. A semi-structured interview will therefore also be constructed in order to gain an appreciation of these factors.

If the psychosocial factors associated with non-adherence to iron chelation therapy can be identified then appropriate interventions can be implemented to reduce this non-adherence. This would serve to reduce the number of medical complications associated with iron overload, thus improving quality of life and reducing costs of treatment. It may also potentially save lives.

7.1 Hypotheses

It is hypothesised that thalassaemic patients who do not adhere to iron chelation therapy will tend to report;

1 Greater psychological distress,

2. Lower psychological well being.

3. Less acceptance of their illness.
4. Lower satisfaction with social support.
5. A tendency to attribute their health related behaviours to external factors
6. Lower levels of self efficacy
7. Lower values of health

A further exploratory question will examine what qualitative factors make it more or less difficult to adhere to iron chelation therapy.

CHAPTER 2: METHODS

Overview

This study examined the relationship between a number of psychosocial variables and adherence to iron chelation therapy (desferal) in patients with thalassaemia. It involved the collection of both quantitative and qualitative data. Fifty two participants completed a questionnaire regarding their psychosocial status. Their current adherence status was measured using reports by the patient, doctor and nurse. In addition, a biological measure was also employed. Twelve patients who had completed the questionnaire were then interviewed in order to investigate the factors that make it more or less difficult for them to take desferal. Two of these were subsequently chosen to be presented as case studies.

1. Participants

The participants were recruited from two London hospitals. In one of them where most of the data was collected (45 participants), potential participants were recruited from one of three settings. Initially they were approached in the day care unit where they were receiving blood transfusions. They were also approached at the consultant's out-patient clinic which took place one evening a week. In addition, participants were approached whilst they were on the overnight ward receiving either intravenous desferal or blood transfusions. In the other hospital, the remaining seven participants were approached on a ward whilst receiving their blood transfusions.

The project was approved by the local research ethics committees of University College Hospitals NHS Trust and Enfield and Haringey NHS Trust (see appendix 1)

All of the people who were approached agreed to take part with the exception of three women. One was pregnant and therefore not taking desferal under the directions of the consultant, another did not speak English and a third reported that she felt uncomfortable talking about herself and did not want to participate. No participant who had agreed to part in the study refused to take part in the semi-structured interview when asked. Twenty nine males (56%) and twenty three females (44%) participated in the quantitative part of this study with a total of 52 participants. In addition, six men and six women were interviewed using a semi-structured interview.

The population of the present study therefore consisted of slightly more men than women with an average age of twenty six and a half. Almost two thirds were single (63%) and one third were in a relationship (36%). With regard to ethnicity, just over a third (35%) were Asian and just under a third were Greek (31%). A fifth (19%) were Turkish and 6% were Cypriot. In addition, 10% of the population fell into the category of "other" which included one Iraqi, one Italian, one Bulgarian, one Chinese and one person of mixed race.

Two measures were used with regard to socio-economic status, namely education after the age of 16 and employment status. The population was generally well educated with nearly a quarter (21%) educated to a degree level (i.e. also having taken 'A' levels) or equivalent and 17% with "A" levels or their equivalent. In addition, nearly

half (44%) had undertaken a vocational qualification such as an NVQ or a BTEC. Only 9 people (17%) had not been in any education since the age of 16.

Only a small number of the population were however employed in the professional (6%) or managerial categories (2%). Twenty five percent fell into the skilled manual category and 17% into the semi/unskilled category. A quarter of the sample were still in education- the same number as those who were unemployed. Of the 13 who were unemployed at the time of the study two had never worked and the rest fell into the skilled, semi / unskilled and managerial categories.

Table 1. Demographics

Gender	Male	29 (55.8%)
	Female	23 (44.2%)
Age	Range	16-47
	Mean	26.63
	SD	7.1
Marital status	Single	33 (63.5%)
	In a relationship	19 (36.5%)
Ethnicity	Greek (Orthodox & Cypriot)	16 (30.8%)
	Turkish	10 (19.2%)
	Asian	18 (34.6%)
	Cypriot	3 (5.8%)
	Other	5 (9.6%)
Education (post 16)	None	9 (17.3%)
	'A' level	9 (17.3%)
	Degree/equivalent	11 (21.2%)
	Vocational	23 (44.2%)
Current Occupation	Professional	3 (5.8%)
	Managerial	1 (1.9%)
	Skilled manual	13 (25%)
	Semi/unskilled manual	9 (17.3%)
	Without income	13 (25%)
	Student	13 (25%)

2. Procedure

2.1 Consent

Patients attending either the day unit / ward or the overnight ward were approached and asked if they would like to participate in the study. They were given an information sheet (see appendix 2) to read and the opportunity to ask any questions before deciding whether or not they would like to participate in the study. Those patients who agreed to participate were then requested to complete a consent form (see appendix 3).

2.2 Questionnaire completion

Those who had agreed to take part in the study were initially asked questions relating to their demographic, medical and adherence status (appendix 4). All participants were then asked to complete the questionnaire. They were advised that the researcher would be available at any stage to clarify any questions that were unclear.

Following completion of the questionnaire, the researcher examined each booklet for missing data. Those participants who had not responded to 100% of the questions were then approached and asked if there was any reason for this. Each responded that this had not been intentional and agreed to complete the missing questions.

3. Psychosocial measures

The participants were given a booklet to complete which incorporated a number of standardised questionnaires (see appendix 5). These are listed below.

Acceptance of illness Scale (AIS: Felton, Revenson & Hinrichsen, 1984). This is an eight item scale on which respondents rate the extent to which they agree / disagree about statements concerning their heath and illness. It focuses on how much participants are able to accept their illness without experiencing negative feelings or responses. Respondents use a five point scale ranging from 1 ('strongly agree') to 5 ('strongly disagree') for their responses to each statement. All statements except for item 6 are in the negative direction (describing a negative attribute of the illness) and are each scored 1-5 with the scoring reversed for item 6. The total range of scores for all eight questions is therefore from 8 (extremely low acceptance / adjustment) to 40 (extremely high acceptance / adjustment). There is evidence of construct validity from the authors' finding of a significant negative correlation between the AIS and the use of wish-fulfilling fantasy as a coping strategy. It also has high internal consistency and a reasonably high test-retest reliability over a seven month period (Spearman's rho = 0.69).

General Health Questionnaire (GHQ- 28: Goldberg & Hillier, 1979). The GHQ was designed as a screening instrument for use with the general population, giving a probability estimate that an individual is a psychiatric case. There is now a wide body of work on the results which have been obtained from different populations. The GHQ-28 provides sub-totals on four scales (somatic, anxiety, social dysfunction and

depression) as well as a total score that represents a probability measure of psychiatric "caseness". Two types of scoring methods are available, the GHQ scoring method (0-0-1-1) or a likert method (0-1-2-3). Responses will be scored using the likert method in the present study in order to increase the sensitivity of this measure with higher scores indicating greater levels of symptomatology.

Psychological well-being (Ryff, 1989). This questionnaire consists of six 9-item scales of psychological well being which measure the dimensions of autonomy, environmental mastery, personal growth, positive relations with others, purpose in life and self acceptance. It represents a short version of the original 14 item scale. Participants respond on a six point scale ranging from strongly disagree (1) to strongly agree (6). Responses to negatively scored items are reversed in the final scoring procedures so that high scores indicate high self ratings on the dimension assessed. Internal consistencies are indicated for each scale and range from .83 to .91.

Short Form Social Support Questionnaire (SSQ6 :Sarason, Sarason, Shearin & Pierce, 1987) This questionnaire is a six-item version of the original 27 - item SSQ which measures social support (Sarason *et al.*, 1983). The SSQ6 yields one quasi-structural measure (SSQ6-N; number of supports) and one global measure (SSQ6-S; satisfaction with support). The number of supports score ranges from 0 (no one identified) to 9 (9 people identified). Thus the total score ranges from 0 to 54. This is divided by 6 to give a mean score. In addition, the satisfaction with support score ranges from 1 (very dissatisfied) to 6 (very satisfied) and so the total score will range from 6 to 36. Again the mean is derived by dividing by 6. It shows high internal

consistency for both the number and satisfaction subscales (Alpha = 0.90 to 0.93) and high test / retest reliability.

The Multidimensional Health Locus of Control Scale form C (Wallston, Stein & Smith, 1994). This questionnaire is a general health locus of control scale that is designed to be condition specific. It has 18 items with 2, 6 item subscales, internality and chance externality as well as two independent three item subscales, doctor and other people. Participants are asked to respond using a six point scale which ranges from strongly disagree (1) to strongly agree (6). None of the items are reversed in the final scoring. The total range of scores for the 2, 6 item scales is therefore between 6 and 36 and the range of scores for the three item subscales between 3 and 18.

Health Value Scale (Lau, Hartman & Ware, 1986). This is concerned with the value an individual places on his or her health. It is a 4 item scale developed to provide a general measure of health value. The seven point response format ranges from 1 (strongly agree) to 7 (strongly disagree). Two of the items are reversed in the final scoring and it is possible to derive a total score of between 4 and 28. In an initial study Lau *et al.* (1986) used a five-point response format and found that the internal consistency as measured by Cronbach's alpha was 0.67 and the test-retest reliability was 0.78. Construct validity was also inferred.

Generalised Self Efficacy Scale (GSES, Schwarzer, 1992). This is a ten item scale which assesses the strength of the individual's belief in his or her own ability to respond to novel or difficult situations and to deal with any associated obstacles or

setbacks. For each item there is a four choice response from "Not at all True" which scores 1 to "Exactly True" which scores 4. The scores for each of the ten items are summed to give a total score The higher the score the greater the individual's generalised self-efficacy belief. High internal consistency ratings have been found for each of the five samples studied and the alphas ranged from 0.82 to 0.93. The retest reliability was found to be 0.47 for men and 0.6 for women over a two year period. It has both concurrent and predictive validity.

4. Additional information

Information was also collected regarding the demographic and medical characteristics of the sample. Participants were asked a number of questions relating to these variables before they were asked to complete the questionnaire (see appendix 4) These questions were administered by the researcher.

4.1 Demographic information:

A. Age

B. Gender

C. Marital Status (single or in a relationship)

D. Ethnicity

E. Education after the age of sixteen.

F. Current occupation or if currently unemployed previous occupation. (These were then categorised according to the 1991 Census).

4.2 Medical information

A. Does anybody else in the family have thalassaemia?

If so, what is their current health status (poor, moderate, good or other).

B. Frequency of blood transfusions?

C. Previous medical complications related to iron overload? (These were then categorised into none, heart problems, diabetes, or multiple).

D. Age of diagnosis? (The ages were then categorised into under 1 year, under 2 years etc.).

E. Method of taking desferal? (Syringe driver or disposable balloon pump / subcutaneous or intravenous or portacath).

F. Recommended dose of desferal per week (measured in hours and days).

5. Adherence measures

Four measures of adherence were employed which included estimates from the patient, the nurse and the doctor. In addition, a fourth measure consisted of the mean serum ferritin level for each participant over a period of eighteen months.

Patient report

Each patient was asked two questions regarding their current adherence status (see appendix 4) by the researcher. Firstly they were asked to state how many times in the previous 4 weeks they had completely failed to take their desferal on an occasion when they had been advised to take it. Secondly, they were asked how many times over the previous 4 weeks they had started to take their desferal but had removed their

treatment before completion of the recommended duration. They were also asked to estimate how many treatment hours they thought they would have missed as a result of terminating their treatment early.

Doctor report

The doctors (consultants) in each setting were also asked to complete an information sheet (see appendix 6) at the end of every week regarding the participants who had been recruited that week. In line with the patient adherence data the doctors were asked to estimate how many times in the previous 4 weeks they believed the patient had completely failed to take desferal when they had been advised to take it. They were also asked to estimate how many times in the previous 4 weeks they thought that the patient had failed to take desferal for as long as had been recommended and how many hours they would have missed as a result.

In addition, the two doctors were also asked to provide information regarding the recommended dose of desferal for each participant. They were asked to record this information in terms of frequency per week and duration per dose (hours).

Nurse Report

One nurse in each setting was also asked to complete the information sheet on a weekly basis (see appendix 7). This information was the same as that requested from the participants and the consultants. Again, this involved completing the relevant information for the patients who had been seen in the proceeding week.

Serum ferritin levels

Information regarding each participant's current serum ferritin levels was taken from the participants themselves and from the clinic database. In addition, each participant's ferritin levels were recorded off the clinic database from September 1997 to February 1999. These results were represented in the form of a line graph for each participant. They were then presented to the doctor based in the hospital where most of the data was collected who blindly rated each.

The doctor noted next to each graph his perception of the patient's past and current adherence status (i.e. 'good' or 'poor'). Any significant trends immediately prior to the participants inclusion in the study were also noted. As a general rule a ferritin of below 2,500 indicated good adherence and above 2,500 indicated poor adherence. This was based on Olivieri *et al.'s* (1994) finding that no major cardiac complications occurred in those whose ferritins were kept below 2,500μg / L or only exceeded this limit in less than 33% of the evaluations.

Participants were then allocated to one of two groups based on their current adherence status by the researcher. Those participants with a clear 'good' or 'poor' adherence status were allocated to their respective groups. Trends were also examined and those patients who were experiencing a significant improvement in their adherence immediately prior to inclusion in the study were allocated to the 'good' group, irrespective of their past adherence status. In addition, those patients experiencing a significant deterioration in their adherence status immediately prior to inclusion in the study were allocated to the 'poor' group irrespective of their past adherence.

6. Qualitative information

Twelve people who had participated in the quantitative part of the study were then asked if they would participate in a short semi-structured interview that would last no longer than thirty minutes. The aim of these interviews was to elicit a detailed account of the factors that make it more or less difficult to take desferal. They were advised that there are no right or wrong answers and about confidentiality. See Appendix 8 for a copy of the interview protocol.

All of those subjects who were asked agreed to take part. These subjects were randomly chosen from the first research centre only and whilst special preference was given to those subjects who had indicated that they had experienced difficulties taking desferal the factors that influenced who was chosen were more practical in nature. For example, participants were interviewed in a small private room off the day unit in order to ensure confidentiality and restricted access played a part in determining who it was possible to interview at any one time.

7. Data analysis

7.1 Qualitative data analysis

Verbal transcripts of all the audiotaped interviews were made and the techniques of interpretative phenomenological analysis were used to interpret the data (Smith, Flowers & Osborn, 1997). This aims to explore in detail the participant's view of the topic under discussion and is concerned with the individual's personal perception of the event (its meaning). In trying to establish an "insider's perspective" it

acknowledges that this cannot be done directly or completely and accepts that access depends upon and is complicated by the researcher's own conceptions. The analysis followed a number of steps;

1. All of the transcripts were read twice and interesting or significant points were noted. Some of these points were attempts at summarising, some were associations or connections and others were preliminary interpretations. Two transcripts were then chosen for further analysis based on the richness of information.

2. These transcripts were subsequently read again and the emerging themes were then listed on a separate sheet and examined for connections. Super-ordinate themes were elicited and a new clustering of themes emerged. At this point certain themes were dropped due to a lack of evidence.

As a check on the analysis an independent audit (Smith, 1996) was conducted. The two transcripts were coded independently by a second researcher experienced in qualitative analysis. Following this coding, the two researchers discussed their readings and came to a general consensus on the theme categories before analysis proceeded further.

7.2 Quantitative data analysis

The quantitative data was inputted into SPSS v. 7.0. Firstly the continuous data was examined to ensure it met the assumptions of parametric testing and transformations were conducted in order to normalise the data where necessary. Correlational analyses

were then conducted to examine the relationships between the psychosocial variables and the measures of adherence and t-tests were used to investigate differences between the biological groups. Multiple regressions were then employed to examine whether a combination of the variables would predict non-adherence or discriminate between the groups.

CHAPTER 3: RESULTS

The results of this study are presented in five sections. The first describes the medical and psychosocial characteristics of the population whilst the second reports the different measures of adherence. Section three reports the reasons why the patients failed to take their treatment and section 4 addresses the first research hypothesis in its exploration of the relationship between non-adherence and psychosocial status. Finally, section five presents the qualitative results regarding the factors which make it more or less difficult to take desferal. This will involve both the presentation of two case studies and a comparison of the quantitative and qualitative findings.

1. Medical and psychosocial characteristics

1.1 Medical characteristics

Forty five thalassaemia major and 7 thalassaemia intermedia patients participated in the study. For most the diagnosis was made at an early age. Sixty seven per cent received a diagnosis before the age of one, 86% before the age of two and everyone had been diagnosed before the age of six. With regard to their health, almost three quarters (73%) had never had any medical complications relating to iron overload, 4 (7%) had experienced cardiac complications, 5 (10%) had diabetes and 5 others (10%) had both cardiac complications and diabetes. In relation to the health of the participants' families, 32 (61%) did not have a family member with thalassaemia. Of those 20 who did, 9 (17%) said that their relative was in good health, 5 (10%) in moderate health and 3 (6%) in poor health. In addition, three family members had died.

With regard to treatment, three quarters of the population had a transfusion once every three (38%) or four weeks (36%) and five different methods of taking desferal were recorded. Half the population (52%) used the balloon pump subcutaneously and 18 (35%) used the syringe driver subcutaneously. The syringe driver and balloon pump taken intravenously were less commonly used (6% and 4% respectively). Only 2 people (4%) used a portacath.

1.1.1 Treatment Recommendations

The patients and doctor were asked to record the recommended dose of desferal. The number of hours that desferal should be taken was then calculated by multiplying the frequency (days per week) by the duration of the dose in hours. Table 1 gives a description of the amount of desferal that the patients believe they should be taking and the amount the doctor prescribed. The results indicate that the patients overestimated their dose when compared to the doctor's recommendations ($t(51) = 3.1$, $p < 0.01$) but that the two reports are strongly correlated ($r = .65$, $p < 0.001$).

Table 1. Dosage from patient / doctor perspectives

	Patient Report(n=52)			Doctor Report (n=52)		
	M	SD	Range	M	SD	Range
Frequency per week	5.1	1.2	2-7	5.1	1.1	2-7
Duration per dose (hours)	13.4	5.2	7-24	11.2	4.3	8-24
Total hours per week	71.2	40.2	24-168	58.4	30.1	16-168
Total hours over 4 weeks	284.8	160.9	96-672	233.5	120.6	64-672

Note. For the purpose of subsequent statistical analyses, all data regarding the recommended dose was subjected to a log 10 transformation to normalise the distributions.

1.1.2 Isolated ferritin result

In order to assess participants' awareness of their serum ferritin they were asked to estimate their current ferritin level. The serum ferritin is a measure of the patient's iron loading. The figure given by the participants was then compared to the most recent ferritin result recorded on the clinic database. The means, standard deviations and range for both reports are presented in Table 2. The two reports correlate highly ($r = .96$, $p < 0.01$) and there is not a significant difference between the means ($t(50) = 1.1$, $p =$ n. s.). This therefore indicates that the patients have an accurate understanding of their current ferritin level.

Table 2. Ferritin Levels

	Current isolated ferritin levels(μg/L)		
	Mean	SD	Range
Patient Report	2349.8	1506.6	500-7000
Computer record	2296.7	1502.8	549-6590

Note: For the purposes of statistical analysis a square root transformation was conducted in order to normalise the distributions.

1.2 Psychosocial characteristics

Table 3 provides the mean, standard deviations and range for each of the psychosocial variables examined. It also provides the results from other studies in order to place the psychosocial scores of this population in a context. However, due to a lack of existing research into the psychosocial characteristics of patients with thalassaemia, comparisons are made with other chronic illness and general populations and should therefore be met with caution.

Table 3. Psychosocial Characteristics

	M	SD	Range	Results from previous studies
GHQ				
Anxiety*	5.6	5.0	0-19	norms
Depression*	3.7	4.4	0-18	not
Somatic symptoms*	7.0	5.0	1-21	available
Social dysfunction*	7.3	3.2	1-19	
Total*	23.7	15.4	7-68	
Locus of Control				
Chance	19.0	5.2	8-29	12.46[a]
Internal	25.2	6.3	7-36	28.67[a]
Doctor	14.5	2.6	9-18	15.99[a]
Other Person	10.6	3.5	3-18	8.48[a]
Self Efficacy*	30.0	4.4	18-40	29.28[b]
Values of Health	14.2	3.9	5-23	22.49[c]
Well-being.				
Environmental mastery	39.0	6.3	25-51	44.8[d]
Personal Growth	39.7	6.9	24-53	49[d]
Purpose in life	39.0	7.4	23-53	47.6[d]
Positive relations with others	42.3	6.4	25-54	44.8[d]
Self Acceptance	37.0	7.3	22-52	45.5[d]
Autonomy	39.7	6.8	22-52	41.3[d]
Well being total	236.7	32.3	168-298	273[d]
Acceptance of Illness	3.7	5.9	17-40	3.5[e]
Social Support				
Number*	2.8	1.6	.33-8.67	4.25[f]
Satisfaction*	5.4	.7.0	2.8-6	5.38[f]

n = 52

* Indicates that these variables were all subjected to a square root transformation to normalise the data.

a = Wallston, *et al.* (1994); b = Schwartzer (1993); c = Lau *et al.* (1986); d = Ryff (1989); e = Felton & Revenson, (1984); f = Sarason *et al.* (1983).

The results indicate that the population of the present study reported lower levels of well-being than university students in a study by Ryff (1989). They did however report similar levels of acceptance of illness to those reported by Felton & Revenson (1984) in an examination of 151 people with either hypertension, diabetes, arthritis or cancer.

The results also indicate that participants reported a higher 'chance' and 'other person' health locus of control and a lower 'internal' and 'doctor' health locus of control than a diabetic population (Wallston *et al.*, 1994). They also reported a lower value of health than ulcer clinic patients (Lau *et al.*, 1986). In relation to social support, the number of reported supports was lower in the present study than those reported in a study of university students (Sarason *et al.*, 1983). However, the reported satisfaction with this support was slightly higher in the present study. Finally, the population in the present study reported similar levels of self efficacy as those reported in a study of 1,660 German adults from a general population (Schwarzer, 1993).

1.2.1 Intercorrelations between the psychosocial variables

Table 4 presents the intercorrelations between the psychosocial variables. However, given the large number of variables the results of these correlations should be met with caution. As would be expected, all of the subscales of psychological distress were positively correlated, as were the well-being subscales. Furthermore, total psychological distress was negatively correlated with well-being as well as with self efficacy and acceptance of illness.

Table 4. Intercorrelations between Psychosocial Variables

	1.GHQTOT	2.LocCH	3. LocOP	4. LocDR	5.LocINT	6. AOI	7. SS1	8. SS2	9. WBTOT	10. SE	11. VoH
1	1.00										
2	.20	1.00									
3	.08	.39**	1.00								
4	-.24	-.04	.05	1.00							
5	-.2	-.25	-.13	.18	1.00						
6	-.51**	-.43**	-.33*	.25	.12	1.00					
7	-.22	-.20	-.22	-.11	-.07	.38**	1.00				
8	-.17	.04	-.12	.05	.19	.23	.02	1.00			
9	-.47**	-.33*	-.37**	-.004	.16	.48**	.20	.36**	1.00		
10	-.34*	-.10	-.22	.12	.06	.33*	.05	.01	.65**	1.00	.
11	-.20	-.28*	-.20	.03	.10	.25	-.11	-.03	.32*	.27	1.00

*p<.05., **p < .01

1= Total psychological distress, 2 = Locus of control (chance), 3 = Locus of control (other person), 4 = Locus of control (doctor),5 = Locus of control (internal), 6 = Acceptance of illness, 7 = Number of social supports, 8 = Satisfaction with support, 9 = Well-being total, 10 = Self efficacy, 11 = Value of health.
All of the GHQ subscales were positively correlated as were the well-being subscales.

Positive correlations were also found between acceptance of illness and the number of social supports, self efficacy and well being. In addition, well being was positively associated with satisfaction with support, value of health and self efficacy. Surprisingly however, the number of supports was not significantly correlated with satisfaction with support. In addition, no association was found between a lack of social support and psychological distress.

Finally, with regard to health locus of control the 'chance' and 'other person' subscales were positively correlated and were both negatively correlated with acceptance of illness and well-being. The 'chance' health locus of control was also negatively correlated with value of health.

2. Measures of adherence

2.1 Patient, doctor and nurse measures

The patients, doctor and nurse were asked to estimate the patients' levels of non-adherence over a period of four weeks prior to participation in the study. In order to calculate the total number of hours missed, estimates regarding the number of times the patients had completely failed to take desferal were firstly multiplied by the number of hours the doctor had recommended they take it per dose. These figures were then added to the number of hours missed as a result of taking it out early to provide an overall estimate.

Table 5 lists provides a description of the patterns of non-adherence as reported by the doctor, nurse and the patient. Due to highly skewed data non-parametric tests were conducted to examine differences in the reported patterns. A Friedman test indicated no significant difference between the three measures regarding the number of hours missed as a result of removing the treatment early ($\chi 2$ (2) = 5.4, p = n. s.).

A significant difference was however found between the three estimates regarding the number of times the patient had completely failed to take their treatment ($\chi 2$ (2) = 20.6, $p < 0.001$). Wilcoxon matched pairs signed ranks tests indicated that there is a significant difference between the patient and the nurse report ($z = 4.9$, $p < 0.001$) and between the nurse and the doctor report ($z = 3.4$, $p < 0.001$). No significant difference was found between the doctor and the patient report ($z = 1.3$, p = n. s.).

Table 5. Patterns of adherence

	Doctor Report			**Nurse Report**			**Patient Report**		
	M	SD	Range	M	SD	Range	M	SD	Range
Times failed to complete treatment	3.8	5.7	0-28	2.8	1.4	0-12	1.6	3.9	0-25
Hours missed as a result of failing to complete treatment	7.4	17.3	0-112	6.7	2.1	0-48	3.6	6.9	0-25
Times completely failed to take treatment	4.5	4.6	0-22	2.1	1.0	0-8	5.2	3.6	0-13
Hours missed due to completely failing to take desferal	55.1	63.3	0-264	25.8	37.1	0-168	59.9	56.8	0-288
Total number of hours missed	62.5	68.5	0-280	32.5	42.7	0-192	63.6	56.8	0-288

n = 52

2.1.1 Percentage of treatment hours missed

The total number of hours missed was then calculated as a percentage of the total recommended number of hours over four weeks. Table 6 reports the percentage of treatment hours missed based on the doctors' recommendations of the dose. The patients estimate higher levels of non-adherence than the doctor or the nurse. Indeed, the nurse estimate of non-adherence is about half that of the doctor and less than half that of the patients' (Wilks' lamda = .60, F = (2,50), 16.47, $p < .001$).

Table 6. Percentage of treatment hours missed.

	Percentage of treatment hours missed		
	Mean	SD	Range
Doctor	25.3%	25.7	0-104%[a]
Nurse	12.7%	13.6	0-45%
Patient	29%	21.2	0-93%

[a] On one occasion the consultant estimated that the patient had missed taking desferal for a longer period than had actually been recommended.
Note: The raw data is presented in the table but for the purposes of statistical analysis these measures were subjected to a square root transformation to normalise the data.

2.1.2 Relationship between the three reports of non-adherence

Correlations were then conducted to examine the strength of association between the three measures. The results are presented in Table 7 and indicate that there are no significant associations between these three measures of non-adherence.

Table 7. Correlations between the measures of adherence

	Doctor	Patient	Nurse
Doctor	1.00		
Patient	.08	1.00	
Nurse	.20	.11	1.00

2.1.3 Correlations between patients' current ferritin result and percentage treatment missed.

Pearson correlations were then conducted in order to examine the relationship between the doctor, patient and nurse report of non-adherence and the current ferritin level as indicated on the clinic data-base. The results indicate that there is a significant relationship between the doctor estimate of non-adherence and patients' ferritin levels ($r = .5$, $p < 0.01$). There is also a significant relationship between the nurse estimate of non-adherence and patients' ferritin levels ($r = .59$, $p < 0.01$). However, there is not a significant relationship between the patient estimate and ferritin result ($r = .14$, $p =$ n.s). This finding suggests that the doctor and the nurse are more likely than the patients to base their estimates of non-adherence on a bio-chemical measure.

2.1.4 Non-adherent vs. adherent groups

In addition, the number of participants who were estimated as having obtained less than 60% of the recommended dose was calculated in order to draw a comparison with the only other study examining non-adherence to iron chelation therapy (Beratis, 1989). Using this criterion, the nurse estimated that no patients obtain less than 60% and the doctor and patients estimated that only 10% obtain less. These results are presented in Table 8 and indicate that the population in the present study are experiencing lower levels of non-adherence than the population in the Beratis (1989) study.

Table 8. Non-adherent vs. adherent groups

	Measures of Adherence			
	Doctor	Nurse	Patient	Beratis (1989)
Adherent	47 (90.4%)	52 (100%)	47 (90.4%)	100 (76.3%)
Non adherent	5 (9.6%)	-	5 (9.6%)	31 (23.7%)

2.2 Biological measure

2.2.1 Group Categorisation of ferritin results

The participants' ferritin levels were also recorded over a period of 18 months from September 1997 to February 1999 and patients were assigned to 'good' and 'poor' groups based on their current adherence status (see methods section for classification criteria). Using this criteria, two thirds of the population were classified as good adherers and one third as poor. Table 9 presents the means and standard deviations for these two groups. As would be expected, the mean ferritins were higher in the poor group when compared to the good group ($t(40) = 3.6$, $p < 0.01$).

Table 9. Group categorisation based on ferritin results over 18 months

	n (%)	Mean (SD)
Good Adherence	27 (64.3%)	2046.5 (1118)
Poor Adherence	15 (35.7%)	3592 (1657.7)

2.3 Summary

The results indicate that whilst patients' overestimate the amount of desferal they have been recommended when compared to the doctor's actual recommendations they do have an accurate understanding of their current ferritin levels. With regard to the three adherence reports the results indicate that patients report the highest levels of non-adherence followed by the doctor and then the nurse. In addition, whilst there are no significant relationships between these three reports, there is a significant relationship between the nurse and the doctor estimates of non-adherence and the patients' current ferritin levels. Furthermore, a comparison of these reports with the results from another study (Beratis, 1989) indicates that participants in the present study experience lower levels of non-adherence.

A biological measure was also employed whereby participants were allocated to either a 'good' or a 'poor' group based on an assessment of their serum ferritin levels. The results of this measure indicate that two thirds of the population are adherent compared to one third who are not. As would be expected the ferritin levels in the non-adherent group were higher than those in the adherent group.

3. Reasons for non-adherence

Participants were asked to state why they had failed to take their treatment as often as had been recommended over the previous four weeks. The answers were then categorised into groups. For those whom the question was applicable (i.e. they had not adhered 100%) most failed to take their treatment because of physical reasons.

Others were on holiday or had social / work constraints. Some were experiencing family difficulties and others just wanted time off or felt that they had been lazy. In addition, two were taking other medication and were not sure about contraindications. These results are presented in Table 10.

Participants were also asked to state why they had removed the pump early. Table 11 indicates that for a lot of people this question was not applicable. Physical side effects and social / work constraints were the most common reason stated and on one occasion someone had experienced some confusion with the timer on the pump.

Table 10. Reasons for completely failing to take desferal

Reason	n (%)
Not applicable (i.e. the patient reported 100% adherence)	8 (15.4%)
No comment	9 (17.3%)
Physical Reason (tired / unwell / pain)	10 (19.2%)
Holiday (either going away or the Christmas holidays)	5 (9.6%)
Social / work constraints	6 (11.5%)
Taking other medication	2 (3.8%)
Family difficulties	2 (3.8%)
Laziness	5 (9.6%)
Just wanting time off	7 (13.5%)

Table 11. Reasons for removing the desferal early

Reason	n(%)
No comment	3 (5.8%)
Not applicable (i.e. they did not remove their treatment early)	34 (65.4%)
Physical side effects	7 (13.5%)
Social / work constraints	7 (13.5%)
Confusion with timer	1 (1.9%)

4. Non-adherence and psychosocial variables

4.1 Continuous measures of adherence and psychosocial variables

Table 12 provides the results of the correlations between the three continuous measures of non-adherence (doctor, nurse and patients reports) and the psychosocial variables. The results indicate a small number of weak significant correlations. With regard to the patient report the results indicate that higher levels of anxiety, somatic symptoms and total psychological distress are all positively associated with non-adherence. There is also a negative relationship between a health locus of control with the doctor and non-adherence, i.e. the more the individual believes that their health is the doctors' responsibility, the more likely they are to adhere.

The nurse measure indicates a positive relationship between a health locus of control with another person and non-adherence. There is also a negative relationship between the number of social supports and non-adherence. Hence, the larger the social support network the higher the likelihood that the patient will adhere. Finally, self efficacy was negatively associated with non-adherence as measured by the doctor. This indicates that the less people believe in their own abilities the less likely they are to adhere.

Table 12. Correlations between the psychosocial variables and the continuous measures of adherence from the three perspectives

	Doctor	Nurse	Patient
GHQ:			
Anxiety	.04	.03	.33*
Depression	.13	.22	.25
Somatic symptoms	.02	.01	.29*
Social dysfunction	.01	.13	.18
Total	.06	.13	.32*
Locus of Control:			
Chance	-.18	.06	-.02
Internal	.02	.11	-.00
Doctor	-.04	.01	-.30*
Other Person	.04	.30*	-.03
Self Efficacy	-.28*	-.15	-.03
Values of Health	-.03	-.01	.13
Well-being			
Environmental mastery	.02	-.14	-.14
Personal Growth	-.05	-.2	-.03
Purpose in life	-.13	-.10	-.09
Personal relations with others	.09	.04	.07
Self Acceptance	.07	-.03	-.07
Autonomy	-.14	-.23	-.01
Total	-.04	-.14	-.05
Acceptance of Illness	-.12	-.20	-.11
Social Support:			
Mean number of supports	.19	-.36*	-.09
Average satisfaction	.07	-.02	-.16

* $p < 0.05$

In addition, there are no significant relationships between the demographic variables of age, gender, marital status, ethnicity and employment and the continuous measures of non-adherence. Furthermore, t-tests revealed that there are no differences in adherence status between those who have medical complications and those without.

4.2 Multiple regressions

Multiple Regressions were then employed in order to examine whether a combination of the variables would predict adherence from each of the three reported adherence perspectives. The demographic variables of age, gender, marital status, occupation and ethnicity were first entered together as a single block. The remaining psychosocial variables (total psychological distress, total well-being, value of health, self efficacy, satisfaction with support, acceptance of illness and external locus of control subscales) were then entered using a stepwise method. A summary of the regression models is presented in Table 13.

Table 13. Multiple regressions of adherence from three perspectives

	R	R2	R2 change	F value for R2 change	Overall F (p)
Model 1: (Doctor)					
Demographics	.07	.01	-	-	.04 (.99)
Self Efficacy	.31	.10	.09	4.6	.80 (.57)
Model 2: (Nurse)					
Demographics	.38	.15	-	-	.16 (.18)
Model 3: (Patient)					
Demographics	.29	.08	-	-	.89 (.49)
Psychological Distress	.44	.19	.11	6.1	1.8 (.11)

The results indicate that demographic and psychosocial variables do not significantly predict non-adherence. However, a lower level of self efficacy was found to significantly contribute to the prediction of non-adherence as measured by the doctor (β = -.33, t = -2.1, $p < .05$). In addition, total psychological distress was found to significantly contribute to the prediction of non-adherence as measured by the patient (β = .36, t = 2.5, $p < .05$).

4.3 Biological measure of adherence and psychosocial variables

With regard to the biological measure of adherence independent t-tests were conducted to examine differences between the two groups in relation to all of the psychosocial variables. No significant differences were found. In addition, chi-square analyses revealed no significant differences between the two groups in terms of gender, marital status, employment status, ethnicity and age (above and below 18). Furthermore, there are no significant differences in adherence status between those with medical complications and those without.

A discriminant analysis was also conducted using the biological measure of adherence and no variables discriminated between the groups.

4.4 Summary

The results indicate that there are a number of reasons why participants failed to take their desferal in the four weeks prior to participation in the study. They also indicate that there are no significant relationships between the three continuous measures of

non-adherence and the demographic variables examined in this study. Furthermore, only a small number of weak relationships were found between these measures and the psychosocial variables. Across the three measures positive correlations were found between non-adherence and anxiety, somatic symptoms, total psychological distress and a health locus of control with 'another person'. Negative correlations were also found between non-adherence and the number of social supports, self efficacy and a health locus of control with the doctor. Multiple regressions then revealed that higher levels of psychological distress and lower levels of self efficacy are predictive of non-adherence as measured by the patients and the doctor respectively.

Finally, the between groups comparison based on the biological measure of non-adherence failed to reveal any significant differences on any of the psychosocial or demographic variables examined.

5. Qualitative interviews

5.1 Selection criteria

The following section presents two case studies from the twelve patients who participated in the interview. Neither was chosen as a special case, nor is it claimed that they are representative of thalassaemia patients in general. Rather, they represent rich examples of the sorts of factors that make it more or less difficult to take desferal at various stages in an individual's life.

5.2 Case study 1

Joe (pseudonym) is a 28 year old man with thalassaemia major. He is of Cypriot origin and is currently unemployed. He has over the past few months been adhering to a strict desferal regime following a long history of non-adherence which eventually resulted in heart failure. For most of his life he has been treated in a different hospital to the one in which the study was conducted and where he experienced a different treatment regime. Four main themes emerged from Joe's interview. These are presented in separate sections.

5.2.1 Denial of thalassaemia and desferal treatment

One of the major themes which emerged as influencing Joe's non-adherence related to his difficulty accepting the fact that he has thalassaemia. None of his friends who did not have thalassaemia themselves knew about Joe's illness. In fact Joe found himself actually forgetting that he had thalassaemia.

Joe had previously had to have blood transfusions once very 8 weeks. This made it easier for him to forget about his illness and treatment. He just put the fact that he had thalassaemia to the back of his mind. In relation to taking desferal he notes;

> "Sometimes I actually did forget. It's like as I said, it's like I didn't feel that I had thalassaemia sometimes and I literally forgot to take it.....But it was always just a nagging thing in the back of my mind to take it more than I should, but I never did.....".

Joe also had difficulties accepting that he would ever have any medical complications related to iron overload. He would compare himself to other thalassaemics who had

died from heart conditions or had higher ferritin levels but would then put his thoughts to the back of his mind;

> "I've seen patients die from various heart conditions about the same age as me. Its always been at the back of my mind but I didn't think it would happen to me."

Additionally, Joe found it difficult to adhere to the desferal regime when he was at home because there were no immediate side effects associated with non-adherence. The ferritin level did not mean anything to him;

> "I'd say the number one thing would be that not having your desferal has no immediate ill effects so you don't notice it.....I suppose because not taking the desferal didn't have any immediate side effects, my ferritins were just a number in the computer."

Joe found himself bargaining with desferal in terms of taking time off and then playing 'catch up'. However, he thought of 'catching up' as something he could do at any stage in his life. He noted that whilst he would put taking desferal off until tomorrow, tomorrow never actually came;

> ".....I think since I was very little I always knew I would have it for life so it was like a big time span in my mind where I thought if I miss out I can always catch up kind of thing.....Odd days here and there, its like a diet that you say you will start tomorrow, but tomorrow never comes."

One of the reasons why Joe did not like taking his treatment was because he had to mix it up himself when he was a teenager. This had been done by his mother when he was a child when he had taken desferal as a matter of routine. He noted that he was not disciplined enough and that he got lazy and relied on IV treatment in hospital. He is also potentially relying on the use of the portacath over the next few years;

> ".....I was relying on the IV desferal at the hospital to take care of it and I still didn't do it enough at home as I should have.....For the next three years I'm probably going to have 24 hour desferal running, whether its in this line or the new

> portacath. So that's no effort at all because I'm just literally connecting the desferal up."

5.2.2 External factors associated with non-adherence

Prior to his heart complications Joe preferred to carry on with his everyday activities rather than adapt his lifestyle to accommodate the desferal regime. This started when he was a teenager and wanted to go out. He did not want to have to deal with the desferal when he came home late. Joe started missing odd days when he was fourteen but when he started work he would sometimes miss a whole week at a time. He would then try and catch up. Whether or not he took the desferal would depend on how busy he was.

Joe acknowledges that adhering strictly to the desferal regime will inevitably limit his social activities in the future and that he will have to change "*quite a lot*". Following his heart difficulties he envisages that that will have to give up work, change his eating habits and exercise less. He also expressed some degree of self consciousness about the pump;

> "I won't want to go certain places and obviously the beach and things like that. I'd be more selective about where I go and who with. If I think that it's going to be a bunch of boisterous lads on a night out I'm more likely to decline now."

5.2.3 Acceptance of treatment but need for balance

Joe's medical complications forced him to take more of a conscious stance in thinking about his illness and the desferal treatment. When talking about these difficulties he describes them as "*a big wake up call*" and comments that he now realises the

importance of desferal. He did however stress the importance of maintaining a balance between taking desferal and leading a normal life;

> "If you go too much one way and think to yourself that you don't have thalassaemia then like me you slip out of routine of taking desferal. And if you concentrate too much on the illness,...I know a few patients and that's all they do, hang round the hospital wards even on their days off from work and then they don't end up having a social life. And even some of them don't hold jobs because they think they are too ill and they're not. They're perfectly fine to work. So you need to find a balance."

Joe believes that parental influences are important in helping people to achieve a balance between taking desferal and leading a normal life. He commented that parents who have children with thalassaemia can be overprotective and therefore the children think that they are not capable of doing things. Joe also warns however about the opposite of this, which was his experience of his parents telling him that would be fine to work and that he could set goals and go for them. He believes that as a result of this he was too ambitious and didn't pay enough attention to his health.

5.2.4 Role of Professionals

Joe expressed some ambivalence about his relationships with the health care staff. On the one hand he believes that it is important that the staff are in touch with the patients and on the other he stated that the doctor could have said anything to him, he only ever listened to himself. Joe commented that where he had previously been treated there was no actual clinic set up and that the individual patient was responsible for making an appointment to meet with the specialist. He believes that this probably also contributed to his non-adherence as he was less likely to have a check up with the specialist who could then "*keep an eye on things*". Joe commented that is important to

be educated about the effects of non-adherence to desferal and stated that he had not been fully aware about heart failure. He believes that early educational interventions would be helpful and that this would help patients maintain their balance;

> "I think that the patients especially when they are young have to be drummed into to find the balance. I think that's the key to leading a normal life without neglecting your treatment at the same time."

5.2.5 Summary

As a result of wanting to be able to hold down a job and go out with his friends Joe sacrificed taking his desferal. He wanted to get on with life and did not want to have to come home and mix up the treatment. Joe did not want to accept that he had thalassaemia and that he had to take desferal. This eventually resulted in cardiac complications and as a result he is now adhering strictly to the desferal regime. Whilst being forced to accept that he has to take desferal if he wants to live, Joe feels that it is important to maintain a balance between taking desferal and leading a normal life. He believes that early education programmes will help people maintain this balance and envisages that he will have to make sacrifices over the next few years as he adheres to the treatment regime.

5.3 Case study 2

Amelia is a married 29 year female of Greek origin who is employed in a skilled manual position. She also has thalassaemia major and is currently adhering to the desferal regime having experienced some difficulties in her teenage years which resulted in heart failure and diabetes. The main themes for Amelia fall into two broad

categories, namely, factors associated with non-adherence and factors associated with adherence.

5.3.1 Factors associated with non-adherence

Physical Side Effects

Amelia acknowledged that there are a number of physical side effects of taking desferal and that whilst she is currently managing to adhere to the regime these side effects can be unpleasant. She spoke of how it can cause pain and bruising and how it can be very uncomfortable. In addition, she has also suffered from Yersinia infection;

> "Desferal, it can be a pain, but, umm, like the difficulties that I have is like when I have bruising on my tummy and it doesn't feel comfortable. I've tried it in my legs and I can't walk."

Treatment Issues

In the past Amelia had to mix the desferal treatment herself. This was described as time consuming and "*a big pain*". In addition, earlier pumps were much heavier which made them difficult to use them at school. Amelia expressed a degree of self-consciousness about the old pump but also acknowledged that you can wear the lighter disposable pumps without people noticing. Whilst she now takes the pump on holiday with her she expressed some ambivalence about using it;

> "You probably get trapped. It feels good not having it. When you've got your pump, you're like all tense and stiff because its there. But when you don't have your pump it feels good and yet there's something not...there's something missing."

Age

Amelia's cardiac complications resulted from her difficulties adhering to the desferal regime when she was a teenager. She acknowledged that adherence to the desferal regime was particularly difficult during her teenage years and that she preferred to go out to taking her treatment. As a result she took the desferal only two or three times a week during that period;

> "Maybe because I was young, I wanted to go out more and I didn't see it was a problem, it wasn't a major important thing to me."

5.3.2 Factors associated with adherence

Acceptance of illness and treatment

When Amelia experienced heart failure she realised the importance of taking desferal. She now believes that she would not be alive after her heart trouble if she had not subsequently adhered to the desferal regime. She also believes that she will not lead a healthy happy married life if she does not continue to take it ;

> "I realise that desferal is important if I want to live, otherwise it is like giving up and I don't really want to give up.....If I want to see the age of seventy I have to continue taking it until something better comes along.....And when I don't have it, I have like withdrawal symptoms, I'm saying like I need to have it otherwise I feel bad if I don't have it."

Amelia also believes that she will not have difficulties with non-adherence in the future as she would feel that she was going to back to where she was before, i.e. ill. When asked if she would take the desferal if she hadn't had the medical complications she replied that she would probably still take it but not as much.

It is important to Amelia to be able to lead a normal / healthy life and she realises the importance of taking desferal in being able to do this. She believes that taking desferal will enable her to do the things that are important to her. She is now married to someone who does not have thalassaemia and would like to be able to do the things that he can do. She has formed a sense of self which is that of a healthy normal person and health is important to her. She also sees desferal as integral to this sense of being normal and healthy. It would therefore appear that Amelia has accepted both the illness and the treatment;

> ".....I see myself as a healthy person, a normal person. Anyone who's healthy, that's how I lead my life. I think that its important to be healthy.....If you use your pump you can become healthy and lead a normal life.....I've overcome that problem where I used to think it was a pain. I take it to work. It's part of me now and when its not there it feels funny not being there".

Family / social / professional support systems

Amelia strongly values the support of her family and friends in giving her meaning in life and thus the ability to continue taking the desferal. She noted that without them she would be '*stuck*'. She states that she would never decide not to take the desferal because she couldn't bear to be without her family and the people who care about her. Her family have encouraged her and made her stronger. She believes that they have given her the courage to use her pump as they have expressed to her the importance of using it. Amelia believes that if you don't take your desferal you are not just letting yourself down you are also letting our family down;

> "My family are supportive and I've got a happy life. If I want to continue that way and if I want to continue having what I've got then I can't give up.....Apart from yourself, you live for your family as well."

Amelia's husband plays a supporting role and gives her lots of encouragement. Again, she states that she would not want to "*let go*" of him by not taking the desferal. She notes that it is important for her husband to think of her as a strong person and that if she does not take her treatment she will not be strong;

> "If I want, I mean, I'm gonna have a healthy, happy, married life as well so I wouldn't want him to go through, I mean, I wouldn't want him to see that I'm not strong enough."

In addition, professional support is also important and Amelia comments that the doctors and the nurses have been "*brilliant*". However, in relation to a question regarding the role of health professionals in helping people to better manage taking desferal Amelia notes;

> "...it's not the doctors or the nurses, because they are not going to be at home with you. It's whatever you do.....They (other thalassaemics) can't just rely on the medical people. They have to stop feeling sorry for themselves, because thalassaemia, it's.....you can lead a normal and a healthy life. *You* have to make it work."

5.3.3 Summary

It would therefore appear that following difficulties with adherence during her adolescent years which resulted in cardiac complications and diabetes Amelia has now managed to integrate the illness and its treatment into a sense of who she is and still feel good about herself. Family and friends have played an important role in her ability to be able to accept her illness and the desferal treatment by providing emotional support and support relating to taking desferal. This support is also associated with a high health value. Professional support has also been important although it would

appear that Amelia believes that she is the ultimately the one who is responsible for her health.

5.4 Comparison of the case studies.

Both Joe and Amelia's difficulties with adherence started during adolescence. At that time, part of the difficulties were associated with mixing up the treatment. This however, is no longer an issue as a result of improved treatment methods. Additionally, they both preferred to go out and socialise rather than take desferal. As a result they experienced heart difficulties which then played the deciding role in them taking desferal again.

One of the major difficulties associated with non-adherence for Joe has been difficulty accepting the fact that he has thalassaemia and the treatment associated with it. Even after his heart difficulties he warns about the importance of maintaining a balance between a normal life and taking desferal. He believes that adhering strictly to the desferal regime will inevitably limit his social activities. This would seem to suggest that Joe still has difficulties accepting his illness and the treatment regime. Amelia on the other hand has managed to incorporate the presence of the illness and its treatment into her self image and feels that she is healthy and normal. Adherence does not limit her lifestyle.

One factor which may have contributed to Amelia's acceptance of illness is the level of social support she receives. Family, spouse and professional support have all helped her to accept her illness and the desferal treatment and to value her health. She also

believes that an individual's health is their responsibility and not the responsibility of the medical team. This is in contrast to Joe who has a tendency to place his health in the hands of the doctor. To conclude, Table 14 and Table 15 provide a summary of the factors which make it more or less difficult to take desferal.

Table 14. Factors which make it easier to take desferal

1. Acceptance of illness and treatment
2. Family Support (emotional and instrumental)
3. High health value
4. Internal health locus of control
5. Medical complications as a result of iron overload
6. Newer pumps
7. Early educational interventions

Table 15. Factors which make it difficult to take desferal

1. Denial of thalassaemia and desferal (reinforced by forgetting, infrequent blood transfusions, secrecy and lack of side effects of non-adherence)
2. Adolescence
3. Health locus of control with the doctor
4. Physical side effects
5. Unrealistic attitude of family members towards thalassaemia
6. Social / work commitments

5.5 Comparison of the quantitative and qualitative data

Where the themes overlap there are inconsistencies in the findings of the quantitative and the qualitative analyses. The quantitative analysis indicates that there is no relationship between acceptance of illness and adherence whereas the qualitative

analysis suggests that this is an important factor. In addition, no differences were found in the quantitative analysis between age and adherence. Again this is inconsistent with the qualitative findings which suggest that adolescence is associated with non-adherence. Furthermore, the quantitative analysis failed to reveal any differences in adherence between those who have medical complications as a result of iron overload and those without. The case studies both indicate that medical complications served as a cue to start adhering.

The qualitative data also indicates that family support in particular can be an important factor in adherence. Whilst not specifically measuring family support, the quantitative analysis failed to find an association between satisfaction with social support and adherence. In addition, an internal health locus of control and a high health value were associated with adherence in the qualitative analysis but not in the quantitative analysis. Furthermore, there are inconsistencies regarding a health locus of control with the doctor. The quantitative analysis indicated that this is associated with adherence and the qualitative with non-adherence.

Finally, there are however consistencies in the reasons given for non-adherence. Physical side effects and social/work commitments are reported in both case studies and by participants in the quantitative analysis.

CHAPTER 4: DISCUSSION

This study aimed to investigate a number of psychosocial factors and their relationship to non-adherence to iron chelation therapy in patients with thalassaemia. Thalassaemia is treated with regular blood transfusions and an iron chelating agent, desferal. Desferal reduces both the number of medical complications associated with iron overload and the number of subsequent deaths as a result of heart failure. It is, however, a lifelong treatment regime, and for most people it involves subcutaneous infusions for eight to twelve hours, five to seven nights a week.

The present study employed both quantitative and qualitative techniques. In the quantitative analysis adherence was assessed from patient, doctor and nurse reports. A biological measure was also employed, whereby participants were allocated into a 'good' or 'poor' adherence group based on their iron loading levels over the previous eighteen months. The relationship between a number of psychosocial variables and non-adherence was then examined.

The results suggested a weak association between a number of the psychosocial variables and the three continuous measures of adherence. In addition, psychological distress was found to contribute to the prediction of non-adherence as measured by the patient and lower levels of self efficacy were found to be predictive of non-adherence as measured by the doctor. Furthermore, no differences were found between the biological groups in relation to any of the psychosocial or demographic variables examined. With regard to the qualitative component, two case studies were outlined in

order to provide an account of the factors that make it more or less difficult to take desferal. A number of themes emerged in each which help to elucidate the quantitative findings.

A discussion of these findings will be presented in five sections. In section one the adherence and psychosocial characteristics of the population will be discussed in the context of previous research. Section two will discuss the findings relating to the research hypotheses alongside the qualitative information regarding the factors that make it more or less difficult to take desferal. Section three will discuss the theoretical implications of the present study whilst section four will discuss its limitations. Finally section five will discuss its scientific and clinical implications.

1. Adherence and psychosocial characteristics

1.1 Incidence of non-adherence

With regard to the three adherence reports the results indicated that the patients rated the highest levels of non-adherence followed by the doctor and then the nurse. In addition, when the participants were allocated to one of two groups by the consultant based on their ferritin records over a period of eighteen months the results indicated that 64% were considered to be adherent and 36% non-adherent.

In order to make comparisons with previous research examining non-adherence to the desferal regime (Beratis, 1989) the percentage of patients considered to be obtaining less than 60% of the recommended dose of desferal was calculated. Using this criteria

Beratis (1989) found that 23% of the population fell into the non-adherent category. In the present study, using the same criteria only 9.6% would be considered to be non-adherent as measured by the doctor and patient reports and 0% as estimated by the nurse. This criterion was not employed to differentiate between non-adherent and adherent groups in present study because of the small numbers in the non-adherent group and because Beratis (1989) did not specify on what criteria this definition of adherence was based.

Previous research indicates that there is a wide range of estimated non-adherence across studies examining its incidence in various chronic illnesses. For example, Kaplan & Simon (1990) reported that estimates range from 15% to 93% and Meichenbaum & Turk (1987) reported that estimates of non-adherence in chronic illness converge at around 30-50%.

It is difficult to draw any conclusions about the incidence of non-adherence to desferal as a result of the many different definitions of non-adherence. The results do however indicate that only one quarter of the population had medical complications related to iron overload and only two people were using a portacath. In addition, when compared to studies in chronic illness thalassaemia patients are at the lower end of the range of non-adherence. Furthermore, using the same criteria as that employed by Beratis (1989) it would appear that this population of adult thalassaemics experience lower levels of non-adherence when compared to a mainly adolescent population. It is suggested that this may be a reflection of age differences between the two populations. Such a finding is consistent with the qualitative data in the present study and the

findings of previous studies in thalassaemia (e.g. Georganda, 1990). It is also consistent across many other chronic illnesses, for example, diabetes (Jacobson *et al.*, 1990; cited in Byron, 1998) and cystic fibrosis (Gudas, Koocher & Wypij, 1991; cited in Byron, 1998).

1.2 Psychosocial characteristics

The norms from previous research enable the reader to place the results of the present study in a context. However, due to the limited amount of research many of the variables in the present study have not been previously examined in relation to people with thalassaemia. Comparisons will be made with other chronic illness and general populations but should be met with caution. In addition, there are limitations due to the fact that it is not possible to determine the statistical significance of such differences due to a lack of information about the comparison samples.

Previous research indicates that patients with thalassaemia experience high levels of psychiatric symptomatology (*Woo et al.,* 1985; Ratip, 1996; Beratis, 1993; Sherman *et al.,* 1985, Georganda, 1988; Tsiantis, 1990) although comparisons cannot be made between the present study and other studies due a lack of existing norms. Thalassaemia patients do however report lower levels of well-being than a group of 129 young men in a study by Ryff (1989). This finding is perhaps not surprising given that the men in Ryff's study were from the general population and not a chronic illness population.

With regard to social support, the actual number of social supports reported in the thalassaemia population are smaller than those presented in a study by Sarason *et al.*

(1983). Again, perhaps this is not surprising as Sarason *et al.'s* population consisted of university students. The reported level of satisfaction with support is however higher in the thalassaemia population. This indicates that whilst thalassaemia patients have fewer social supports than a student population, they are more satisfied with the support they get. Indeed, satisfaction with support was positively correlated with well-being.

In relation to acceptance of illness the results of the present study are similar to those reported in a study by Felton & Revenson (1984). This study included 151 people with one of four chronic illnesses, namely, hypertension, diabetes, arthritis or cancer. In addition, the health locus of control results indicate that thalassaemia patients have a lower 'internal' and 'doctor' health locus of control but a higher 'chance external' and 'other person' health locus of control than those reported by a diabetic population (Wallston *et al.,* 1994).

Furthermore, thalassaemia patients reported a much lower health value than ulcer clinic patients in a study by Lau *et al.* (1986). The value of health measure has not been extensively used in health research and has instead been used to explore the health locus of control measure. In relation to this, Lau *et al.* (1986) note that there is no reason to expect that people will have internal health locus of control beliefs if they do not value their health highly, particularly if some other conflicting behaviour is more highly valued. As indicated above, the results of this study do indeed indicate that thalassaemia patients have a lower internal health locus of control than a diabetic

population. Finally, the population of the present study reported similar levels of self efficacy to 1,660 German adults from a general population (Schwartzer, 1993).

2. Psychosocial status and non-adherence

2.1 Demographic characteristics and non-adherence

Contrary to Ratip's (1996) findings the results of the present study indicate that thalassaemia patients are well educated, with one fifth educated to degree level. However, consistent with the literature, no relationships were found in the quantitative analysis between any of the demographic variables and any of the measures of non-adherence. The reviews by Haynes et al. (1979), Kaplan & Simon, (1990) and Meichenbaum & Turk (1987) all indicate that the majority of studies fail to find an association between adherence and the patients' socio-demographic variables. It is surprising however that the quantitative analysis of the present study failed to reveal any relationship between age and non-adherence.

Previous thalassaemia research (Beratis, 1989; Georganda, 1990) indicates that adolescence is associated with non-adherence to the desferal regime. Indeed, the qualitative data in the present study support these findings. It is suggested that the failure to find a relationship between age and non-adherence in the quantitative analysis may be related to the fact that the mean age of participants was 27 years (range 16-47) and therefore does not incorporate many adolescents for whom non-adherence may be an issue.

2.2 Psychosocial characteristics and non-adherence

This section will discuss the findings of the relationships between the psychosocial variables and non-adherence. It will place these findings in the context of previous research and where the themes overlap it will discuss the inconsistencies between the qualitative and the quantitative data. Whilst the qualitative results should be met with caution as they do not represent the experience of thalassaemia patients in general they can be employed in some instances to inform the suggestions as to why the quantitative analysis either failed to confirm the research hypotheses or only revealed weak associations. For clarity, the terms adherence and non-adherence are employed to differentiate between greater and lesser levels of adherence along a continuum.

2.2.1 Psychological Distress

The quantitative results indicate that greater levels of psychological distress are associated with non-adherence, as measured by the patients only. Correlations revealed weak positive associations between anxiety, somatic symptoms, total psychological distress and non-adherence. No associations were found between depression and non-adherence. This is surprising given that the literature indicates that anxiety (Nelson *et al.*, 1978) and depression (Blummenthal *et al.,* 1982) are powerful predictors of non-adherence. As a result stronger associations would have been expected. In addition, no association was found between non-adherence and psychological well-being. In this case, comparisons cannot be made with previous research as no existing study has examined this relationship.

It is hypothesised that the relationship between psychological distress and non-adherence may have been weakened by an association between psychological distress and adherence. The results indicate that there are a number of reasons why people may not take their treatment. These include, amongst others, pain and social / work commitments. It suggested that the experience of pain and a reduction in social activities associated with adherence may in turn be associated with an increase in psychological distress, as might be the simple act of taking the treatment itself.

Furthermore, it is suggested that the reverse is also possible. Deciding not to adhere and instead lead an active social life / live without the pain of treatment may be associated with a reduction in psychological distress. Indeed, this hypothesis links with a finding by Meichenbaum & Turk (1987) who reported that treatment non-adherence may not invariably be maladaptive and that in some circumstances it may even be adaptive, reflecting a logical and rational decision making process. Non-adherence may represent the patients attempts to gain some control over the illness and its psychosocial impact.

It is further suggested that this hypothesis may also explain the failure to find an association between lower levels of well-being and non-adherence. It is possible that this relationship may also have been weakened by an association between higher levels of well-being and non-adherence. For example, going on holiday was one reason given for not taking desferal. It is suggested that holidays are generally a time when people feel well and can relax and that in this situation non-adherence may in fact be

associated with higher levels of well-being and not lower levels of well-being as originally hypothesised.

2.2.2 Acceptance of illness

The findings of the quantitative analysis do not support the hypothesis that lower levels of acceptance of illness are associated with non-adherence. Again, no previous studies have examined this relationship and so comparisons cannot be made. Past research examining this concept does however indicate that people who are more accepting of their illness show less anxiety and depression (Hogg *et al.*, 1994). The results of the present study support this finding. Higher levels of psychological distress were associated with lower acceptance of illness and higher levels of well-being were associated with greater acceptance of illness.

However, the results of the quantitative and qualitative analysis are inconsistent as the qualitative analysis indicates a strong association between acceptance of illness and adherence behaviour. The results highlight a positive relationship between acceptance of illness and adherence and that factors such as family support and value of health may be important in this relationship. On the reverse, the results also indicate that low levels of acceptance of illness and treatment are associated with non-adherence. Georganda (1990) reported that when the individual has a chronic illness the illness is part of them and this is can be a very difficult idea to accept. Difficulties with acceptance of illness in the qualitative analysis were associated with being secretive about the illness, forgetting about it and bargaining with the treatment.

This notion of secrecy about thalassaemia has been identified in other studies (e.g. Ratip, 1996). Furthermore, in a study of adolescents, Georganda (1988) reported that thalassaemia patients did not want to be reminded of the illness and that they actually wanted to forget that they had it. In the present study, forgetting was reinforced by infrequent blood transfusions, infrequent contact with health professionals and a lack of immediate side effects of non-adherence. Indeed, Meichenbaum & Turk (1987) reported that lowest levels of adherence occur with patients who have chronic disorders and when no immediate risk or discomfort is evident.

It is hypothesised that the inconsistencies in the findings may be a result of the limitations of the acceptance of illness measure. This measure focused directly on the extent to which participants are able to accept their illness without experiencing negative consequences. In doing so it makes the assumption that people accept that they have an illness. Given the fact that in the absence of medical complications the thalassaemia patient can feel well (as long as they have their blood transfusions), their perceived susceptibility to the illness may be low. Their perception of the severity of the illness may also be low. It is hypothesised that this may have one of two effects. It may either make the illness easier to accept, or alternatively, it may make it easier to deny. It is suggested that if thalassaemia patients deny that they have an illness they may then deny that they have to take desferal.

It is therefore hypothesised that the relationship between lower acceptance of illness and non-adherence in the quantitative analysis was weakened by an association between higher levels of acceptance of illness (as measured by the acceptance of illness

scale) and non-adherence. For example, individuals may only be able to state that their illness does not stop them from doing the things that they like to do most (i.e. high acceptance of illness) because they are denying that they have to take desferal and can therefore continue with their normal activities. It is therefore suggested that it is important to distinguish between the concept of acceptance of illness and the concept of acceptance of treatment as one does not necessarily imply the other.

2.2.3 Social Support

The results of the quantitative analysis indicate that the larger the social support network patients have, the more they are likely to adhere. It is however surprising that no association was found between lower levels of satisfaction with support and non-adherence as was initially hypothesised. Indeed, Warren & Hixenbaugh (1998) reported that the diabetes research indicates that an individual's perceptions of the nature and function of relationships is a better indicator of non-adherence than more objective measures such as network size.

This failure to find a relationship between satisfaction with social support and adherence is also inconsistent with the findings of the qualitative data. The qualitative findings indicate that family support in particular is positively associated with adherence. Family support was identified as playing an important role in being able to value one's health, accept thalassaemia and accept desferal treatment. Two particular types of support were identified as being important, namely, emotional and instrumental support (Cohen & Wills, 1985). Emotional support is related to feelings of being loved whereas instrumental support is related to support and encouragement

in taking desferal. This association between social support and adherence is consistent with the vast body of literature which indicates that social support is an important factor in adherence (e.g. Doherty *et al.,* 1983).

However, the qualitative results also highlight potential limitations to family support. Overprotection by parents was identified as being unhelpful in that it can reduce patients' beliefs that they are capable of doing things for themselves. This not only links with the finding that thalassaemia patients are overprotected by their parents (Ratip, 1996; Woo *et al.*, 1985) it is also links with the concept of self efficacy (Bandura, 1977). In addition, family difficulties were one of the reasons why people had failed to take desferal in the four weeks prior to participation in the study.

Furthermore, the results suggest that parents need to be realistic about the limitations of their child. This again links with Tsiantis'(1990) finding that parents of children with thalassaemia can exert excessive pressure on their child. The results of the present study suggest that if parents do not make children aware of the limitations associated with living with thalassaemia then other factors such as work and social life can interfere with adherence. How others perceive the illness is therefore also important to adherence and links with Georganda's (1990) finding that how the illness is perceived and dealt with by others may cause more of a problem than the illness itself. Georganda (1990) also noted that the child is greatly influenced by how the adults view him or her.

It is hypothesised that the failure to find a relationship between lower levels of social support and non-adherence in the quantitative analysis was weakened by an association between increased satisfaction with social support and non-adherence. It is suggested that people may be satisfied with the social support they receive for different reasons. Some may be satisfied with the support that they receive in relation to illness related tasks such as acceptance of illness and its treatment (emotional and instrumental support). This would then suggest a positive relationship between satisfaction with support and adherence. For others however, satisfaction with social support may be associated with the opportunity of being able to go out and socialise (social companionship), particularly during adolescence. It is suggested that this form of social support may be negatively associated with adherence, particularly if the individual is secretive about their illness.

2.2.4 Health locus of control

In relation to patients' health locus of control the quantitative results are inconsistent with the hypothesis that non-adherence would be associated with an external health locus of control. This supports Horne & Weinman's (1998) findings that existing research findings are inconsistent.

The results indicate that one external health locus of control dimension (other person) is positively associated with non-adherence whilst another (doctor) is negatively associated with non-adherence. Therefore patients who believe that another person has a controlling influence on their health adhere poorly and those who believe that the doctor has a controlling influence adhere well. The first finding is consistent with the

research hypothesis but the second indicates that an external health locus of control is associated with adherence and not non-adherence as was initially hypothesised. This finding is also inconsistent with the qualitative findings which indicated that a health locus of control with the doctor is associated with non-adherence. It is suggested that for some, a health locus of control with the doctor is associated with both adherence and non-adherence. It may be associated with adherence whilst the patient is in hospital receiving intravenous treatment or if they have a portacath inserted. It may also be associated with non-adherence when they do not adhere to the subcutaneous infusions at home, preferring to place responsibility for their health in the hands of the doctor.

In contrast, the qualitative data indicated that an internal health locus of control is positively associated with adherence. This finding therefore supports the theory that internals on the multidimensional health locus of control will be more likely to engage in health promoting activities.

2.2.5 Health Value

No associations were found between non-adherence and a lower value of health in the quantitative analysis although a high health value was found to be associated with adherence in the qualitative analysis. No comparisons can be made with the literature, as Lau *et al.* (1986) note that the concept of health value has not been applied in any systematic and theoretically sophisticated manner to health research. It has been used instead to explore the health locus of control concept.

The results indicate that thalassaemia patients experience lower values of health than ulcer clinic patients (Lau *et al.*, 1982). It is hypothesised that the perceived barriers to taking desferal may contribute to the reasons for this. It may be that at times thalassaemia patients consider other factors such as maintaining a 'normal' life to be more important than their health. Even those patients who value their health highly may at times value the ability to be able to lead an active social life and avoid pain more than they value their health - at least in the short term. It is therefore suggested that the relationship between a low value of health and non-adherence was weakened by an association between a high health value and non-adherence when the perceived barriers to treatment are valued more highly than health.

It is further suggested that the experience of medical complications may be associated with adherence as indicated in the qualitative analysis. However, given the failure to find such an association in the quantitative analysis it is hypothesised that medical complications may serve as a cue to adherence but may be short lived as the patient values the ability to be able to continue with their 'normal' activities more than they value their health.

2.2.6 Self Efficacy

Finally, the quantitative results indicate that lower levels of self efficacy are associated with non-adherence as measured by the doctor only. This finding supports the initial hypothesis and indicates that the less patients believe in their abilities, the less likely they are to adhere to the treatment regime. This is consistent with the literature which

suggests that self efficacy beliefs can be powerful predictors of adherence (e.g. Kaplan *et al.*, 1984) although a stronger association might have been expected.

It is hypothesised that the reason for this weak association may be that patients consider their ability to be efficient in other areas of their life (e.g. work) to be more important than the ability to take their treatment. Bandura (1977) noted that the individuals' efficacy expectations will vary greatly depending on the particular task that confronts them. Indeed, this hypothesis is further supported by the qualitative findings of the present study. These results indicate that families may not be aware of the limitations associated with living with thalassaemia and that as a result individuals may be encouraged to believe in their abilities in other areas, for example the workplace. This may then impact on their ability to be able to adhere.

2.3 Multiple regressions

Multiple regressions revealed that total psychological distress significantly contributes to the prediction of non-adherence as measured by the patients. No other variable contributed significantly to this model. In addition, lower self efficacy is predictive of non-adherence as measured by the doctor with no other variable contributing significantly to this model. No comparisons can be made with other studies due to a lack of research in this area. It is suggested that the failure to predict a significant model of non-adherence based on the variables examined is a result of the complexity of the relationships between the specific variables and non-adherence already discussed.

2.4 Summary

Where the themes overlap the results indicate that there are inconsistencies between the qualitative and the quantitative analyses. The results of the quantitative analysis support the research hypothesis that non-adherence is characterised by greater psychological distress. This finding was however weak and it is suggested that this may be a result of additional associations between greater levels psychological distress and adherence and lower levels of psychological distress and non-adherence. Furthermore, it is also suggested that the failure to find an association between lower levels of well-being and non-adherence is the result of an association between higher levels of well-being and non-adherence.

With regard to acceptance of illness the results between the qualitative and quantitative analyses are inconsistent. The quantitative analysis found no relationship between lower levels of acceptance of illness and non-adherence whereas the qualitative analysis indicated a strong relationship. It is suggested that the failure to confirm the quantitative research hypothesis is a result of the limitations of the acceptance of illness measure employed.

The results of the quantitative and the qualitative analyses are also inconsistent in relation to the association between satisfaction with social support and adherence. It is suggested that the failure to find an association between lower levels of satisfaction with support and non-adherence was weakened by an association between increased satisfaction with social support and non-adherence. Furthermore, the qualitative data suggest that it is the type of support that is important in determining this relationship.

The findings are also inconsistent with regard to the relationship between health locus of control and non-adherence. It is suggested that whilst an internal health locus of control is associated with adherence, a health locus of control with the doctor can be associated with both adherence and non-adherence. In addition, the quantitative analysis failed to find a relationship between non-adherence and lower values of health. It is suggested that this relationship may have been weakened by an association between a high health value and non-adherence when the perceived barriers to treatment have a higher personal value than health. It is further suggested that this may be the reason why the quantitative analysis only revealed a weak relationship between lower levels of self efficacy and non-adherence. It is suggested that people may believe in their abilities in other areas of their life (e.g. work) more that their ability to take their treatment.

The findings of the quantitative and qualitative analysis therefore indicate that it is difficult to establish direct relationships between any one specific variable and non-adherence and that there are likely to be a complex interplay of factors associated with non-adherence behaviours. This finding is supported by Meichenbaum & Turk (1987) who reported that a number of researchers often attempt to examine the relationship between specific variables and non-adherence and that whilst this research can yield useful findings, actually a number of highly complex interdependent factors are operating. It is therefore to a theoretical model that we now turn in order to discuss the findings of the present study.

3. Theoretical Issues

As a result of the developments in health and social psychology a number of different theoretical frameworks or models have been proposed in an attempt to explain adherence behaviour. Given the nature of the constructs examined and identified in the quantitative and the qualitative components of the present study it is proposed that the health belief model (Rosenstock, 1974) provides the most useful framework in order to discuss the findings.

The original model (Rosenstock, 1974) proposed that in the context of an individual's psychological and demographic characteristics the likelihood of someone carrying out a particular health behaviour (e.g. adhering to the desferal regime) is a function of their personal beliefs about the perceived threat of the disease and an assessment of the perceived risk/benefits of the recommended course of action. The model proposed that the perceived threat is derived from the perceived seriousness of the threat and the individual's perceived susceptibility to it. The individual then weighs up the perceived benefits of an action against the perceived barriers to the action. In 1975, Becker and Maiman added a further component when they indicated that a cue to action must occur to trigger the behaviour. In addition, further variables have been added such as general health motivation.

The health belief model therefore predicts that the likelihood of adherence is increased if the perceived threat of the disease is high, if the benefits of the behaviours are thought to outweigh the barriers and if certain cues are in place. It is however important to acknowledge that the present study was not designed to assess the

validity of such a theoretical model and as a result some of the constructs were not directly examined. In these instances hypotheses will be discussed based on related constructs.

3.1 Demographic and psychological characteristics

The health belief model proposed that diverse demographic, personality and social factors can in any given instance indirectly affect an individual's health motivations. The results of the present study indicate that age and psychological distress are important demographic and psychological factors associated with non-adherence.

3.2 Perceived susceptibility and severity of the illness

Whilst these constructs are not directly examined in the present study it is hypothesised that in general, given the lack of immediate side effects of non-adherence to desferal the individual's perceived susceptibility to the illness may be low. It is further hypothesised that given the fatal nature of non-adherence the individual may perceive the severity of the illness as high. This hypothesis links with the research into HIV-preventative behaviour. Sheeran and Abraham (1996) note that the consequences of HIV infection are delayed and that this may produce a general failure to acknowledge personal susceptibility. They also note however that the consequences are fatal and that this increases levels of perceived severity of the illness. Sheeran and Abraham (1996) note that such ceiling and floor effects may limit the extent to which these measures can distinguish between those who do and those who do not take precautions against HIV. It is therefore suggested that these measures may be limited

in distinguishing between those who do and those who do not adhere to the desferal regime.

In addition, Sheeran and Abraham (1996) also note that increasing perceptions of threat among individuals who already acknowledge personal susceptibility may prompt maladaptive coping in the form of denial and thereby increase the likelihood of HIV risk behaviour. It is hypothesised that this may also be true for patients with thalassaemia. It is possible that patients who acknowledge the difficulties associated with taking the treatment may then deny that they have to take it as a maladaptive coping mechanism. This links with the concept of acceptance/denial of illness/treatment and it would be interesting to further examine this construct in relation to the constructs of perceived susceptibility and severity.

3.3 Perceived benefits/barriers

The results of the present study indicate that there are a number of perceived barriers to treatment with few benefits. This finding may however reflect the fact that participants were asked directly about the barriers to treatment but were not asked about the benefits. In relation to the benefits of taking desferal the qualitative component indicated that adherence to the desferal regime was associated with being able to live a healthy life. However, the perceived barriers included social/work commitments, physical side effects (feeling tired, pain, unwell), family difficulties and taking other medication. On the reverse, feeling well and going on holiday were also perceived barriers. Given that the benefits were not specifically examined in the present study it is suggested that future research examine this construct.

In addition, there has also been some debate regarding the construct of self efficacy and whether this can be considered a component of the perceived barriers (Janz & Becker, 1984) or whether it should be added as additional theoretical construct (Rosenstock, Strecher & Becker, 1988). Self efficacy has been found to be an important predictor of HIV preventative behaviour (e.g. Siegel, Mesagno, Chen & Christ, 1989) and in a review of the literature, Sheeran and Abraham (1996) note that amongst other measures, perceived self efficacy is a more important predictor of HIV-preventative behaviour than health belief model-specified variables. Self efficacy was also found to be associated with adherence in the present study and therefore the results would support the inclusion of the construct of self efficacy into the health belief model. However, more research is needed to specify the interactions between beliefs and self efficacy and to further the development of this construct into a theoretical framework.

3.4 Health motivation/cues to action

Sheeran and Abraham (1996) note that the cues to action and health motivation have been neglected in empirical tests of the health belief model and that this may be a result of the lack of clear construct definitions. With regard to health motivation, the qualitative results of the present study indicate that an internal health locus of control is associated with adherence as is a high value of health. In addition, the quantitative results also indicate that that a health locus of control with another person and with the doctor are associated with adherence behaviours. It is important to note however that further research is needed to clarify the relationship between health motivation and the related constructs of health locus of control and value of health (Sheeran & Abraham,

1996). Furthermore, it is proposed that medical complications as a result of iron overload may serve as a cue to action as might educational interventions and instrumental social support (i.e. support and encouragement taking desferal).

3.5 Summary

In discussing the findings of the present study in relation to a theoretical framework it is important to note that this study did not directly examine the validity of the health belief model . Instead it examined a number of psychological and social factors that have been found to be associated with non-adherence in the general chronic illness research. Indeed, the health belief model has been criticised on a number of different levels. One general criticism is that it does not provide any operationalization instructions and therefore has to be operationalized as a series of independent variables. This inevitably limits its status as a coherent model (Sheeran & Abraham, 1996).

Another criticism of the model is that it lacks construct definition. As a result of this lack of definition a number of constructs examined in the present study have been linked to those in the model. For example, it is suggested that the acceptance of illness construct may be related to susceptibility/severity of illness constructs. It is further suggested that the health locus of control and health value constructs may be related to the health motivation construct. However, it is important to note that further research is needed before any conclusions can be made. The issue of the utility of the construct of susceptibility/severity of illness has also been brought into question given the hypothesis that ceiling and floor effects are possible.

Furthermore, the model specifies that demographic and psychological factors only indirectly affect an individual's motivations. The results of the present study indicate that there are some direct associations. Finally, the results of the present study indicate the need to include the construct of self efficacy into the model although further research is needed in order to theoretically define its position.

4. Limitations of research

4.1 Generalisabilty

There are limits to the external validity of this study as a result of the limited number of participants in the quantitative analysis. In addition, whilst the two case studies served to provide examples of peoples' experience of taking desferal, they do not represent the experience of thalassaemia patients in general. In order to increase external validity it is important to replicate this study, or parts of it, with a larger sample of adults with thalassaemia.

4.2 Research design

This study was cross sectional in its design and therefore provides a 'snap shot' of the situation for participants at one point in time only. Past research indicates that adherence is a complex and dynamic construct that changes over time - a finding which is also supported by the qualitative data in this study. As a result, the actual design of this study also constitutes one of its limitations.

In addition, a major part of this study was correlational. It is important to note that correlations cannot be used to make unequivocal inferences about the relationships between variables. As a result it is not possible to move beyond the strength of associations between variables to make inferences about causality. This study represents only a preliminary step in causal explanation.

Furthermore, this study incorporated a large number of independent and dependent variables and the possibility of Type I errors cannot be ruled out. As a result, all findings should be met with caution as they were significant at the 0.05 level only. A large number of variables were also entered into the multiple regressions which also means that Type I errors cannot be ruled out.

Whilst the design of the present study was essentially quantitative, the qualitative data provided a wealth of information about peoples' experiences of the difficulties associated with taking desferal. More emphasis on the qualitative component may have yielded more in-depth data and provided information which could then be used as the basis of future quantitative studies. It may also have avoided the difficulties associated with the validity of the measures of adherence which are discussed in section 4.3.1.

4.3 Measures

4.3.1 Adherence measures

Adherence is a difficult concept to define. The measures of adherence employed in this study tried to account for all of the variability of adherence over a four week period. The questions asked were therefore very specific and over a long time period. As a result, it is possible that either the raters did not understand the questions or that they could not accurately estimate such specific questions over such length of time. Furthermore, the patients were asked questions relating to their adherence by the researcher which may have limited the validity of the measure. In addition, the patients overestimated their recommended dose of desferal which may indicate that they also overestimated their levels of non-adherence.

Furthermore, the validity of the doctor and the nurse reports is also limited. In some cases they had not been in contact with the patient for several months. The doctors also reported that they do not actually ask patients whether they remove their treatment early and that they had to guess this information. In addition, the results indicate that the doctor and nurse reports were associated with the patients current ferritin status and not with the patient report. Ferritin levels are known to vary according to medical status of the patient and they may therefore not be an accurate reflection of the four week period. Again this suggests that there are limitations to the validity of these measures.

Finally, the validity of the biological measure of adherence is also limited. For some of the participants there was a great deal of missing data. A limited number of ferritin results would not provide an accurate mean for their ferritin over the previous 18 months. In addition, the graphs of patients' ferritin results over the preceding eighteen months were rated by one doctor only and may therefore be subject to bias. Furthermore, the participants were allocated to one of the two groups by the researcher only. Again this casts doubt on the validity of the measure.

4.3.2 Psychosocial measures

There are a number of limitations to the psychosocial measures employed in this study. Firstly, in order to increase its sensitivity a likert scoring method was employed. This limited comparisons with other studies which tend to employ the GHQ scoring method. In addition, the GHQ (Goldberg & Hillier, 1979) was found to be sensitive to the patient report of non-adherence but not to the doctor or nurse reports. It is possible that this is because the GHQ asks about peoples' health over the past few weeks. The patients themselves may have reported their adherence over this time period but the evidence suggests that the doctor and the nurse reports were based more on patients' ferritin levels and therefore may not accurately represent the time period in question. Furthermore, Ratip *et al.* (1996) note that the GHQ focuses on recent change in affect so answers may suggest no psychosocial morbidity among patients who have been coping with a serious problem over many years.

Furthermore, the limitations of the acceptance of illness measure (Felton & Revenson, 1984) questionnaire have already been mentioned. This questionnaire makes the

assumption the patients have already accepted their illness and does not account for those who were in denial. In addition it does distinguish between acceptance of illness and acceptance of treatment. Finally, there are also limitations to the social support measure (Sarason *et al.,* 1987) employed in the present study as it examined the number of social supports and satisfaction with support only. The results of the qualitative analysis suggested that it may be more important to examine the relationship between different types of social support and non-adherence, rather than simply satisfaction.

5. Implications of research

5.1 Scientific implications

5.1.1 Research design

As noted previously there are limitations to a cross sectional study. Given the dynamic nature of the concept of adherence a longitudinal study could be employed in future research in order to examine factors associated with adherence over time. Such a design would improve the external validity of the findings.

It is also suggested that further research should include both qualitative and quantitative components. Future quantitative studies could examine the relationships investigated in the present study, building on the findings of both the quantitative and qualitative analysis. Any one of the variables employed in the present study could be used in future research. It is however recommended that fewer psychosocial variables

are examined and that future research examines potential mediating factors in the relationships between the variables. For example, it would be interesting to examine the influence of perceived barriers (social life / pain / work) to treatment in the relationship between psychological distress or well-being and non-adherence. It may also be interesting to examine the role of family support in the relationship between acceptance of illness and adherence.

In addition, qualitative analyses could be employed to further our understanding of the factors associated with non-adherence which could then be used to inform future quantitative analyses. A 'methodologically pluralistic' approach is advocated where appropriate methods are employed for the research questions under investigation (Barker, Pistrang & Elliot, 1994).

5.1.2 Adherence measures

In order to improve the validity of this study simpler measures of adherence should be employed. This could include a simple Likert scale. No one measure of adherence is foolproof and this measure could also be given to the doctor and the nurse. In this situation, ensuring that the doctor or the nurse had recent contact with the patient would improve the validity of this measure. These reports could also be used in combination with other measures such as prescriptions counts or an electronic measuring device when they become more widely available (e.g. Matsui *et al.*, 1994, cited in Myers & Midence 1998) .

In addition, the biological marker of adherence, could be employed in further studies. A number of factors could improve the validity of this measure. These include regular monitoring of each patients serum ferritin levels and stricter criteria for rating the graphs. Olivieri *et al.* (1994) reported that no cardiac complications occurred in those whose ferritin levels were kept below 2,500 or exceeding this limit in less than 33% of the evaluations. More formal calculations based on this criteria would improve the validity of this measure. In addition, a second rating by another doctor would provide a measure of inter-rater reliability and would also improve its validity. Furthermore, it is suggested that group allocation should also be undertaken by a doctor with a second doctor providing a measure of inter-rater reliability.

5.1.3 Psychosocial measures

It is suggested that the employment of any measure of psychological distress will lead to difficulties in any study of adherence as it is not possible to differentiate between general psychological distress associated with the chronic illness and increased psychological distress that is directly associated with non-adherence. Ratip *et al.* (1996) employed an instrument specifically directed at the problems associated with thalassaemia. Whilst this semi-structured interview could be criticised because of it subjectivity further development of this measure might yield more useful findings. In addition, employing a measure of social support which examines the association between different types of support on adherence would provide interesting data. One such scale is the Inventory of Socially Supportive Behaviours (Barrera, 1981). This is a 40 item measure of four types of support (emotional, instrumental, information appraisal and socialising). Finally, it is suggested that the development of an

acceptance of treatment questionnaire, possibly based on qualitative information would provide a further useful measurement tool.

5.2 Clinical implications

The results of this study indicate that adherence is a dynamic and complex concept that changes over time. It also indicates the complexities of the relationship between psychosocial factors and adherence. Further research is needed before any firm recommendations can be made regarding the clinical implications of the relationship between psychosocial status and non-adherence. Given the complexity of factors affecting adherence no one clinical intervention would be appropriate for all individuals. However, a number of general suggestions can be made.

Given that the rates of non-adherence in this population were low when compared to other chronic illnesses it is suggested that existing practice may encourage adherence. Indeed, Ratip *et al.* (1996) note that the perception of psychosocial burden varies amongst doctors and is greatly influenced by the doctors personality. In the clinic where most of the data was collected staff worked hard to ensure adherence amongst their patients. The results indicate that patients were well educated about the effects of non-adherence as measured by the fact that they had an accurate awareness of their ferritin levels. There was also an evening clinic once a week and the facility for evening blood transfusions so as to ensure minimum interference with the school or work of the patients. In addition, an understanding and personal relationship between the staff and patients was stressed (Massaglia & Carpignano, 1985; Politis *et al.*, 1990)

and a Clinical Psychologist was attached to the clinic in order to assess non-adherence and provide appropriate psychological interventions.

The results of the quantitative and qualitative analyses indicate that there are a number of factors potentially associated with non-adherence. These include, psychological distress, low levels of self efficacy, low acceptance of illness and its treatment, an 'external' health locus of control and a lack of social support associated with adherence behaviours. It also highlights that there are a number of perceived barriers to treatment, for example, pain, social life, family difficulties, work and holidays. It is suggested that an assessment of risk of non-adherence should include these variables alongside an assessment of the individual's perceived susceptibility to the illness and perceived severity of the illness.

Given the association between non-adherence and adolescence it is further suggested that it is important to maintain continuity between child and adolescent services in order to avoid the potentially traumatic referral to other units in adolescence (Politis, 1990). Ratip *et al.* (1996) suggest that the patients opinion should be sought before the transfer and that an overlap between services can alleviate the psychosocial impact of such a move. Continuity of care may also be helpful in an adult setting (Meichenbaum & Turk, 1987). The qualitative analysis suggested that one of the factors associated with difficulties with acceptance of illness involved, amongst other things, a lack of frequent contact with the health care provider. This may be particularly relevant for those patients who have a doctor health locus of control.

In addition, one of the suggestions made in the semi-structured interview was the need for early educational interventions. Matthews & Malios (1976) note that the psychosocial burden of thalassaemia can be better managed if an educational programme is directed towards the adolescent. It is suggested that this may include information regarding the disease and the benefits of its associated treatment. Books such as "What is Thalassaemia?" (Porter, 1996) are currently available. Support for the adolescent could also be extended in their other systems such as school or higher education services (Achenbach, 1992, cited in Ratip *et al.,* 1996). This could further help to ensure that the thalassaemia patient can lead as normal a life as possible. Furthermore, thalassaemia support associations are also important in the education of both patients and provide the opportunity to meet peers, form relationships and participate in social activities. These associations may also help patients be less secretive about their illness and help them to strike a balance between taking desferal and leading a 'normal' life.

Enlisting the support of the thalassaemia patients family could also improve their adherence. Interventions could be targeted at expressing the importance of emotional and instrumental support and at maintaining a balance between parental overprotection and a realistic understanding of the limitations associated with the illness. It could also aim to encourage communication regarding the illness so as to avoid secrecy.

Finally, psychological intervention could also be aimed at addressing issues relating to acceptance of illness and its treatment, accepting responsibility for one's health and at increasing levels of self efficacy in relation to illness related tasks. The type of

psychological intervention employed should be based upon a thorough assessment of the nature of the individual's experience of non-adherence.

5.3 Summary / conclusions

Having to live with a chronic illness can have a profound effect on an individual's psychological and social status. The present study represents an initial investigation into the psychosocial factors associated with non-adherence to iron chelation therapy (desferal) in adults with thalassaemia major and thalassaemia intermedia. It examined the relationship between specific psychosocial variables and non-adherence and whilst some specific relationships were identified the results suggested there are in fact a number of highly complex interdependent variables operating. Adherence is a complex and dynamic phenomenon and each individuals experience will be based on a complex interaction of a number of factors.

It is suggested that given the lack of immediate side effects of non-adherence to desferal and the barriers to adherence, non-adherence may in fact be based upon a rational, logical and adaptive decision making process. It may represent an attempt to gain some control over the illness and its psychosocial impact. Given that maintaining one's health is associated with subcutaneous infusions of desferal for 8-12 hours, five to seven nights a week, thalassaemia patients may at times value the ability to continue with a 'normal' life more than they value their health. For the thalassaemia patient non-adherence may at times in fact be associated with lower levels of psychological distress, increased feelings of well-being and an active social life.

This study therefore highlights the complexity of the concept of adherence and further research is needed to examine the relationship between psychosocial status and adherence in patients with thalassaemia, only then can any conclusions be made. Furthermore, only then can effective interventions be developed. These interventions should be targeted not only at improving adherence, but improving adherence in the context of a 'normal' life - whatever that implies for the particular individual concerned.

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APPENDIX 1: ETHICS APPROVAL

The project was approved by the local research ethics committees of University College Hospitals NHS Trust and Haringey NHS Trust. Letters confirming ethical approval are included on the following two pages.

UCL
HOSPITALS

The University College London Hospitals

Research and Development Directorate
9th Floor, St Martin's House
140 Tottenham Court Road, London W1P 9LN
Fax. 0171-380 9937

R&D Directorate Manager:
Simon Robinson, Tel. 0171-380 9833
Administrative Assistant:
Philip Diamond, Tel. 0171-380-9833

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Office/Ethics Committees Administrator:
Iwona J Nowicka, Tel. 0171-380 9579
Assistant Director of Finance R&D:
Liesa Jones, Tel. 0171-380 9833/9579

Dr Chris Barker
Senior Lecturer
Department of Health Psychology
UCL
Gower Street

10 June 1998

Dear Dr Barker

Re: Study 98/0084
Psychosocial factors influencing adherence to iron chelation therapy in patients with homozygous beta thalassaemia

The above application is now approved by the Trust and you may go ahead with your research.

Yours sincerely

RL Souhami
Director of R&D

Enfield Haringey
HEALTH AUTHORITY
Where health matters

Chairman: Peter Dixon
Chief Executive: Christine Outram

11 January 1999

Rhiannon Cobner
Clinical Psychologist Training
The University College London Hospitals
Sub-department of Clinical Health Psychology
1-19 Torrington Place
London

Dear Ms Cobner

606 - Psychosocial factors influencing adherence to iron chelation therapy in patients with homozygous beta thalassaemia

I write to inform you that the above study submitted to the Local Research Ethics Committee has been approved, Chair's action having been taken.

Please quote the above number on any future correspondence.

The committee look forward to receiving a copy of an interim report in six months time or at the end of the study if this is sooner.

Yours sincerely

L H Lipson

Mrs L H Lipson
Chair
Enfield & Haringey LREC

h:\lrec\letters\606.doc

Holbrook House, Cockfosters Road
Barnet, Hertfordshire EN4 0DR
Tel: 0181-272 5500

APPENDIX 2: INFORMATION SHEETS

Information sheets supplied to patients inviting them to participate in the study are supplied on the following two pages, one for each hospital. Both information sheets invite patients to participate in the quantitative study, and an additional invitation to be interviewed for the qualitative component is included in the first information sheet.

The University College London Hospitals

THALASSAEMIA & SICKLE CELL UNIT
DEPARTMENT OF HAEMATOLOGY
University College Hospital, Grafton Way, London WC1E 6AU
Direct Line: Dr. J.B. Porter 0171 380 9638
Fax: 0171 380 9911

Psychosocial factors influencing adherence to iron chelation therapy in thalassaemia

Information sheet

We invite you to take part in a research study. This information sheet tells you about it. It is important you understand this information and that you know what will happen to you if you decide to take part. Whether or not you do take part is entirely your choice. All of the information will be treated in the utmost confidence.

Who is being invited to participate in the study?

People with thalassaemia who are currently being described desferal by DR Porter are being invited to participate in this study.

What is the goal of the research?

The goal of the research is to try and find out why people do not take their desferal as often as prescribed. If we can get a better idea why people do not take their desferal, then we can identify them and try to get them the best treatment.

What would involvement mean in practical terms?

Involvement in this study would mean completing a questionnaire during one of your visits to hospital. This will not involve an extra visit to the hospital. The questionnaire examines possible factors that may affect whether or not the treatment is taken as often as prescribed. You may also be invited to take part in a semi-structured interview which would last no longer than 30 minutes. The interview will examine in a bit more depth your feelings about taking the treatment.

Are there any risks?

There are no physical or psychological risks of taking part in this study. If however after completing the questionnaires or the semi-structured interview you are left with any uncomfortable feelings, you will be given an opportunity to discuss them.

You do not have to take part in this study if you do not want to. If you decide to take part you may withdraw at any time without having to give a reason. Your decision to take part or not will not affect your care or management in any way. All proposals for using human subjects are reviewed by an ethics committee before they can proceed. This proposal was reviewed by the joint UCL/UCLH Committees on the Ethics of Human Research.

Name of Investigators: DR Chris Barker & Ms Rhiannon Cobner
Address: Sub-Department of Clinical Health Psychology, University College London, WC1E 6BT
TEL: 0171-380-7897

THE NORTH MIDDLESEX HOSPITAL

An Associated University Hospital

Haematology Department
Tel: 0181 887 2428
Fax: 0181 807 9644

Sterling Way
London N18 1QX
0181 887 2000

Psychosocial factors influencing adherence to iron chelation therapy in thalassaemia

Information sheet

Psychosocial factors influencing adherence to iron chelation therapy in thalassaemia

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Name of Investigators: DR Chris Barker & Ms Rhiannon Cobner
Address: Sub-Department of Clinical Health Psychology,
University College London, WC1E 6BT
TEL: 0171-380-7897

Direct Line

Direct Fax

APPENDIX 3: CONSENT FORMS

After agreeing to participate in the study each patient was asked to complete a consent form thereby officially confirming their involvement. Consent forms for each hospital are included on the following two pages.

THALASSAEMIA & SICKLE CELL UNIT
DEPARTMENT OF HAEMATOLOGY
University College Hospital, Grafton Way, London WC1E 6AU
Direct Line: Dr. J.B. Porter 0171 380 9638
Fax: 0171 380 9911

Confidential **Pat. No.....**

Psychosocial factors influencing adherence to iron chelation therapy in thalassaemia

Written Informed consent

Have you read the information sheet about this study?.....YES/NO

Have you had an opportunity to ask questions and discuss this study?.....YES/NO

Have you received satisfactory answers to all your questions?.....YES/NO

Have you received enough information about the study?.....YES/NO

Who have you spoken to about the study?.....

Do you understand that you are free to withdraw from this study:
At any time?.....YES/NO
Without giving reason for withdrawing?.....YES/NO
Without affecting your future medical care?.....YES/NO

Do you agree to take part in this study?.....YES/NO

Patients Signature.....Date.....
Name of Patient.....

Investigators Signature.....Date.....
Nameof Investigator.....

Name of Investigators: DR Chris Barker & Ms Rhiannon Cobner
Address: Sub-Department of Clinical Health Psychology,
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Confidential Pat. No.....

Psychosocial factors influencing adherence to iron chelation therapy in thalassaemia

Written Informed consent

Have you read the information sheet about this study?.....YES/NO

Have you had an opportunity to ask questions and discuss this study?.....YES/NO

Have you received satisfactory answers to all your questions?.....YES/NO

Have you received enough information about the study?.....YES/NO

Who have you spoken to about the study?.....

Do you understand that you are free to withdraw from this study:
- At any time?.....YES/NO
- Without giving reason for withdrawing?.....YES/NO
- Without affecting your future medical care?.....YES/NO

Do you agree to take part in this study?.....YES/NO

Patients Signature.....Date.....
Name of Patient.....

Investigators Signature.....Date.....
Nameof Investigator.....

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APPENDIX 4: ADDITIONAL INFORMATION

During interview sessions the researcher asked the patients a series of questions, recording the results on the information sheets below.

Psychosocial factors influencing adherence to iron chelation therapy in patients with thalassaemia.

Demographic, medical and adherence characteristics.

DEMOGRAPHIC:

1. **Age:** _____.
2. **Gender:** *Male / Female*
3. **Marital Status:** *Single / In relationship*
4. **Ethnicity:** _____.
5. **Education post 16 ?**

Details _____.

6. **Current Occupation** (paid or unpaid) if any: _____.

(If currently unemployed please state previous occupation if any) _____.
_____.

MEDICAL:

1. **Does anybody else in the family have thalassaemia ?** *Yes / No*

Health status of family member: *Poor* *Moderate* *Good* *Other:*

2. **Frequency of blood transfusions:** _____.
3. **Age at diagnosis of thalassaemia:** _____.

4. **Previous medical complications related to iron overload:** _____.
   _____.
   _____.
5. **Method of taking desferal:** *Syringe Driver or Disposable Balloon Pump*
   Subcutaneous or Intravenous
6. **Recommended dosage of desferal per week** (include frequency and duration): _____.
7. **Current ferritin level** (patient report): _____.

ADHERENCE

1. **The number of times over the past 4 weeks the patient has completely failed to take their desferal:** _____.
   Reason: _____.
   _____.
   _____.
   _____.
2. **The number of times over the past 4 weeks the patient has started to take desferal but stopped before the recommended duration**. (Include the number of times and total estimated hours missed): _____.
   Reason: _____.
   _____.
   _____.
   _____.

The following information was gathered from the patients notes:

1. **Current ferritin level:** _____.
2. **The number of times a week the patient was advised to take desferal.** _____.
3. **The recommended duration of each dose of desferal.** _____.

APPENDIX 5: QUESTIONNAIRE

The following questionnaire was given to all participants in the study.

Psychosocial factors influencing adherence to iron chelation therapy in patients with thalassaemia

This study aims to try and identify reasons why people may at times have difficulty taking desferal. If we can get a better idea about what sort of things make it difficult to take, then we can try and find better ways to help people have the best treatment.

Please complete the following questionnaire. All of the answers you give will be confidential. There is no need to think too long about your answers - we are interested in your immediate response. There are no right or wrong answers. If you do not understand any of the questions then please ask Rhiannon Cobner who will explain. Please try to answer all of the questions.

In this set of questions please respond by circling a number from 1-5 on the scale next to the items which you feel best describes your response

1. I have a hard time adjusting to the limitations of my illness

Strongly Agree	*1*	*2*	*3*	*4*	*5*	*Strongly Disagree*

2. Because of my health, I miss the things I like to do most

Strongly Agree	*1*	*2*	*3*	*4*	*5*	*Strongly Disagree*

3. My illness makes me feel useless at times

Strongly Agree	*1*	*2*	*3*	*4*	*5*	*Strongly Disagree*

4. Health problems make me more dependent on others than I want to be

Strongly Agree	*1*	*2*	*3*	*4*	*5*	*Strongly Disagree*

5. My illness makes me a burden on my family and friends

Strongly Agree	*1*	*2*	*3*	*4*	*5*	*Strongly Disagree*

6. My health does not make me feel inadequate

Strongly Agree	*1*	*2*	*3*	*4*	*5*	*Strongly Disagree*

7. I will never be self sufficient enough to make me happy

Strongly Agree	*1*	*2*	*3*	*4*	*5*	*Strongly Disagree*

8. I think people are often uncomfortable around me because of my illness

Strongly Agree	*1*	*2*	*3*	*4*	*5*	*Strongly Disagree*

Please read this carefully.

We would like to know if you have had any medical complaints, and how you health has been in general over the past few weeks. Please answer all the questions on the following pages by circling the answer which you think most nearly applies to you. Remember that we want to know about recent complaints, not those that you had in the past.

Have you recently:

1.	Been feeling perfectly well	*Better than usual*	*Same as usual*	*Worse than usual*	*Much worse than usual*
2.	Been feeling in need of a good tonic?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
3.	Been feeling run down and out of sorts?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
4.	Felt that you are ill?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
5.	Been getting any pains in your head?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
6.	Been getting a feeling of tightness or pressure in you head?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
7.	Been having hot or cold spells?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
8.	Lost much sleep over worry?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
9.	Had difficulty in staying asleep once you are asleep?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
10.	Felt constantly under strain?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
11.	Been getting edgy and bad tempered?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
12.	Been getting scared or panicky for no good reason at all?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
13.	Found everything getting on top of you?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*

14. Been feeling nervous and strung up all the time?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
15. Been managing to keep yourself busy and occupied?	*More so than usual*	*Same as usual*	*Rather less than usual*	*Much less than usual*
16. Been taking longer over the things you do?	*Quicker than usual*	*Same as usual*	*Longer than usual*	*Much longer than usual*
17. Felt on the whole you were doing things well?	*Better than usual*	*About the same*	*Less well than usual*	*Much less well*
18. Been satisfied with the way you've carried out tasks?	*More satisfied*	*About the same*	*Less satisfied*	*Much less satisfied*
19. Felt that you are playing a useful part in things?	*More so than usual*	*Same as usual*	*Less than usual*	*Much less than usual*
20. Felt capable of making decisions about things?	*More so than usual*	*Same as usual*	*Less than usual*	*Much less than usual*
21. Been able to enjoy your normal day-to-day activities?	*More so than usual*	*Same as usual*	*Less than usual*	*Much less than usual*
22. Been thinking of yourself as a worthless person?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
23. Felt that life is entirely hopeless?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
24. Felt that life isn't worth living?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
25. Thought of the possibility that you might do away with yourself?	*Definitely not*	*I don't think so*	*Has crossed my mind*	*Definitely have*
26. Found that at times you couldn't do anything because your nerves were too bad?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
27. Found yourself wishing you were dead and away from it all?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
28. Found that the idea of taking your own life kept coming to you?	*Definitely not*	*I don't think so*	*Has crossed my mind*	*Definitely have*

The next set of questions ask about people who provide you with help or support. Each question has two parts. For the first part, list all the people you know, excluding yourself, whom you can count on for help or support in the manner described. Give each persons initials and their relationship to you (see example). Do not list more than one person next to each of the numbers beneath each question. Do not list more than nine people per question.

For the second part, using the scale below, circle how satisfied you are with the overall support you have.

6	*5*	*4*	*3*	*2*	*1*
Very satisfied	*Fairly satisfied*	*A little satisfied*	*A little dissatisfied*	*Fairly dissatisfied*	*Very dissatisfied*

If you have no support for a question, tick the words 'NO one', but still rate your level of satisfaction. The example below has been completed to help you.

Example,

Who do you know whom you can trust with information that could get you into trouble?

(a) No one

1) *DO (boyfriend)*__	4) _____	7) _____
2) *EB (friend)* ____	5) _____	8) _____
3) *HM (friend)*____	6) _____	9) _____

(b) How satisfied

6 (5) *4* *3* *2* *1*

---

1. Whom can you count on to distract you from your worries when you feel under stress?

(a) No one

1) _____	4) _____	7) _____
2) _____	5) _____	8) _____
3) _____	6) _____	9) _____

(b) How satisfied

6 *5* *4* *3* *2* *1*

2. Whom can you really count on to help you feel more relaxed when you are under pressure or tense?

(a) No one

1) _____	4) _____	7) _____
2) _____	5) _____	8) _____
3) _____	6) _____	9) _____

(b) How satisfied

6 5 4 3 2 1

3. Who accepts you totally, including both your best and your worst points?

(a) No one

1) _____	4) _____	7) _____
2) _____	5) _____	8) _____
3) _____	6) _____	9) _____

(b) How satisfied

6 5 4 3 2 1

4. Whom can you really count on to care about you regardless of what is happening to you?

(a) No one

1) _____	4) _____	7) _____
2) _____	5) _____	8) _____
3) _____	6) _____	9) _____

(b) How satisfied

6 5 4 3 2 1

5. Whom can you really count on to help you feel better when you are feeling generally down in the dumps?

(a) No one

1) _____	4) _____	7) _____
2) _____	5) _____	8) _____
3) _____	6) _____	9) _____

(b) How satisfied

6 5 4 3 2 1

6. Whom can you count on to console you when you are very upset?

(a) No one

1) _____	4) _____	7) _____
2) _____	5) _____	8) _____
3) _____	6) _____	9) _____

(b) How satisfied

6 *5* *4* *3* *2* *1*

For each item please choose a number from 1-6 from the scale which you feel best describes your response.

SCALE:

Strongly Agree	*1*	*2*	*3*	*4*	*5*	*6*	*Strongly Disagree*

1. Being happy with myself is more important than having others approve of me ____
2. For me, life has been a continuous process of learning, changing and growth. ____
3. I am an active person in carrying out the plans I have set for myself ____
4. I am good at juggling my time so that I can fit everything in that needs to be done ____
5. I am not afraid to voice my opinions, even when they are in opposition to the opinions of most people ____
6. I am not interested in activities that will expand my horizons. ____
7. I am quite good at managing the many responsibilities of my daily life ____
8. I do not enjoy being in new situations that require me to change my old familiar ways of doing things ____
9. I do not fit very well with the people and the community around me ____
10. I don't have a good sense of what it is I'm trying to accomplish in life ____
11. I don't have many people who want to listen when I talk ____
12. I don't want to try new ways of doing things - my life is fine the way it is ____
13. I enjoy making plans for the future and working to make them a reality ____
14. I enjoy personal and mutual conversations with family members or friends ____
15. I feel like many of the people I know have gotten more out of life than I have ____
16. I feel overwhelmed by my responsibilities ____
17. I gave up trying to make big improvements or changes in my life a long time ago. ____
18. I generally do a good job of taking care of my personal finances and affairs ____
19. I have been able to build a home and a lifestyle for myself that is much to my liking ____
20. I have confidence in my own opinions, even if they are contrary to the general consensus ____
21. I have difficulty arranging my life in a way that is satisfying to me ____

22. I have not experienced many warm and trusting relationships with others _____
23. I have the sense that I have developed a lot as a person over time _____
24. I judge myself by what I think is important, not by the values of what others think is important _____
25. I know that I can trust my friends, and they know they can trust me _____
26. I like most aspects of my personality _____
27. I live life one day at a time and don't really think about the future _____
28. I made some mistakes in the past, but I feel that all in all things have worked out for the best _____
29. I often change my mind about decisions if my friends or family disagree _____
30. I often feel lonely because I have few close friends with whom to share my concerns _____
31. I sometimes feel as if I've done all there is to do in life _____
32. I tend to be influenced by people with strong opinions _____
33. I tend to focus on the present, because the future nearly always brings me problems _____
34. I tend to worry about what other people think of me _____
35. I think it is important to have new experiences that challenge how you think about yourself and the world. _____
36. I used to set goals for myself, but now that seems like a waste of time _____
37. In general I feel confident and positive about myself _____
38. In general, I feel I am in charge of the situation in which I live _____
39. In many ways I feel disappointed about my achievements in life _____
40. It seems to me that most other people have more friends than I do _____
41. It's difficult for me to voice my own opinions on controversial matters _____
42. Maintaining close relationships has been difficult and frustrating for me _____
43. Most people see me as loving and affectionate _____
44. My attitude about myself is probably not as positive as most people feel about themselves _____
45. My daily activities often seem trivial and unimportant to me _____
46. My decisions are not usually influenced by what everyone else is doing _____
47. People would describe me as a giving person, willing to share my time with others _____
48. Some people wander aimlessly through life, but I am not one of them _____

49. The demands of everyday life get me down ____

50. The past has had its ups and downs, but in general, I wouldn't want to change it. ____

51. There is truth to the saying that you can't teach an old dog new tricks ____

52. When I compare myself to friends and acquaintances, it makes me feel good about who I am ____

53. When I look at the story of my life, I am pleased with how things have turned out. ____

54. When I think about it, I haven't really improved much as a person over the years ____

For each item please circle the number that best describes the extent to which your disagree or agree with the statement. Only circle one number per item.

1 = Strongly disagree (SD)
2 = Moderately disagree (MD)
3 = Slightly disagree (D)
4 = Slightly agree (A)
5 = Moderately agree (MA)
6 = Strongly agree (SA)

	SD	MD	D	A	MA	SA
1. If my thalassaemia worsens, it is my own behaviour which determines how soon I feel better again	1	2	3	4	5	6
2. As to my thalassaemia, what will be will be	1	2	3	4	5	6
3. If I see my doctor regularly, I am less likely to have problems with my thalassaemia	1	2	3	4	5	6
4. Most things that affect my thalassaemia happen to me by chance	1	2	3	4	5	6
5. Whenever my thalassaemia worsens, I should consult a medically trained professional	1	2	3	4	5	6
6. I am directly responsible for my thalassaemia getting better or worse	1	2	3	4	5	6
7. Other people play a big role in whether my condition improves, stays the same, or gets worse	1	2	3	4	5	6
8. Whatever goes wrong with my thalassaemia is my fault	1	2	3	4	5	6
9. Luck plays a big part in determining how my thalassaemia improves	1	2	3	4	5	6
10. In order for my thalassaemia to improve, it is up to other people to see that the right things happen	1	2	3	4	5	6
11. Whatever improvement occurs with my thalassaemia is largely a matter of good fortune	1	2	3	4	5	6

12. The main thing which affects my thalassaemia is largely a matter of good fortune	1	2	3	4	5	6
13. I deserve the credit when my thalassaemia improves and the blame when it gets worse	1	2	3	4	5	6
14. Following doctors orders to the letter is the best way to keep my thalassaemia from getting worse	1	2	3	4	5	6
15. If my thalassaemia worsens, its a matter of fate	1	2	3	4	5	6
16. If I am lucky, my thalassaemia will get better	1	2	3	4	5	6
17. If my condition takes a turn for the worse, it is because I have not been taking proper care of myself	1	2	3	4	5	6
18. The type of help I receive from other people determines how soon my condition improves	1	2	3	4	5	6

Indicate the extent to which you agree with the four following statements using the scale below. Write the appropriate number in the blank space to the right of each statement

Strongly agree		*Moderately agree*		*Moderately disagree*		*Strongly disagree*
1	*2*	*3*	*4*	*5*	*6*	*7*

1. There is nothing more important than good health
2. Good health is only of minor importance in life
3. If you don't have your health you don't have anything
4. There are things I care about more than my health

For each item please circle the number that best describes the extent to which your disagree or agree with the statement. Only circle one number per item.

	Not at all true	*Barely true*	*Moderately true*	*Exactly true*
1. I can always manage to solve difficult problems if I try hard enough.	*1*	*2*	*3*	*4*
2. If someone opposes me, I can find means and ways to get what I want.	*1*	*2*	*3*	*4*
3. It is easy for me to stick to my aims and accomplish my goals.	*1*	*2*	*3*	*4*
4. I am confident that I could deal efficiently with unexpected events.	*1*	*2*	*3*	*4*
5. Thanks to my resourcefulness, I know how to handle unforeseen situations.	*1*	*2*	*3*	*4*
6. I can solve most problems if I invest the necessary effort.	*1*	*2*	*3*	*4*
7. I remain calm when facing difficulties because I can rely on my coping abilities.	*1*	*2*	*3*	*4*
8. When I am confronted with a problem, I can usually find several solutions.	*1*	*2*	*3*	*4*
9. If I am in a bind, I can usually think of something to do.	*1*	*2*	*3*	*4*
10. No matter what comes my way, I'm usually able to handle it	*1*	*2*	*3*	*4*

APPENDIX 6: DOCTOR REPORT

The following forms were completed by the doctors after their patients had agreed to participate in the study.

Psychosocial factors influencing adherence to iron chelation therapy in patients with thalassaemia

Patient Adherence Form
Doctor Report

Please complete the following information for each of the patients listed on the sheet. We are interested in their levels of adherence to desferal in the four weeks prior to today. If you have not seen the patient very recently then please estimate their levels of adherence over the past 4 weeks based on your previous experience of them. If you don't know exactly what their current adherence status is, then please give your nearest estimate.

Please state in the relevant columns:

A. The date of your last contact with the patient

B. How many times in the past 4 weeks the patient has taken desferal but for less than the recommended duration.

C. The total number of hours missed in the past 4 weeks as a result of taking desferal for less than the recommended duration

D. How many times in the past 4 weeks the patient has failed to take desferal completely.

E. Recommended dose (days per week and hours per dose)

F. Any relevant comments

Patient	Times patient has failed to take desferal for as long as is recommended in past 4 weeks.	Total number of hours missed as a result of failing to take desferal for as long as is recommended in the past 4 weeks.	Number of times patient has completely failed to take desferal in past 4 weeks.	Recommended dose (times per week and hours per dose)	Comments

APPENDIX 7: NURSE REPORT

The following forms were completed by the nurses after their patients had agreed to participate in the study

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Psychosocial factors influencing adherence to iron chelation therapy in patients with thalassaemia

Patient Adherence Form
Nurse Report

Please complete the following information for each of the patients listed on the attached sheet. We are interested in their levels of adherence to desferal in the four weeks prior to today. If you have not seen the patient very recently then please estimate their levels of adherence over the past 4 weeks based on your previous experience of them. If you don't know exactly what their current adherence status is, then please give your nearest estimate.

Please state in the relevant columns:

A. The date of your last contact with the patient

B. How many times in the **past 4 weeks** the patient has taken desferal but for less than the recommended duration.

C. The total number of hours missed in the **past 4 weeks** as a result of taking desferal for less than the recommended duration

D. How many times in the past **4 weeks** the patient has failed to take desferal completely.

E. Any relevant comments

Patient	Times patient has failed to take desferal for as long as is recommended in past 4 weeks.	Total number of hours missed as a result of failing to take desferal for as long as is recommended in the past 4 weeks.	Number of times patient has completely failed to take desferal in past 4 weeks.	Comments

APPENDIX 8: INTERVIEW PROTOCOL

The following questions were used by the researcher as a framework for the semi-structured interview.

Psychosocial factors influencing adherence to iron chelation therapy in patients with thalassaemia

Semi-structured interview protocol

Instructions to all Participants

"Thank you for completing the questionnaire. I would now like to ask you some questions about desferal and about the sorts of things that affect how easy or difficult it is for you to take it. Again, it is important to remember that there are no right or wrong answers. The interview will be recorded, but as before, all of your answers will be confidential."

1. Can you tell me a little about what it is like for you, having to take desferal, how it makes you feel?

2. What factors influence whether or not you take desferal?

3. Are you currently having any difficulties taking your desferal?

4. Have you experienced any difficulties taking desferal in the past?

5. Do you envisage any difficulties in the future?

6. Has anyone said anything to you about taking desferal that has been particularly helpful or unhelpful?

7. Is there anything that there health care staff could do to help people better manage to take their desferal?