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**Assessing the effect of Addison's disease on patient quality of life
within the South African context**

by

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Supervised by Professor Mark Solms

Neuropsychology Masters Degree

Department of Psychology

University of Cape Town

2008

COMPULSORY DECLARATION

This work has not been previously submitted in whole, or in part, for the award of any degree. It is my own work. Each significant contribution to, and quotation in, this dissertation from the work, or works, of other people has been attributed, and has been cited and referenced.

Signature:

Date: 28, 10, 2008

Signed by candidate

Acknowledgements

This project would not have been possible without the support of my supervisor. Many thanks to Professor Mark Solms, who read my numerous revisions and helped to give this project structure and coherence.

I owe a debt of gratitude to Dr Oz Omeen for acting as an informal consultant and for providing financial support for my research.

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Thanks to Frank De Gouveia who compassionately helped for editing.

Abstract

Addison's disease (AD) is a chronic, lifelong disorder caused by adrenal gland insufficiency, and it requires lifelong daily therapy with cortisol replacement, which is a steroid hormone. Since cortisol is a stress hormone, one can expect fatigue, sleep disturbance, depression, anxiety and a generally low quality of life (QOL). Studies have shown that cortisol replacement therapy has a great effect on the health perception, general well-being and QOL of patients with AD.

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As studies of the disease to date have been conducted mostly in Europe, it is necessary to establish how applicable they are to South Africa, bearing in mind that South Africa is a developing country with different needs. Specifically, answers need to be found to the question of whether we can apply the European findings and their treatment packages to South African patients and whether they are able to have the same QOL as the Europeans. This study finds that our patients do indeed have the same QOL, and that we should therefore be able to apply the European findings here. Measuring QOL alone, however, gives us very general information which is not sufficient for our study. The second aim of this research is to compare different aspects of QOL in AD, as this has not been researched before. This knowledge should help clinicians to recognise QOL impairment better, which will enable modifiable risk factors to be adjusted with early intervention. (For example, psychological impairment can be reduced with counselling.) This study also finds that some AD patients who suffer a combination of other autoimmune diseases have a lower QOL. The main instrument used for this research was the Rotterdam QOL questionnaire. We also used the Beck depression scale, and the Spielberger anxiety inventory. Our sample consisted of 100 patients with a confirmed diagnosis of AD from all around South Africa, and a control group who did not have AD or any other autoimmune diseases, matched for age and gender. This study was a double blind study.

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CHAPTER ONE

Literature review

Introduction

In 1855, in London, Thomas Addison for the first time described what is now called Addison's disease. This is a lifelong, chronic disease characterised by lack of cortisol and aldosterone which are two important steroid hormones made by the adrenal cortex. Cortisol mobilises nutrients in the body, modifies the body's response to inflammation, stimulates the liver to raise the blood sugar and helps to control the amount of water in the body. Aldosterone regulates salt and water levels which affect the blood volume and blood pressure. Cortisol production is regulated by another hormone, adrenocorticotrophic hormone (ACTH) which is made in the pituitary gland. Classical AD results from the loss of cortisol and aldosterone secretion due to the total or partial destruction of both the adrenal glands. This condition is also called primary adrenal insufficiency. Secondary adrenal insufficiency similarly causes a loss of cortisol secretion, but this is a distinct entity. In this case the ACTH is deficient, resulting in insufficient cortisol production, although aldosterone may remain adequate (Shomon, 2002).

In about 70 percent of cases Addison's disease is an autoimmune condition. This means that the destruction is caused when the body's own immune system attacks the adrenal cortex as if it were a foreign body. The cortex becomes inflamed and the outer layer shrinks. The other 30 percent of cases are caused by infections (such as tuberculosis), tumours and other diseases of the glands (Shomon, 2002).

Addison's disease symptoms

Primary insufficiency

The symptoms of AD do not normally appear until over 90 percent of the adrenal cortex has already been destroyed, so that very little adrenal capacity is left. This can take any time from months to years. Symptoms of the disease, once advanced,

include severe fatigue and weakness, loss of weight, increased skin pigmentation, a feeling of faintness, low blood pressure, nausea, vomiting, salt cravings and painful muscles and joints. Because of the rather non-specific nature of these symptoms and their slow development, they are often missed or ignored until, for example, a relatively minor infection leads to an abnormally long convalescence which prompts an investigation. Frequently, it is not until an Addisonian crisis is precipitated that attention is turned to the adrenals (Colditz, 2001).

Secondary insufficiency

Secondary adrenal insufficiency is sometimes described as “Addison’s”, although it has a very different cause. It typically occurs when a pituitary tumour (such as an adenoma) forms. The pituitary gland is a very important component of our endocrine system. It lies below the optic chiasm at the base of the brain. It releases hormones in the thyroid, adrenals and gonads. The anterior pituitary produces six hormones: thyroid-stimulating hormone, growth hormone, Adernocortoctropine, luteinising, prolactine and follicle-stimulating hormone. Pituitary active adenoma is caused by the disruption of the hypothalamic inhibitory hormone, dopamine, which leads to excess secretion of prolactine (Johnson and Lightman, 1996).

In secondary adrenal insufficiency, the pituitary gland no longer triggers the adrenals to produce cortisol, and dehydroepiandrosterone (DHEA) production is also believed to decline. In most cases of secondary adrenal insufficiency, however, aldosterone is still produced, as its production is stimulated by other hormonal regulatory systems. The pituitary hormone which triggers cortisol production is called ACTH. It is responsible for the skin hyperpigmentation found in primary Addison’s. People with secondary adrenal failure do not suffer the hyperpigmentation found in primary Addison’s, because their ACTH levels are declining (Colditz, 2001).

Long-term use of high doses of steroid drugs to treat other illnesses (for example, high-dose prednisone for bowel disease, emphysema or asthma) can also cause temporary or permanent loss of adrenal function. This is often referred to as secondary adrenal suppression.

Weakness and weight loss of 1 to 15 kg are universal features of AD in adults. The symptoms are: nausea, vomiting, diffuse abdominal pain (present in approximately 90 percent of patients and usually indicating an impending Addisonian crisis), diarrhoea (in approximately 20 percent of patients), mood disturbances (including depression, and irritability), and decreased concentration (Shomon, 2002).

What is cortisol?

Adrenal glands are located above the kidneys and normally produce cortisol. It belongs to a class of hormones called glucocorticoids, which affect almost every organ and tissue in the body. The major function and responsibility of cortisol are to respond to stress (Talbot, 2002). Cortisol is normally present in the body at higher levels in the morning, and is at its lowest level at night. Although stress isn't the only reason that cortisol is produced, it has been termed "the stress hormone" because it is also secreted at higher levels during the body's "fight or flight" response to stress, and it is responsible for several other stress-related changes in the body (Greenberg, 2006).

Among its other vital tasks, cortisol helps to maintain blood pressure and cardiovascular function; to slow down the immune system's inflammatory response; to balance the effects of insulin by breaking down sugar for energy; and to regulate the metabolism of proteins, carbohydrates, and fats. Cortisol is involved in the inflammatory response, provides a quick burst of energy in survival situation, heightens memory functions, provides a burst of increased immunity, lowers sensitivity to pain, and helps maintain homeostasis in the body (Talbot, 2002).

Although we regard cortisol as a very important hormone, it is necessary to consider the effects of having too high a dose of cortisol or over-replacement of cortisol. According to Greenberg (2006), it can have negative effects on the body; such as impaired cognitive performance, suppressed thyroid function, blood sugar imbalances (for instance, hyperglycaemia), decreased bone density, decreased muscle tissue, higher blood pressure and lowered immunity and inflammatory responses in the body; another consequence, increased abdominal fat, is associated with greater health problems than fat deposited in other areas of the body. Some of the problems

associated with increased stomach fat are heart attacks, strokes, the development of higher levels of “bad” cholesterol (LDL) and lower levels of “good” cholesterol (HDL), which can lead to further health problems.

Guided imagery, journaling, self-hypnosis, exercise, yoga, listening to music, breathing exercises and meditation are some useful methods to relax the body and mind that can assist the body to maintain healthy cortisol levels (Greenberg, 2006).

Treatment of Addison’s disease

Generally, the first step in the treatment of the disease is the replacement of the hormones cortisol and aldosterone. Hydrocortisone, which functions like both of these hormones, is often a good prescription. Further treatment includes a combination of glucocorticoids and mineral corticoids to compensate for the adrenal insufficiency. Hydrocortisone and fludrocortisone are also commonly prescribed. Higher doses of medication are usually required during childbirth, injury, surgery, dehydration, during severe stress and during serious infections. During stressful events, the patient may develop adrenal failure which is characteristic of an Addisonian crisis in which his or her body is not able to produce enough cortisol. If medication is not received, a serious drop in blood pressure can cause shock, which may in turn prove fatal.

Since patients with adrenal failure have lower sodium levels, it is necessary for them to supplement their diets with extra salt (sodium chloride), especially when weather conditions are hot and humid, or after heavy exercise. As AD sufferers retain potassium, they should avoid salt substitutes, which usually contain potassium chloride (Margiorios & Chrousos, 2001).

What is quality of life?

Quality of life (QOL) is a term that refers to people’s emotional, social and physical wellbeing, and their ability to function in the ordinary tasks of living (Bowling, 1992). Factors contributing to QOL include psychological state, physical function, social relationships and social roles (Bowling, 1992).

In 1984 the World Health Organization defined health as being not only the absence of disease and illness but also the presence of physical, mental, and social well-being (Rubin, 2000).

The importance of QOL is explained succinctly by the Northern Centre for Healthcare Research (1996) when they say that “quality of life is regarded as a subjective report of the patient’s experience of disease and treatment. Assessing quality of life is meant to enhance the insight into the consequences of the disease and its treatment, indicate groups of patients at risk for developing high levels of distress, and enable the comparison of the effectiveness of treatment and thus support decision making in clinical oncology.” QOL has different aspects, including; psychological, physical and daily activity aspects (De Haes, 1996).

Physical well-being

Physical well-being is probably the first component of health that comes to mind when considering QOL. According to Bowling (1992), physical well-being is defined in terms of a person’s functional activity for which performance has been assumed to reflect physical health, such as self care, mobility, lack of pain or the symptoms of any illness and activities (e.g. walking or climbing the stairs). In addition, sleep, nutrition and sexual health are considered in the physical health category (Donatelle, 2006). Accordingly, physical well-being is described when we meet the following terms:

1. We are free of pain
2. Our basic needs for food, water, sleep and shelter are met
3. We have enough energy to accomplish our daily tasks and fulfil our recreational desires
4. Our brains can maintain sufficient alertness and focus to enable our mental processes to function well
5. We are able to achieve satisfying sexual experiences, within our own frame of reference.

Psychological well-being

Psychological well-being is a positive state of mind engendering a sense of well-being that enables a person to function effectively within society. Individuals who have good mental health are well-adjusted, are able to relate well to others, and basically feel satisfied with themselves and their role in society (Barry, 2002). Moods, thoughts, feeling, self-control and life satisfaction – feeling satisfied with what we have achieved in life – are necessary to measure states of psychological well-being (Bowling, 1992).

In 2004 Brim, broke down the areas which contribute to psychological well-being, into:

Self-acceptance: having positive thoughts about yourself; acknowledging and accepting multiple aspects of self; feeling positive about your past life; and being able to say, "when I look at the story of my life, I am pleased with how things have turned out so far"(Brim, 2004).

Personal growth: having feelings of continued development and potential and being open to new experiences; feeling increasingly knowledgeable and effective; and being able to say, "for me, life has been a continuous process of learning, changing, and growth."

Purpose in life: having goals and a sense of direction in life; feeling that both present and past experiences are meaningful.

Environmental mastery: feeling capable of managing a complex environment; choosing or creating personally appropriate contexts; and being able to say, "I am good at managing the responsibilities of life."

Autonomy: being self-determining, independent, and regulating your behaviour internally; resisting social pressures to think and act in certain ways; evaluating yourself by personal standards; and being able to say, "I have confidence in my own opinions, even if they are different from the way most other people think."

Positive relations with others: having warm, enjoyable, trusting relationships; being concerned about others' welfare and conditions; being capable of strong empathy, affection and intimacy; understanding the give-and-take of human relationships, and being able to say, "people would describe me as a giving person, willing to share my time with others" (Brim, 2004).

Activities of Daily Living

Activities of Daily Living (ADL) is one of the important components of a QOL measurement as it is designed to describe, for clinical purposes, the basic tasks of everyday life, such as eating, bathing, dressing, toileting, transferring (walking) and continence (Bowling, 1992). When people are unable to perform these activities, they need help, either from other human beings or from mechanical devices, or both.

Although persons of all ages may have problems performing the functions of ADL, the prevalence rates are much higher for the elderly. Within the elderly population, ADL prevalence rates rise steeply with advancing age and are especially high for persons aged 85 and over (Rivlin and Wiener et al, 1988). However, the ADL in this research does not only measure the normal daily activities such as eating, bathing, dressing, toileting and transferring (walking), but it also measures the daily performance at work (is the patient able to work according to his or her best ability?), and in society and social life (does the patient have the same quality of social life as he / she used to have?).

Overall quality of life

The link between physical well-being and emotions has been recognised by the medical field for centuries. A holistic approach called Psychoneuroimmunology focuses on well-being that considers body, mind and spirit in connection with illness and disability. According to Sheinfeld & Arnold (2006), it is well documented that high levels of stress can have a deleterious effect on health, well-being and the functioning of the immune system. Conditions ranging from depression and low self-esteem, to nervous breakdowns and burnout, and to high levels of stress have been shown to undermine immune system functioning, making individuals more susceptible to a host of illnesses. Therefore when we assess QOL, even though we assess each component to see how the illness has affected it, we need to have an overall assessment as well, because all these components are related to each other.

The result of a complete overview on QOL and its components shows that when one measures a QOL it is important to clarify what the results are both in general and in

detail. This is because one can then discern which aspect of the QOL is specifically impaired and needs to be improved.

Because the treatment of AD is a lifelong course of hormone replacement therapy there have been many articles focusing on patients' QOL. None of these have, however, specifically compared the components of QOL to find out which aspect of QOL is more impaired in AD patients. This research argues that it is important to adjust patients' treatment packages according to their need and based on the South African context. There are of course many difficulties due to the lack of resources in South Africa. The result is that a large number of the patient population often cannot afford medical resources, especially as most of them do not have medical aid.

Many patients are members of the casual wage system and their payment is per hour, making it difficult for them to take any time off work. As a result, it is difficult for them to consult with physicians on a regular basis. In addition, the multicultural nature of our society, the high rate of crime and the average South African's perception that society is unsafe contribute to the argument that we must adjust our treatment packages to patients' specific needs. The level of stress and anxiety is much higher than in those patients who live in European societies with lower levels of crime and different social stressors. This research examines two questions: first, if we get the same result as the European research, how do we know which aspects of QOL in South African and European patients with AD are more or less impaired? Second, do the QOL component impairments of South African patients differ from those of European patients?

Overview of psychological and clinical literature

Cooper (1991) conducted one of the earliest studies on the relationship between endocrine disease and psychological distress. As he had previously documented the link between other autoimmune diseases and psychological problems, we decided to use his study as a point of departure, especially considering that we wanted to investigate whether the coexistence or co-morbidity of other autoimmune diseases aggravates the QOL in AD patients.

Cooper emphasised the role and existence of “psychic traumas” prevalent in pituitary disease in his research. He concluded that patients suffering from Cushing’s syndrome experienced stressful and uncontrollable events as significantly more “negative” and “independent” than his control groups. His main conclusion was that major depressive disorders are a severe and life-threatening complication that can occur in concurrence with endocrine disorders such as Cushing’s syndrome, Addison’s disease, hyperthyroidism, hypothyroidism and hyperprolactinemic amenorrhea. Other psychiatric symptoms, ranging from anxiety to psychotic disturbances and cognitive impairment may be present, though to a lesser degree than depression.

Cooper’s data show that the occurrence of an organic affective syndrome in endocrine disease may not simply be the consequence of increased hormonal levels, but the expression of a more general suprapituitary derangement. He emphasised that a depressed mood may have a profound influence on the AD sufferer’s QOL (including his or her interactions with others) and on how he or she experiences the endocrine disease. He postulated a treatment regime primarily directed at the physical condition as more effective than antidepressant drugs in organic affective syndromes. This is supported by the effect of steroid synthesis inhibitors on depression in patients with Cushing’s syndrome and by the action of antithyroid drugs on anxiety in patients with hyperthyroidism.

When comparing the QOL components, our research results showed how our AD patients’ treatment regime had a more significant effect on physical condition than psychological conditions or their daily activities.

It is interesting to note that none of the researchers after Cooper followed his guidelines. In another study following this one, Cooper measured depression and the psychological aspect of QOL only. This is limiting as it ignores the fact that QOL is also affected by physical impairment and ADL levels.

Cooper (1991) attributed the occurrence of an organic affective syndrome in endocrine disease to factors other than increased hormonal levels. However, other researchers took a different view. Riddle *et al.* (1993) initiated a study into the QOL of patients with AD. Their objective was to examine the effect of different doses of

cortisol replacements on the perception of health and general well-being in patients with primary adrenocortical failure. For research purposes, they placed 14 adults (eight females and six males, in a randomised double-blind cross-over design) into a treatment experiment in which all of the patients were given three regimes of cortisol for one week each (regime I: 20 mg 2 times a day; regime II: 30 mg 2 times a day; regime III: placebo in the morning and 30mg cortisol in the evening). They then tracked the patients' progress over three weeks and gathered data from three questionnaires administered at the end of the period to assess QOL (Addison's questionnaire, Basler Befindlichkeits-skala and Beschwerde-liste).

The results revealed that general well-being in terms of the patients' subjective contentment levels was best established during regime I in 64 percent of the patients; 29 percent in regime II and 14 percent in regime III. The differences between regimes II and III were significant, and the conclusion reached was that QOL in Addison's patients is influenced by the dose of cortisol replacement therapy (i.e. regime I, which was the 20 ml cortisol, which had a better impact on patients' QOL than regime II, which was 30 ml cortisol). However, the study did not examine which aspect of QOL improved most, the result being that it is difficult to determine which aspect is most defective. This finding is applicable to the South African context, as most South Africans experience generally high levels of anxiety and stress which necessitate different dosages of cortisol replacement therapy. A specific study would need to be developed, though, to get more detailed information.

Riddle (1993) and his colleagues carried out a second study that linked the levels of hormones in the body to low QOL in AD patients. Their research documented the QOL of 80 AD patients who were on long-standing replacement therapy with cortisone acetate and fludrocortisone. The patients demonstrated high levels of impairment in terms of their physical QOL component. Specifically, they reported a lowered perception of their general health, decreased vitality and increased fatigue, with the latter suggesting a substantial lack of energy as the most prominent clinical problem. The authors also found significant impairment in the QOL in women, but the reasons for this were not clear as they had not clarified which aspects of QOL were most impaired (psychological, physical or ADL levels). This information is necessary to enable clinicians to offer improved treatment programmes

that detail expected experiences and provide more flexibility to modify components when patients are in distress.

Hunt *et al* (2000) undertook a similar project, focusing on the improvement in mood, fatigue, well-being and sexual function after DHEAS replacement in AD patients. In their trial, which was conducted over 12 months, they examined 106 AD patients (44 males, 62 females) with a median age of six, using a randomised double-blind, parallel, placebo-controlled study. They concluded that Addison's patients are at risk from osteoporosis and that DHEA treatment has been shown to increase bone marrow disease in postmenopausal women and the aged. These parameters were measured by dual energy x-ray absorptiometry (DEXA) as additional major study end points. They concluded that a dose of 50 mg DHEA balances this deficiency, and allows for significant improvement in some aspects of psychological function. Using a well-known psychometric instrument, they found significant improvement in patients' self-esteem with a tendency toward general improvement in well-being. Their study also revealed significant changes in mood and fatigue after DHEA treatment. One commendable aspect of this research is that it considered the psychological and physical aspects of QOL. However, other aspects of QOL, such as ADL and overall QOL were not examined.

Li Voon Chong *et al.* (2001) questioned whether hydrocortisone replacement dosage could influence intraocular pressure in patients with primary and secondary hypocortisolism. This question is significant, as patients taking cortisol on a daily basis are at risk of ocular hypertension and glaucoma, which would also affect their general well-being and health. Li Voon Chong studied 17 patients aged 24 to 58 years with a mean of 42.7 years, and 20 control subjects aged 20 to 59 years, with a mean of 38.7 years. His results showed that

Intraocular pressures during the day are influenced by the morning hydrocortisone replacement dosage with significantly higher intraocular pressure levels in the early afternoon following 20 mg compared with 10 mg. A morning hydrocortisone dose of 10 mg leads to a greater physiological intraocular pressure profile during the day. This data supports the view that a daily replacement dose of 30 mg hydrocortisone may be excessive Li Voon Chong *et al.* (2001).

Riddle (1993) and Hunt (2000) attributed low QOL to hormone replacement therapy, while Li Voon Chong *et al.* (2001) found that low QOL could be linked to daily doses of hydrocortisone replacement.

Lovas (2002) also initiated a study to ascertain the correlation between the illness and the medication. He examined subjective reports given by 79 AD patients with confirmed primary adrenal failure to research the issue. As he wanted to emphasise the importance of fatigue, he included a separate questionnaire on this subject. He then compared the results of the survey with normative data from the general population and concluded that general health and the perception of vitality were most consistently impaired in patients with AD.

Lovas also found that the scores on physical and social functioning, and physical and emotional roles were low in female patients. However, it must be noted that these results were confined to patients with autoimmune polyendocrine syndromes who displayed lower scores than patients with solitary AD. In this study, fatigue levels were higher than normal for men and women; while the working disability between the ages of 18 and 67 years was 26 percent, compared with 10 percent in the corresponding general population. This trend increased with age and was higher in sub-groups with concomitant endocrine diseases. Most subjective health parameters were lower among the disabled compared to the employed patients (Lovas, 2002). His study showed that female patients reported reduced physical functioning, which might in turn have been due to adrenal androgen depletion. Mental health seemed to have been more influenced by concomitant endocrine diseases, so mental fatigue might be a specific feature in adrenal failure. Lovas' study is limited by the fact that in emphasising the physical aspect of QOL it excludes the psychological aspect and ADL. Overall QOL is also not examined in this study. One possibility, which needs to be further examined, is that psychological impairment may also have an interrelationship with low physical impairment conditions (such as fatigue).

Since cortisol is a stress hormone, it can affect patients' quality of sleep, which in turn affects their QOL on a daily basis. According to Lovas (2003), most hormones show circadian variation regulated by hypothalamic pacemaker cells. Apart from the presence and functioning of melatonin, a hormonal feedback mechanism on the

timing of the sleep-wake cycle has not yet been explained. Many associations have been described between the hypothalamic-pituitary-adrenal (HPA) axis and sleep architecture. The balance between growth hormone-releasing hormone (GHRH) and Corticotropin-releasing hormone (CRH) appears to play a key role in sleep regulation. CRH inhibits slow-wave sleep (SWS), which is a major component of the restorative non-rapid eye movement (NREM) sleep. ACTH primarily affects sleep through its effects on cortisol secretion. Cortisol enhances SWS possibly by the reaction inhibition of CRH. High levels of glucocorticoids inhibit rapid eye movement (REM) sleep (Lovas, 2003). However, low cortisol levels also interfere with normal REM sleep in patients with adrenal insufficiency. Currently, the adrenal androgen precursor DHEA is under scrutiny for its effects on neurons, and its possible influence on sleep is also being considered. To date, the predominance of sleep problems in AD sufferers has not been satisfactorily explained. Lovas (2003) suggests that high CRH levels, low cortisol levels and a reduction in DHEA levels during the night might interfere with physiological sleep and perhaps cause subjective sleep disturbances.

Patients with primary adrenal failure (AD) require normal levels of cortisol and dehydroepiandrosterone. To examine this further, Lovas (2003) and his colleagues studied the prevalence and characteristics of perceived sleep disturbances in a large group of patients with AD on standard replacement therapy. They invited 60 patients to participate in the study and divided them into groups, comprising AD sufferers only, autoimmune polyendocrine syndrome type I (APS I) and autoimmune polyendocrine syndrome type II (APS II) for sub-group analysis. The results showed increased daytime fatigue, but this was not rated as higher than normal. This finding supports Li Voon Chong's research (2001).

Stewart *et al.* (2004) produced a paper in which it was suggested that over-replacement of cortisol may increase developmental delays, short stature, obesity, reduced bone mineral density and, arguably, premature vascular mortality in adults. Under-replacement of cortisol carries the risk of recurrent adrenal crises or failure of suppression of adrenal hyperandrogenism in patients with congenital adrenal hyperplasia. Such patients fail to mount an adrenocortical response to stress. Based on studies that defined the cortisol response to illness and surgical stress, patients were advised to double or triple their daily cortisol replacement in the face of undercurrent

illnesses (such as a febrile illness) and to take hydrocortisone in doses of 100 to 200 mg per day should they be undergoing major surgery. It is interesting to note that the researchers provided hardly any advice about psychological effects. Instead, they contended that such psychological stresses as anxiety and depression had conflicting results as compared with endurance exercises. This reflects the lack of an evidence base and confirms the need to undertake an in-depth investigation into the psychological distress that Addison's disease causes.

Despite many years of study in this area, scientists still question the relationship between psychological distress and endocrine diseases. Sonino *et al.* (2004) examined the frequency and characteristics of psychological distress in a heterogeneous population of patients suffering from endocrine diseases during and after adequate treatment. The study was conducted on 146 patients (31 males and 115 females) using semi-structured clinical interviews to assess psychiatric (structured clinical interview for DSM-IV) and psychological (diagnostic criteria for psychosomatic research [DCPR]) diagnoses. The psychosocial index, the medical outcome study short form and the general health survey were also used to help the patients form an idea of their own QOL. The results showed that 81 percent of the group presented with at least one psychiatric (DSM-IV) or psychological (DCPR) diagnosis. The most frequent diagnostic findings were generalised anxiety disorder (29 percent), major depression (26 percent), irritable mood (46 percent), demoralisation (34 percent) and persistent somatisation (21 percent). Using self-rating instruments, patients with at least one DSM-IV or DCPR diagnosis reported considerably more stressful lives, psychological distress and impaired QOL compared to those who had none. Sonino concluded that long term examination of endocrine patients showed a high prevalence of psychological distress. He further stated that thorough considerations of a patient's overall QOL was vital to increase therapeutic effectiveness. Sonino (2004). It can therefore be concluded that, in contrast to Lovas' (2002) findings, the endocrine patient's QOL is in fact adversely affected by the disease.

Since 2002, more researchers have studied the effects of hormone replacement therapy on patients' QOL. Rose (2004) tested a hypothesis based on QOL assessments completed by patients with successful hormone substitution. He aimed to establish whether patients with successful hormone replacement therapy continued to

experience poor QOL or whether they recovered. He concluded that the possibilities available for the somatic treatments of the disease are insufficient, and that other psychosocial factors, such as the emotional coping strategies of patients, should be taken into greater account in therapy. However the aspects of QOL are not clear and Rose does not specify which aspects of QOL were more impaired.

Hahner *et al.* (2006) produced another study that assessed the QOL in patients with AD. They studied 348 patients with AD and administered three standardised questionnaires (SF-36, GBB24, HADS) assessing their health-related QOL. They found that AD sufferers' QOL was significantly impaired in comparison to age- and gender-matched control groups from a representative random sample of the general population. They also noted that the failure of DHEA to fully restore well-being indicates the need for further improvement of glucocorticoids replacement strategies. Their research also gives a very general perspective on QOL and AD patients, and has not specified the QOL's different aspects – the question still remains over which aspect of QOL is more impaired. Do these patients suffer mainly from physical impairment, psychological impairment or do they have low performance in their daily activities? How can physicians help their patients with more details? Besides the AD cortisol replacement therapy what other therapies can be beneficial for them?

According to the literature reviewed for this paper, AD has a significant impact on QOL, sleep and well-being. However, as most studies have been conducted in Europe, they would need to be further examined before they could be applied to the South African context. In fact, it is necessary to conduct this research as a uniquely South African study to determine how relevant the European studies and their treatment programmes are in our context. South Africa is too varied on too many levels compared to Europe to enable a simple comparison to be made. Psychological impairment in the QOL of South Africans is affected by the insecurity of having our personal safety constantly threatened, while our crime rate has a direct effect on our mental health by heightening anxiety and causing stress. Another differentiating factor is the lack of access to health care and medical facilities for many citizens. South Africa is a developing country and as such there are differences in terms of social, political and economic aspects of overall QOL.

The literature surveyed for this paper does not explain which QOL component is impaired for AD patients. The question therefore arises as to whether clinicians should advise their patients that they will have a low *general* QOL or whether they should provide details. In order to provide more information to patients they would need to know which QOL component is more damaged. With this knowledge, physicians should be able to intervene in the early stages of the disease and raise the AD sufferer's QOL before it deteriorates. If, for example, they know that the patients' psychological component is more likely to be impaired, they would then be able to refer him / her for counselling to counter potentially high levels of depression and anxiety. Similarly, physical impairment might require physiotherapy or exercise. Finally, knowing further details about QOL could shed light on the possible causes of its decline.

Another issue that needs further investigation concerns the fact that some patients have AD without any other diseases, while others have a combination of AD and another autoimmune system disease. The existence of other diseases in the patient may contribute to a reduction in psychological well-being. Such a patient would then need special care, such as referral to a psychologist. In this manner clinicians will gain insight into the underlying causes which make such patients vulnerable.

Aims of the study

An overview of the AD, cortisol insufficiency and QOL literature allows us to conclude that the impairment in QOL in patients with AD is significant. However, as previously mentioned, we know of no study of these symptoms in South African AD patients. Therefore our physicians need to know that the overall QOL of South African AD patients is adversely affected due to conditions in our country such as:

- The lack of resources available to most South Africans
- The financial effect on patients (e.g. some patients cannot afford the medication nor can they attend regular medical consultations to monitor the treatment programme)
- Insufficient medical resources
- The high level of crime and social insecurity
- Environmental stressors in our society

- No access to medical aid.

Regarding pre-existing research conducted in a European context, how similar / dissimilar are our results? Do we need to adjust our patients' treatment packages to meet their needs according to their QOL? Our research therefore aims to investigate the similarity between South African and European patients' QOL to determine whether the European findings can be applied to South Africa. The central hypothesis is: H_1 . South African patients with AD have the same QOL as European patients.

Since QOL measures different aspects of a person's life, such as physical well-being, psychological well-being, daily activity and overall well-being, it is important to investigate in detail what the results for each component are. If we were only to report that these patients' QOL is low, how would we know which aspect of their quality of life is compromised as a result of AD or the hormone replacement therapy? In addition, patients with other autoimmune diseases could also have a low QOL, but what are the differences between the QOL assessment of each disease in the event of co-morbidity? Do we need to add physiotherapy to our patients' treatment packages or would they require psychological support such as counselling sessions to deal with their psychological impairment as a result of the AD? Furthermore, physicians need to know what the main effect of the treatment regime on their patients will most likely be. These questions are echoed by Rapley (2003) when he stated that QOL measures could serve to assist physicians in discerning amongst various treatments; to inform patients about the side-effects of treatment regimes; to monitor treatment efficacy from the patient's perspective; and to allow clinicians to better plan and coordinate treatment packages.

The second topic of this study is a comparison of the various QOL components. The literature review shows that AD patients suffer from low QOL, but research has thus far failed to analyse the components of QOL to clarify where the impairment lies. Patients have either been assessed physically (for example, AD and fatigue), or psychologically (for example, AD and depression), but in the absence of any other information, all that we are able to discern is that AD patients have a low QOL. It is important for clinicians to help their patients improve their QOL, and to maintain it at a higher level. There are some factors of QOL that are modifiable and some that are not. This will allow the patients to adjust to some of the disease's symptoms and its

treatments. So analysing the components of QOL will allow us to find out where the impairment lies. Therefore the second hypothesis of this study is: H₂. The three components (physical, psychological, ADL) will not activate uniformly.

Finally, this study aims to compare the differences between two groups of AD patients. Some have a combination of AD and other autoimmune syndromes, while others have only AD. Generally, the former could have a lower QOL. Knowledge of this sort will help clinicians to design effective treatment plans. This paper contends that AD patients with other autoimmune diseases have a lower QOL compared to patients who only suffer from AD.

CHAPTER TWO

Method

Sample

The minimum eligibility criterion for this study was whether patients had primary adrenal failure. To test our assertions, eligible subjects were enlisted from the South African Addison's disease database, which comprises all known Addison's disease patients living in South Africa. These patients have all been diagnosed with Addison's disease over differing periods of time. Dr Ian Ross, consultant endocrinologist, generated the list of patients with the assistance of other specialist physicians throughout South Africa. Ethical approval was granted for the 140 patients who were eligible for the study, and a total number of 100 patients were ultimately interviewed, for reasons outlined below. The subjects were interviewed telephonically. The interviewer was blind as to whether the subject was a patient or a control.

Control group

A matched control group was selected by identifying an individual of the same gender and approximate age residing in the patient's household. Additional criteria for selection included an assessment by the interviewer's assistant of their eligibility (e.g. they should not have had any earlier disease, or chronic illness), their willingness to give consent and their availability in terms of being present at the same time that the interview was conducted with patients. These individuals therefore already knew that an interviewer would telephone them on a certain date at a stipulated time.

Instruments

Three questionnaires were administered: the Rotterdam QOL questionnaire, the Beck depression inventory and the Spielberger anxiety inventory:

- **Rotterdam quality of life questionnaire**

The Rotterdam QOL questionnaire was chosen as it accurately measures different aspects of QOL, such as physical, psychological, daily activity, and overall QOL that were needed for this study. In addition it can be conducted telephonically.

- **Beck depression inventory**

The Beck depression inventory (BDI) is a widely used instrument to measure mood. It comprises a 21-item test presented in multiple-choice format that attempts to measure the presence and degree of depression in adolescents and adults. We used the 1978 self-administered version (see appendix C).

- **Spielberger anxiety scale**

The Spielberger anxiety scale (SAS) includes 20 items, each of which has four answers to choose from. The questionnaire provides norms for clinical patients, high school and college students and working adults and it can be administered either individually or in a group. It differentiates clearly between the temporary condition of “state anxiety” and the more general and long-standing quality of “trait anxiety”. It assists professionals in distinguishing between a client’s feelings of anxiety and their depression. The scale’s simplicity makes it ideal for evaluating individuals with lower educational backgrounds. The SAS has been translated into more than 40 languages and is the leading measure of personal anxiety worldwide (Caci *et al.* 2003).

Ethics

The study protocol was approved by the University of Cape Town’s Department of Psychology and Groot Schuur Hospital’s Ethics Board. All participants gave telephonic consent prior to testing, and any questions they might have had were answered.

Procedures

Initially the interviews were conducted on a face to face basis. However, three problems arose. The first was that skin hyperpigmentation made the patients clearly distinct from the controls. The second was that the patients seemed obliged to either downplay their symptoms or exaggerate them in face-to-face interviews. To minimise the interviewees’ discomfort, they were asked to complete the questionnaire on paper. This however, did not completely eliminate the problem and also raised a new one: illiterate or uneducated interviewees were unable to complete the questionnaire. The third problem was that since patients were scattered around the country, it was not possible to travel to interview them. Telephonic interviews were the best solution,

eliciting the most honest and unbiased answers and it was therefore decided to continue with data collection this way.

The interviews were conducted between 9 a.m. and 7 p.m. Weekends were avoided. Interviewees were informed about the research and its aims by the co-researcher and were told that they would get a call on an arranged date and time for the interview. Respondents were then asked whether it was an appropriate time for them to answer the questions and whether they were still willing to participate in the study. They were informed that it would take only 10 to 15 minutes to conduct the interview. The interviewees were then asked whether they had any questions before they were requested to keep a pen and paper ready to write the possible answers down. For those who were not able to write, the options were repeated for each question.

Each interview started with the Rotterdam QOL questionnaire, which has shorter questions. This was followed by the Beck questionnaire. The interviewer explained that the respondents should choose the option which most closely related to their feelings and also reminded them that if they needed to have the options repeated, as often as required, they should not hesitate to ask. The Spielberger questionnaire was then given, which again has shorter questions to avoid fatigue or boredom. At the end of each interview the respondents were thanked for their participation in this research.

Groote Schuur Hospital granted ethical approval to conduct the study on 140 endocrine clinic outpatients. At the start of the trial, the study population was 140 patients, but only 100 of them were available for interview. The patients and members of the control group were informed that a researcher, who had no knowledge of whether they were patients or not, would contact them. Separate questionnaires were used for each interviewee. All analyses were carried out using the STATISTICA package. The results are described in the next chapter.

CHAPTER THREE

Results

This research attempted to answer the following questions:

A: What is the QOL of South African AD patients, and does it differ from the QOL in European studies?

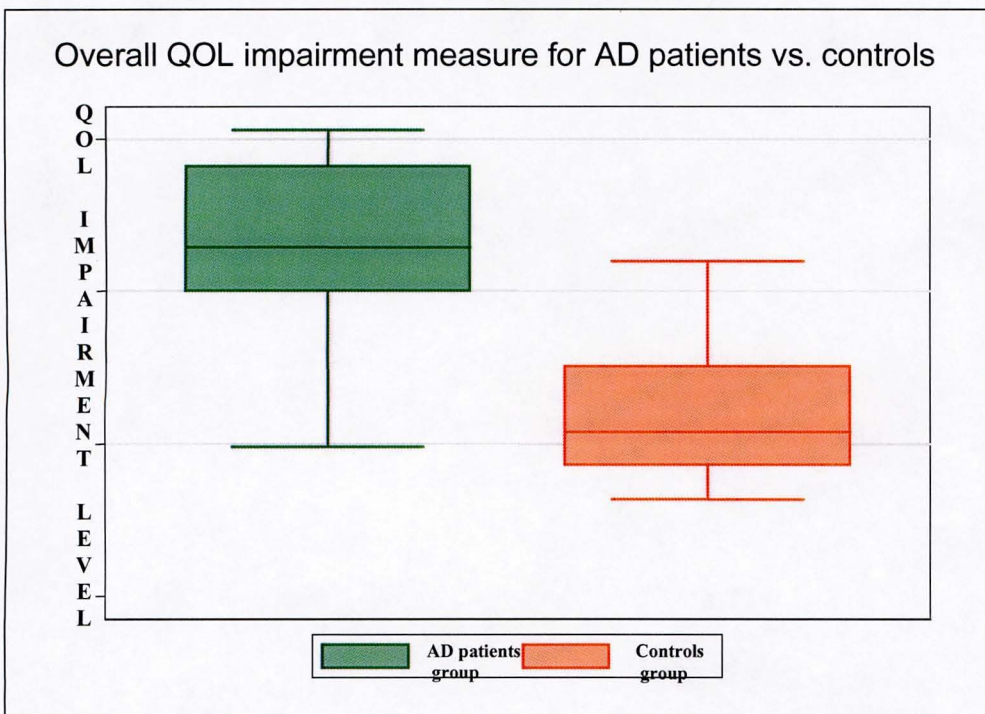
B: What is the difference between the QOL components and do they affect QOL uniformly?

C: Is there a difference in the QOL of the patients who have only AD with those who have both AD and another autoimmune disease?

Analysis of the data indicates that the overall QOL of South African Addison's disease patients is lower than the control group's overall QOL – AD patients averaged a score of 59.19 (sd 21.99), compared to the average score of 114.66 (sd 24.46) for the controls. This also indicates that, South African AD patients do not differ from the Europeans as well.

Since our groups were matched and we expected the clinical group to have worse QOL than the control group, t-tests were used to determine group differences so one-tailed t-tests were conducted. There was strong evidence that ($p > 0.0001$) the overall QOL in the clinical group was lower than the control group's overall QOL. (See Figure 1).

Figure 1: Overall QOL AD patients group vs. control group



This study scrutinised the components of QOL. Since all the scores were standardized from raw scores into scores on a 100 point scale in a systematic way. This made results more easily interpretable. Moreover, the level of quality of life impairment in the different scales became compared more easily.

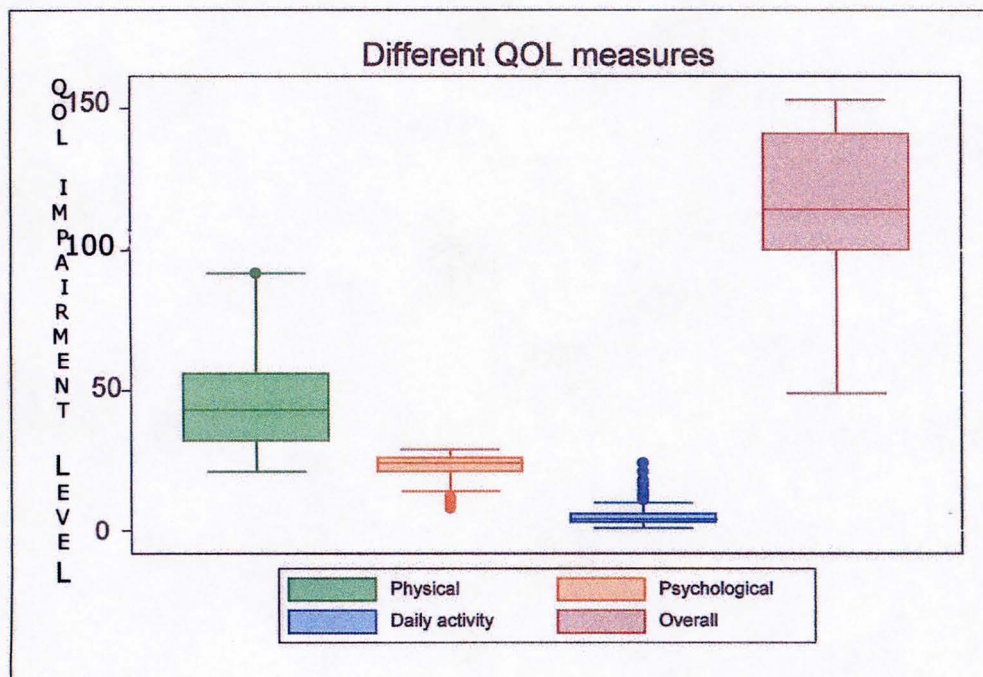
We investigated the differences of QOL components which were the psychological aspect, physical aspect, and daily activity level. This is what was missing in the European research. Analysis of the QOL components showed they do not affect the QOL uniformly. The disease had the least effect on the patients' work performance, social life and daily activity level, then their psychological level, while the effect of the disease on their physical health was on the highest level. Reviewing the literature, however, gives the impression that AD patients have low QOL because they suffer from psychological impairments, whereas the difference between the physical impairment level (average 115.82) and the psychological impairment level (average 33.45) is significantly larger. (See Table 1)

Table 1: Descriptive statistic for psychological level, physical level, Daily activity level of AD patients' group vs. control group

	Clinical group			Control group		
	Psychological level	Daily activity level	Physical level	Psychological level	Daily activity level	Physical level
Mean	33.45	13.42	115.82	6.16	1.41	22.25
Sd	10.11	5.34	26.19	5.26	0.64	5.69

Bearing in mind that AD is a physical illness, it does not surprise us that patients' physical complaints are greater than their psychological problems. Reviewing the literature gave us the impression that AD patients have psychological impairment but did not indicate the degree to which their psychological problems are different from their physical problems while they are under treatment. So our results show that, although AD patients suffer from psychological problems, their physical complaints are still more than their psychological complaints; they may alternatively be an indication that they have psychosomatic problems which we need to test for in future. Clearly the treatment packages can be improved to support the patients' mental and physical health, as a result of which their daily activity level will improve as well.

Figure 2: Quality of life impairment level in physical, psychological, daily activity and overall in AD patient's group.



Regression was used to find out which one of the components had more impact on the QOL. The indication from the beta-coefficients was that physical impairment has the most importance. Howell (2002) suggests that the relative size of the t-values used for significance testing are perhaps the best for judging relative importance. By that standard, physical impairment ($B = -203$; $t = -8.6$; $p < .001$) would be the most important predictor. The results show that it is primarily the physical impairment which causes low QOL and it is then the psychological impairment which aggravates the QOL.

Since most of the previous research had found that AD patients have psychological damage, we decided to investigate patients' psychological impairment more closely by assessing their anxiety and depression separately. The results show that they have more or less the same levels of anxiety and depression which are higher than those of the control group (See Table 2).

Table 2: Descriptive statistic

	AD patient group		Control group	
	Beck depression scale	Spielberger anxiety inventory	Beck depression scale	Spielberger anxiety inventory
Mean	34.72	35.07	23.56	21.72
Sd	12.71	11.83	9.96	7.79

The result of the t-test on the Beck depression scale also show that the groups differ ($p > 0.000$), with the clinical group showing a higher level of depression than the control group. On the Spielberger anxiety inventory, both the groups also show differences ($p > 0.000$), with the clinical group showing higher levels of anxiety as well.

Figure 3: Depression level AD patients group vs. control group

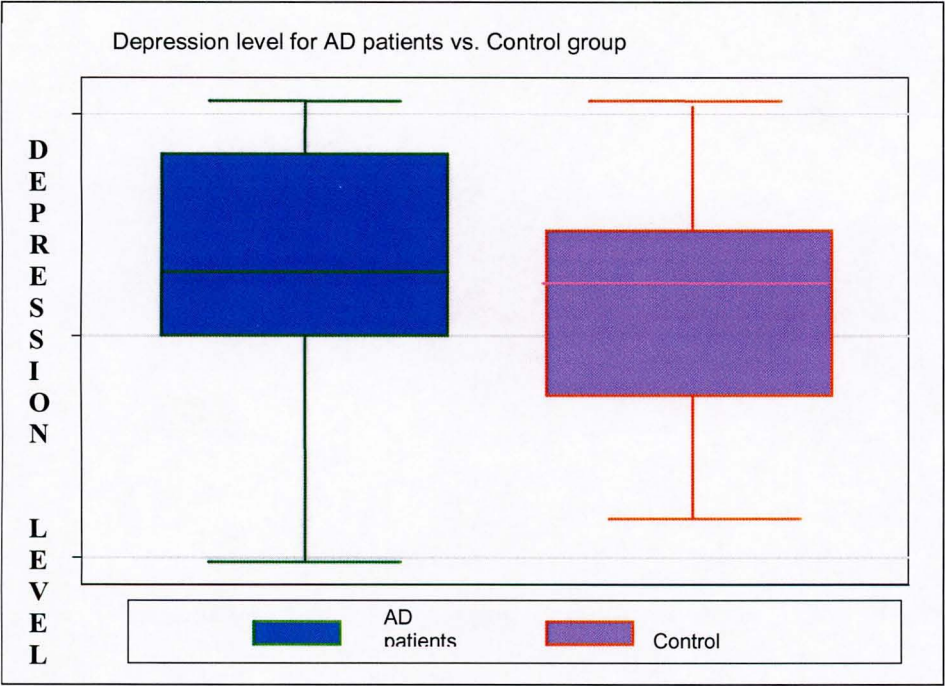
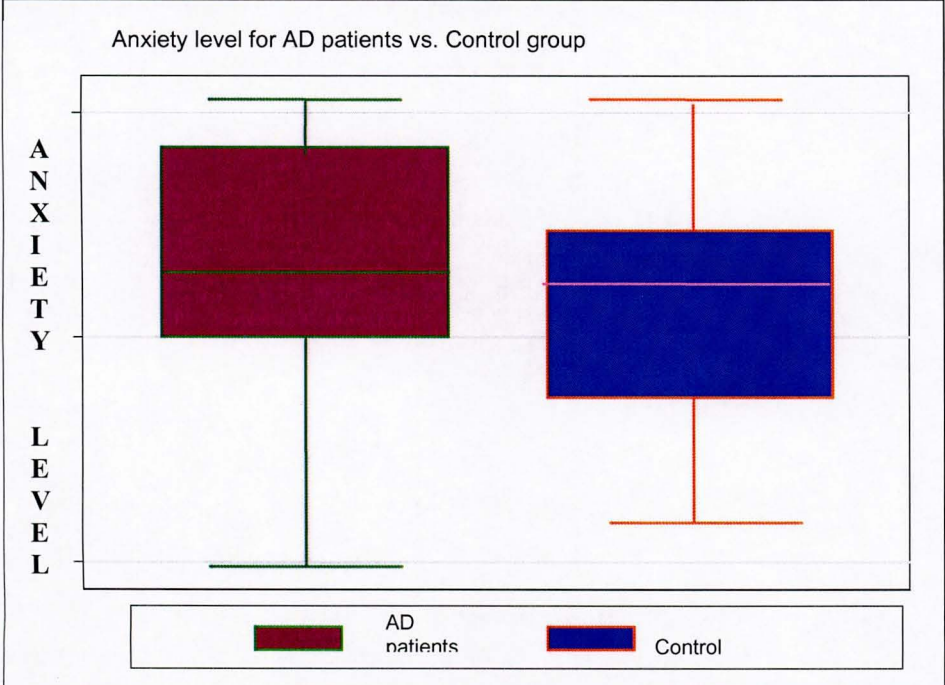


Figure 4: Anxiety level AD patients group vs. control group



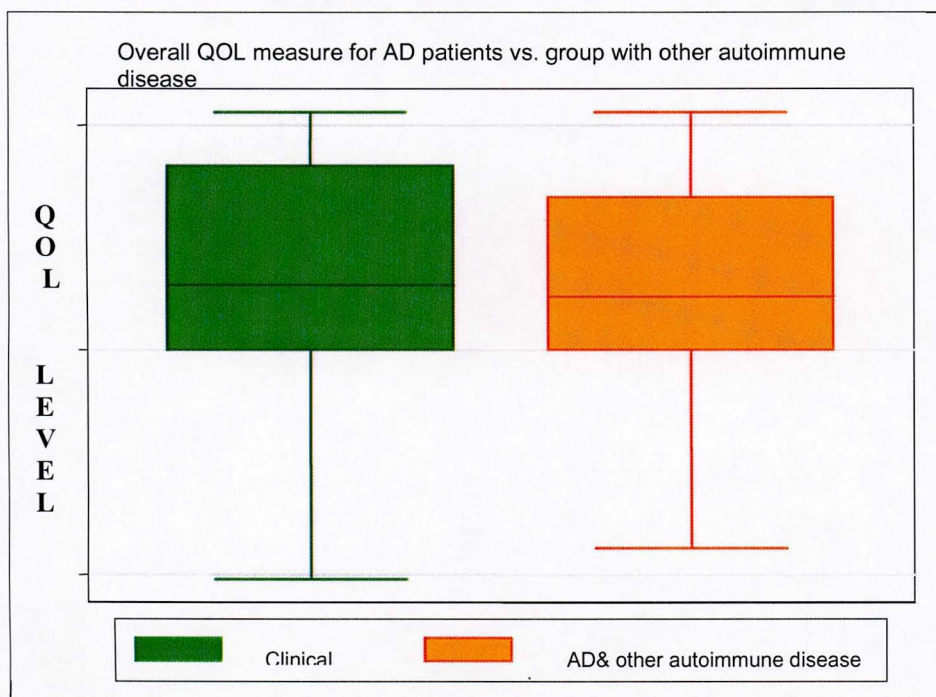
The last question of the research was how different is the QOL of the patients who only have AD from those who have both AD & another autoimmune disease? The results show that QOL of patients with Addison's disease does not differ that much from the patients who have AD as well as another autoimmune disease. (See Table 3)

Table 3: Descriptive statistic

	Overall QOL clinical group Patients with AD	Overall QOL control group Patients with AD and another autoimmune disease
Mean	115.82	114.66
Sd	26.19	24.45

And finally the two groups of AD and AD with another autoimmune disease were compared. Since they were not a matched pair, we used the independent t-test. The results show that $p=0.3733$ and therefore patients with other autoimmune disease have equal levels of QOL compared with patients with AD only.

Figure 5: Graph box overall QOL in AD patients vs. overall QOL in AD patients and other autoimmune disease



The box plot of the AD group and the group of AD and another autoimmune disease show a high degree of overlap, which shows that their QOL impairment is very similar, and both have quite a high prevalence, indicating that another autoimmune disease does not significantly aggravate the QOL .

The reason that we used the overall QOL separately from its components is that European studies have only looked at QOL in overall and in this study while we are looking at the components of QOL we want to be able to compare our study to theirs too.

CHAPTER FOUR

Discussion

Consistent with our original hypothesis, AD patients demonstrated a greater degree of impairment in their quality of life. A reduction in physical capabilities accounted for the greatest portion of this impairment, with psychological symptoms also contributing to the overall impairment, with psychological symptoms also contributing to the overall impairment, daily activity being impacted the least. AD patients demonstrated higher levels of both depression and anxiety, compared to controls. However, QOL was not different in AD patients when compared to AD patients comorbid autoimmune disease.

As discussed earlier, Addison's disease is a chronic, lifelong disorder caused by adrenal gland insufficiency and as such it requires lifelong cortisol replacement therapy. For years scientists have explored the relationship between endocrine disease and psychological distress, with particular focus on the relationship between Addison's disease and the QOL of patients. They found that endocrine disease does in fact affect QOL and can cause depression and anxiety. They also found that different modes of cortisol replacement therapy affect mood and that AD sufferers frequently experience fatigue daily. Such sufferers also exhibit noticeably reduced working ability and reduced health (Lovas, 2000).

As previously stated, there is to date no study on the effect of Addison's disease on the QOL of patients in SA. Equally, there are no studies on which aspect of QOL is affected and what QOL means for each patient. Research findings have so far only provided physicians with a general insight into the disease. Three important questions arise:

1. How can physicians give adequate advice on the potential deleterious effects of AD when there is so little accurate information with which to manage their patients' overall convalescent needs?
2. How can physicians know what to expect during the treatment programme they have prescribed to their patients when there is very little specific information available?
3. How can physicians establish modifiable factors that allow for early intervention

before symptoms become worse?

This study began in response to the need for clearer information to help answer the questions above. To this end, we wanted to explore the QOL of AD patients and to clarify the differences between its components.

A further question that we have attempted to clarify is whether studies based on a European subject group would be valid and applicable in the South African context, given that South Africa is a developing country with a heterogenous population delineated along distinct economic and social lines which are different from European socio-political exigencies. Further differences in the subject groups are that the access to medical aid and health care in this country and other developing countries are different from those found in Europe. Such differences in health care provision leads to the deduction that the average South African's and European's psychological health differs also. The psychological health of South Africans is further exacerbated by high rates of crime, poverty and social insecurity.

The last question that this study has attempted to answer is whether AD patients with other autoimmune diseases have worse QOL as compared to patients who only have AD. As the presence of other autoimmune diseases can already cause a low QOL we wanted to establish whether there is any difference between their QOL in comparison to other groups of patients who only have AD. An example would be a patient with Coeliac disease who, as a result of this illness, has become infertile or has had a miscarriage and is therefore already experiencing depression. Coeliac disease is an autoimmune disease that affects the intestines, and has shown a high rate of co-morbidity with AD.

To answer this question, we decided to assess our patients with a QOL test (the Rotterdam QOL questionnaire that covered the four components of QOL: psychological, physical, daily activity and overall QOL levels. We found the test suitable for gathering more information about the QOL of AD patients, allowing us to compare the four components of QOL and to determine which ones would be more affected and modifiable. To improve the accuracy of this study, we added the Beck depression inventory and the Spielberger anxiety test.

In comparing our results to other research, it is necessary to have a short overview of the literature. In 1991 Cooper concluded that patients with endocrine disorders tend to suffer from various psychiatric disturbances and cognitive impairments, specifically including symptoms of major depressive disorders and generalised anxiety disorders. Later, in 1993 he did further research concerning AD and the impact on patients of different doses of cortisol replacement therapy. This study produced the results showing that patients' QOL is adversely affected by the increased doses of cortisol. This information however, is too indistinct and does not allow physicians to have a clear understanding of the AD patients' QOL. The studies by Cooper determined that while psychological impairment is a factor that needs to be addressed by physicians treating AD patients, greater focus and attention must be placed on the physical impairment and its effects. While valuable, this information is incomplete as there is no comparative data about the other components of QOL. The similarity between our research and the Cooper research is that we also found that AD patients have higher psychological impairment than the control group, but our study was able to show that patients' physical impairment is higher than their psychological impairment. Cooper did not look at all the components of QOL and, as such, we are not able to make any comparative conclusions which might provide physicians with information on all the components of the QOL to determine which of these are modifiable.

Later in 1993 Riddle and his colleagues also found that patients' general health is affected by the levels of cortisol in their treatment programmes. Like Cooper's, this study gives a vague understanding of patients' QOL and the quality of their physical and psychological health. The study found that the patients' general health is adversely affected but our research could determine in greater detail whether patients' physical well-being was more damaged than all other components. This study also showed that the patients' psychological impairment and their daily activity level was higher than the control group's. The advantage of our finding was that we were able to determine the differences across the four components of QOL and could further determine the quality of each component as well as which component most aggravates the QOL. The similarity between Riddle's research and ours is that we also concluded that AD patients suffer from depression and anxiety but that is not the only reason which causes the low QOL. Our research, however, also found that the physical

impairment level is still higher than their psychological impairments, and that the difference is substantial.

Then in 2001 Hunt *et al.* concluded that the self esteem and well-being of AD patients are hugely affected by their hormone replacement therapy. Again, we can see the same problem here: the information is too general; and we still do not know what the qualities of the components of QOL are, and how they differ from each other.

In 2002 Lovas found that AD patients in general experience fatigue and they have an impaired general health. Lovas also concluded that their physical and social functioning is greatly impaired. He looked at specific areas such as physical and social functioning, but the rest of his research still has the same approach as the earlier studies, giving very general information. It does not examine how other components are affected by AD, although, unlike other researchers, who had mainly focused on the psychological aspect, he looked at the physical factors. We still, therefore, need to look at all the other factors of QOL. However, even though his findings are focused on the physical aspect of QOL, the study supports our conclusion that physical damage is greater than psychological and daily activity level damages.

In 2004 Stewart *et al.* concluded that over-replacement of cortisol also leads to adverse physical health reactions, and they determined that this would lead to increased developmental delays, short stature, obesity, reduced bone mineral density and premature vascular mortality in adults. Their study focused particularly on the physical component of the QOL and did not look at other aspects of QOL. This confirms the necessity of research which looks at every single component and explains exactly how each component affects a patient's QOL. Their finding does, however, support our conclusion that AD patients have more physical than psychological complaints, but that their psychological impairment is much greater than the control group.

In 2004 Sonino's research was focused narrowly on psychological distress and the psychological component of the QOL; it proved that AD patients can suffer from a range of different psychological or mental problems. Our study can partly relate to these findings, as we also found psychological impairment in our study, but we

looked at other components of QOL as well. The main feature of our findings in comparison to Sonino's is that, while the psychological component is important, the patients have more physical impairment than psychological or daily activity level impairment.

Hahner's findings in 2006 were also too vague and general. They merely concluded that the QOL of AD patients is impaired. This does not provide an explanation of the quality of each aspect of the study, nor of the components contributing to QOL.

When we look at all the research to date we find that varying conclusions about the effect of AD on the psychological aspect of QOL or the physical aspect or QOL in general have been made. This study adopts a more holistic approach to the subject: it looks at all the components of QOL and compares them with each other. Our study shows the comparative results for each of the QOL components, and it gives a better understanding to physicians and patients of the deleterious aspects of this disease and the effect it has on each aspect of life.

An overview of the literature gives the strong impression that AD sufferers have low physical QOL but, as Riddle (1993) and his colleagues showed, the psychological component of the disease causes great distress too.

Many sectors of the population dealing with AD in varying capacities can benefit from this research, and even more detailed studies on the overall effects of AD on QOL in the future.

Within the medical population, the first group who can derive benefit from this research is the endocrinologists, who would gain a better understanding of the effects of AD on their patients' overall well-being. This information allows endocrinologists to make a more comprehensive assessment of which component of the QOL is aggravated by AD, and also gives supportive evidence in advance of any changes in treatment packages for their patients. Of course, in order to do this most effectively one would need to have complete information about the effect of AD on all the components of QOL rather than just one of them.

While the physical damages of AD are considerable, the psychological component of QOL is also affected. Therefore the second group of medical professionals who would benefit from the results of research discussed in this paper are psychologists. While endocrinologists concentrate on managing the physical aspects of this disease, the assistance and input of psychologists during the convalescent period are almost equally important. This is due to the immense psychological distress suffered by those patients with AD. This research has specified, through the use of the Spielberger anxiety test and the Beck depression test, the high frequency of anxiety and depression which accompanies AD, but this is a fairly two dimensional perspective on psychological distress which can be almost as debilitating as Addison's itself.

Patients and their families also need to have a better knowledge and understanding about this disease and its symptoms. They need to know what to expect and how to monitor the problem. The vital information is which parts of the patient's QOL is most likely to be affected; what type of physical, mental and emotional assistance will they require; and what will be the likely effect of this disease on their overall mood and on their overall functioning.

Knowing such details of the disease as are described in this study will also help government and medical aid companies to help patients in a more efficient way, so that their comprehensive needs are covered. By knowing that AD patients have a lower than average QOL, government and medical aid companies can measure the requirements of the treatment protocol for AD. This would include knowing the likelihood of patients needing physical and psychological support such as physical therapies, nutrition education, psychological counselling sessions, as well as regular medical check-ups with a physician qualified to monitor AD and the effects of cortisol, prednisone, etc on the patients. In this way, effective, comprehensive treatment packages could be budgeted more pragmatically and efficiently.

Our results showed that the QOL of South African AD patients is indeed affected by the disease. Our patients' overall QOL impairment levels are higher than the overall QOL in our control group or, in other words, AD patients had much lower QOL than members of the control group. When reviewing all the components, and the Beck and Spielberger inventories, we found that all of the components in our clinical group had

lower means in comparison with the control groups. The physical impairment level had the highest mean compared to other components in our clinical group. The daily activities showed very low variability between the clinical and control groups but this component had the lowest impairment in both groups also. This informs us that most patients do not suffer with daily activity dysfunction. As this finding demonstrates, the QOL in our clinical group is much lower than our control group and we can report with confidence that our finding is matched with what we found in the literature. We did not, however, stop investigating at this point since we wished to determine which one of the QOL components is most affected.

As stated above, the QOL measures physical impairment, psychological impairment and daily activity impairment. The results of the study showed that the most affected component was physical, while the psychological impairment level was less affected, followed by the impairment in daily activity. While the frequency of physical and psychological impairment was quite high, the daily activity impairment was fairly low. From this, it can be determined that it is the physical impairment in AD patients which primarily causes the low QOL and that the psychological impairment is the second cause for their low QOL – with both of these factors needing to be taken into account to improve patients' QOL.

Considering that most of the research cited gives evidence of the component impairment discussed in the previous paragraph, further exploration would be necessary to determine the exact nature of the psychological distress, to ensure that the physical impairment is not exacerbated by psychosomatic symptoms.

Although Addison's disease affects patients' physical health it does not seem to have a significant effect on their daily activities. Their psychological impairment seems to be less affected than the physical components, but this does not mean that they are not psychologically damaged. The Beck and Spielberger inventories showed that the mean depression and anxiety in the clinical group is much higher than in the control group. It is therefore possible to assert that Addison's disease and the cortisol replacement therapy do indeed cause high levels of stress and anxiety. We concluded that the South African AD study matches its European counterpart in general, but that the latter excludes a comparison of the components of QOL and its modifiable factors.

While comparing the various components we found that physical impairment is lower in QOL in general, but psychological damage is found as well, and that the level of stress is greater than the level of depression.

Therefore one of the modifiable factors within the QOL components is the prevalence of high stress and anxiety levels which can be reduced with early intervention. Such early intervention could include any psychological and life skills counselling, stress management lectures or stress control techniques such as creative art, meditation, relaxation and yoga, to assist patients while being treated.

A comparison was also made between patients who had AD with the patients who had a combination of AD and at least one other autoimmune disease. We concluded that patients with AD have slightly lower QOL than patients who have AD and another autoimmune disease, but their overall QOL impairment is very much the same. One can therefore deduce that the co-morbidity of some other autoimmune disease with AD does not necessarily aggravate the QOL.

Limitations of the study

Our sample group comprised patients who had been diagnosed with AD for varying periods. Since the duration of the disease in our patients and their individual treatment programmes differed, we acknowledge that this could affect research consistency.

Additionally, we question whether changing our interview techniques during data collection from personal to telephonic interviews could have had an effect on the accuracy of our data. Telephonic interviewing techniques are not able to determine the clues and congruency levels that physical characteristics such as the person's appearance, presentation and expressions provide, these being important contributing factors in psychological assessments.

Suggestions

We would like to suggest that other studies include children in their research. Generally, children live less stressful lives than adults, mainly because they have less responsibility. Comparing their QOL with adults could clarify the effect of AD on

QOL. Research of this sort would be additionally valuable if it included specific information on how each of the QOL components is affected by AD.

The occurrence of AD and its subsequent treatment with a cortisol replacement therapy or equivalent require a period of convalescence and adjustment, during which additional physical therapies would be useful to alleviate the effects of cortisol depletion on the body. While most studies we examined specified that the component most affected by AD was the physical one, none specified which of the symptoms occurred most frequently. This information would be useful, by emphasising the need for further research. Physicians and endocrinologists would then be able to determine which support therapies the patients may need in the treatment of their symptoms. For example, symptoms of the disease, include severe fatigue and weakness, loss of weight, a feeling of faintness, low blood pressure, nausea, vomiting, salt cravings and painful muscles and joints, indicating the need for additional physical therapies to aid in recovery.

A further suggestion would be to examine a typical treatment package (as opposed to the disease itself) of AD using different curative strategies for stress, anxiety and depression. By doing this, physicians can then more accurately discern the major psychological malady accompanying AD, and can make recommendations to augment the treatment programme with particular therapies that are show to be effective. For example, based on a chief complaint being some form of generalised anxiety, a physician may refer a patient for cognitive behavioural therapy (CBT) and relaxation techniques to facilitate the improvement of their QOL. A comparative study could then be undertaken with AD patients who have not received CBT in their treatment programme, and such factors such as recuperation time and improvement in QOL can be assessed.

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Appendix A

Consent form

Appendix B

Rotterdam Symptom Checklist Confidential

In this questionnaire you will be asked about your symptoms. Would you please, for all symptoms mentioned, indicate to what extent you have been bothered by it, by circling the answer most applicable to you. The questions are related to the past week. Example: Have you been bothered, during the past week, by headaches not at all a little quite a bit very much have you, during the past week, been bothered by lack of appetite not at all a little quite a bit very much.

1-Irritability

not at all a little quite a bit very much

2-tiredness not at all a little quite a bit very much

3-worrying not at all a little quite a bit very much

4-sore muscles not at all a little quite a bit very much

5-depressed mood not at all a little quite a bit very much

6-lack of energy not at all a little quite a bit very much

7-low back pain not at all a little quite a bit very much

8-nervousness not at all a little quite a bit very much

9-nausea not at all a little quite a bit very much

10-despairing about the future

not at all a little quite a bit very much

11-difficulty sleeping not at all a little quite a bit very much

12-headaches not at all a little quite a bit very much

13-vomiting not at all a little quite a bit very much

14-dizziness not at all a little quite a bit very much

15-decreased sexual interest

not at all a little quite a bit very much

16-tension not at all a little quite a bit very much

17-abdominal (stomach) aches

not at all a little quite a bit very much

18-anxiety	not at all	a little	quite a	bit very much
19-constipation	not at all	a little	quite a	bit very much
20- diarrhea	not at all	a little	quite a	bit very much
21-acid indigestion	not at all	a little	quite a	bit very much
22-shivering	not at all	a little	quite a	bit very much
23-tingling hands or feet	not at all	a little	quite a	bit very much
24-difficulty concentrating	not at all	a little	quite a	bit very much
25-sore mouth/pain when swallowing	not at all	a little	quite a	bit very much
26-loss of hair	not at all	a little	quite a	bit very much
27-burning/sore eyes	not at all	a little	quite a	bit very much
28-shortness of breath	not at all	a little	quite a	bit very much
29-dry mouth	not at all	a little	quite a	bit very much

A number of activities is listed below. We do not want to know whether you actually do these, but only whether you are able to perform them presently. Would you please mark the answer that applies most to your condition of the past week.

1- Unable, 2- only with without help, 3-without help, 4- with difficulty
--

1-Care for myself (wash etc.) O O O O

2-walk about the house O O O O

3-light housework/household jobs O O O O

4-climb stairs O O O O

5-heavy housework/household jobs O O O O

6-walk out of doors O O O O

7-go shopping O O O O

8-go to work O O O O

All things considered, how would you describe your quality of life during the past week?

excellent

good

moderately good

neither good nor bad

rather poor

poor

extremely poor

Would you please check whether you answered all questions?

Thank you for your help.

Patient number__

Appendix C

Beck Depression Inventory

In this questionnaire are groups of statements. Please read each group of statements carefully. Then pick the one statement in each group which best describes the way you have been feeling the *Past Week. Including Today!* Circle the number beside the statement you picked. If several statements in the group seem to apply equally well, circle each one. Be sure to read all the statements in each group before making your choice.

1. a. *I do not feel sad.*
b. *I feel sad.*
c. *I am sad all of the time, and I can't snap out of it.*
d. *I am so sad or unhappy that I can't stand it.*

2. a. *I am not particularly discouraged about the future.*
b. *I feel discouraged about the future.*
c. *I feel that I have nothing to look forward to.*
d. *I feel that the future is hopeless and that things cannot improve.*

3. a. *I do not feel like a failure.*
b. *I feel that I have failed more than the average person.*
c. *As I look back on my life, all I can see is a lot of failures.*
d. *I feel I am a complete failure as a person.*

4. a. *I get as much satisfaction out of things as I used to.*
b. *I don't enjoy things the way I used to.*
c. *I don't get real satisfaction out of anything anymore.*
d. *I am dissatisfied or bored with everything.*

5. a. *I don't feel particularly guilty.*
b. *I feel guilty a good part of the time.*
c. *I feel quite guilty most of the time.*
d. *I feel guilty all of the time.*

6. a. *I don't feel I am being punished.*
b. *I feel I may be punished.*
c. *I expect to be punished.*
d. *I feel I am being punished.*

7. a. *I don't feel disappointed in myself.*
b. *I am disappointed in myself.*
c. *I am disgusted with myself.*
d. *I hate myself.*

SPIELBERGER STATE-TRAIT ANXIETY INVENTORY (STAI-S)

Directions:

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number to the right of the statement to indicate how you feel right now, that is, at this moment. There are no right or wrong answers. Do not spend too much time on any one statement, but give the answer which seems to describe your present feelings best.

	Not at all	Somewhat	Moderately	Very much
I feel calm	1	2	3	4
I am tense	1	2	3	4
I feel upset	1	2	3	4
I feel frightened	1	2	3	4
I feel nervous	1	2	3	4
I am relaxed	1	2	3	4
I am worried	1	2	3	4
I feel confused	1	2	3	4