The Quality of Life in Patients with Diffuse and Limited Systemic Sclerosis

Naomi Reay

Submitted in accordance with the requirements for the degree of

Doctor of Philosophy, the University of Leeds, School of Healthcare and

School of Medicine

October 2008

I confirm that the work submitted is my own and that appropriate credit has

been given where reference has been made to the work of others.

Acknowledgements

Abstract

Systemic Sclerosis (SSc) is a rare, autoimmune, connective tissue disease. It has potentially severe physical and psychological impacts on the individual. SSc has two sub-types, diffuse cutaneous systemic sclerosis (dcSSc) and limited cutaneous systemic sclerosis (lcSSc). This study had three aims: to develop a framework to describe and understand the impact of SSc on Quality of Life (QoL) in SSc; develop a measure of QoL in SSc; and test the hypothesis that levels of quality of life will differ between disease sub-type.

To achieve the study aims a mixture of qualitative and quantitative methods were used. In order to develop the descriptive framework of QoL in SSc, qualitative data was gathered from 31 interviews and a focus group of people with SSc. The data was analysed using thematic analysis and the themes used to form the descriptive framework.

The descriptive framework of SSc QoL consisted of thirty themes which form four overarching themes of Emotion, Physical adaptation, Impact on/with others, and Self.

To develop the SSc QoL scale, potential items were identified through a process of item selection from the qualitative data. Together with comparator measures, a 90 item draft SSc QoL was posted to 336 patients randomised from the National Scleroderma Database (NSD), with a return rate of 61 % (203). Items not fitting the Rasch model of item response theory were deleted: 39 items were retained. The 39-item questionnaire was

administered to a second population of 369 SSc patients randomised from the NSD. 159 were returned and respondents received a second copy, 117 of these were returned within four weeks (74% of first returns). Further Rasch analysis resulted in a 29 item SSc QoL measure.

The SSc QoL (29) showed reliability of 0.764 over two-time points. Non-parametric testing showed that sub-type of disease had no significant impact of levels of QoL (p, 0.836). However, Structural Equation Modelling revealed an indirect influence of disease sub-type on QoL, this being related to disability associated with disease sub-type.

Contents

List of Figures

List of Tables

Abbreviations

AS - Ankylosing Spondylitis

DcSSc - Diffuse Cutaneous Systemic Sclerosis

Dd - Disease duration

DI F- Differential Item Functioning

FSS - Fatigue Severity Score

HAD - Hospital Anxiety and Depression score

HAQ - Health Assessment Questionnaire

HRQoL - Health Related Quality of Life

IRT - Item Response Theory

ICDH - International Classification of Disability, Handicap

ICF - International Classification of Disease, Functioning and Health

LcSSc - Limited Cutaneous Systemic Sclerosis

LHS - London Handicap Scale

OMERACT -Outcome Measures in Rheumatology

PAH – Pulmonary arterial hypertension

PRO - Patient Reported Outcome

PROM - Patient Reported Outcome Measures

QALY - Quality Adjusted Life Years

QoL - Quality of Life

RA - Rheumatoid Arthritis

SEM - Structural Equation Modelling

SCTC - Scleroderma Clinical Trials Consortium

SHAQ - Scleroderma Health Assessment Questionnaire

SLE - Systemic Lupus Erythematosus

SSc - Systemic Sclerosis

SWB - Subjective Well Being

UKF I - UK Functional Index

Publications and Presentations relating to this study

Publications

- Reay N, Firth J (2008) – Records management guidance and its implications for research. <u>Nurse Researcher</u>; **15** (3): 26 – 31

- Firth J, Reay N (2008) – Clinical and research databases in healthcare research. <u>Nurse Researcher</u>; **15**: (4) 27 – 34

- Reay N (2007) – An exploration of the NHS end of life care programme and its potential use for patients with end-stage systemic sclerosis. <u>Musculoskeletal Care</u>. Sep: **5** (3): 130-8

- Yung, A. Reay N, Goodfield, MD - Improvement in digital flexibility and dexterity following ingestion of sildenafil (Viagra) in limited systemic sclerosis (2005) – <u>Arch Dermatol</u>. Jul: **(7)**: 831-3

Invited Conference Presentations

- Reay N - Levels of Fatigue in Diffuse and Limited Systemic Sclerosis. British Health Professionals in Rheumatology (BHPR), ARC Silver Medal Prize for Clinical Research. British Society of Rheumatology, Liverpool, 2008.

- Reay N - Quality of Life in Systemic Sclerosis. Second International Systemic Sclerosis Forum Actelion sponsored. Paris, 2008

Conference Presentations

- Reay N, Hill J, Hale C, Emery P, Tennant A (2008), – "A Needs-based Quality of Life Measure For Systemic Sclerosis: The SSc QoL" British Society of Rheumatology (Liverpool)

Poster Presentations

- Reay N, Denton, CP, Hill J, Hale C, Emery P, Tennant A (2007) – A Study of Levels of Fatigue in Diffuse and Limited Systemic Sclerosis. British Health Professionals in Rheumatology (Birmingham)

- Reay N (2007) – A Search for consensus in the assessment of depression in systemic sclerosis patients. British Society of Rheumatology (Birmingham)

1. Introduction

Systemic Sclerosis (SSc) is an autoimmune disease with the highest disease mortality of all the rheumatological diseases. It has two sub-types, diffuse cutaneous SSc (dcSSc) and limited cutaneous SSc (lcSSc). It can have a devastating effect on the heart, lung, kidney, blood vessels, skin and connective tissue leading, in some cases, to a premature death. Recent advances in treatment for some aspects of this disease have meant that more people are surviving to live with the long-term impact of SSc. Research into the physical and psychological effects of dcSSc and lcSSc continues to emerge. However, there is no framework to describe the impacts of SSc on patient's perceptions of their Quality of Life (QoL), and little research into the effects of disease sub-type on patient-perceived QoL.

The aims of the study are to:

1. Develop a framework to describe and understand the impact of systemic sclerosis (SSc) on quality of life

2. Develop a questionnaire to measure quality of life in people with SSc

3. Use the questionnaire to test the hypothesis that there will be differences in the level of quality of life between people with different subtypes of SSc

The following methodologies will be used to generate the descriptive framework of SSc QoL and to test the research hypothesis:

Qualitative research methods will be used to explore the effect of SSc on patient-perceived QoL and generate a descriptive framework of SSc QoL.

Qualitative data will be used to provide potential items for use in development of the SSc QoL measure. Quantitative techniques, including Rasch analysis, will be used to test the psychometric qualities of the SSc QoL

Both non-parametric and statistical modeling techniques will be used to test the study hypothesis, examining the relationship between disease sub-type and levels of QoL in SSc using the SSc QoL measure.

The thesis is structured as follows:

Chapter Two presents a review of the literature around SSc and its sub-types, outlining its diagnostic criteria, epidemiology, physical and psychological impacts, and its current and future treatments. Rationale for an exploration of patient-perceived QoL, and the research hypothesis is presented. Use of a system to classify the impact of SSc is explored, that of the World Health Organisation (WHO) classification structure, the International Classification of Functioning Disability and Health (ICF, 2001).

Chapter Three presents the developmental history and conceptual viewpoints of QoL in healthcare. The model of QoL chosen for this research, the needs-based model, is explored together with the rationale for its choice.

Chapter Four details the methods used to meet the three study aims. The three aims are met using three separate methodologies. The first study aim, to develop a descriptive framework of QoL in SSc is achieved using qualitative data collection techniques (interviews and a focus group). Techniques for data analysis are discussed and the method selected, thematic analysis, is described in detail. The second study aim, development of a needs-based measure of QoL in SSc is achieved by applying item

selection techniques to qualitative data in order to produce the items of the SSc QoL measure. Rasch analysis is described as the tool used to test the psychometric properties of the SSc QoL and rationale for this choice is explored. Thirdly, in order to test the hypothesis that disease sub-type is reflected in levels of QoL in SSc, a description of statistical approaches is given. This includes exploration of Statistical Equation Modelling (SEM), together with a rationale for its selection in this study.

Chapters Five, Six and Seven present the study results. Chapter Five describes the descriptive framework of SSc QoL and the themes identified from the qualitative data. Chapter Six provides details of the development and psychometric testing of the SSc QoL, and the parametric testing of the study hypothesis. Chapter Seven presents the results of hypothesis testing through the use of Structural Equation Modelling (SEM).

Chapter Eight presents a discussion of the study findings and their implications for clinical practice. The chapter concludes with a summary of key findings and a plan for a future programme of SSc research.

2. Systemic Sclerosis (SSc)

2.1 Introduction to SSc

This chapter describes SSc and demonstrates the potentially devastating nature of this disease and its sub-types. SSc is the systemic form of scleroderma (from the Greek, meaning 'hard-skin'). Scleroderma represents a spectrum of diseases classified as connective tissue autoimmune diseases. The range of diseases labelled as scleroderma span from those which affect only local areas of skin (examples of this form of the disease include conditions called morphea and linear scleroderma) to systemic forms (SSc) which are classified into the sub-types of limited cutaneous systemic sclerosis (lcSSc) and diffuse cutaneous systemic sclerosis (dcSSc).

For many years knowledge of the physical and psychological impacts, pathology and treatment of this rare disease has been sparse. However, in recent years this body of knowledge has substantially increased and this chapter explores this literature, including a description of the diagnostic criteria, aetiology, pathogenesis, epidemiology and treatments for SSc, with particular emphasis on the impact of disease sub-type. A case study is used to illustrate the reality of living with SSc and the care pathway provided for that individual.

Use of the World Health Organisation (WHO) International Classification of Disease, Functioning and Health (WHO 2001) is explored as a framework for the classification of the impact of SSc.

This literature review has been drawn from a search of key databases including Medline, Cinhal and Embase, these searches supplemented by key author searches and a snowball technique of reference discovery.

2.2 Systemic Sclerosis; definition, classification and aetiology

Literally meaning 'hard skin', scleroderma describes a collection of diseases, which at their extreme can result in skin so tight that it can encase the patient making it difficult to move fingers, limbs or the face. This disease is succinctly described as an:

'incurable and potentially life-threatening disease, often associated with a high degree of morbidity and suffering'

(Senecal et al. 2005) p. 1646

There is no single medical specialism taking sole care for these patients (Johnson et al. 2006). Care is commonly dictated by symptoms and therefore patients with SSc may be seen in a range of clinical specialities. In the UK, many patients with the localised form of the disease, (Table 2.1), are cared for by dermatologists specialising in the impact on their skin. Those with the systemic forms of the disease, (SSc), are more commonly cared for by rheumatologists.

There is evidence from a Spanish study that SSc has up to a four fold increase in mortality in comparison with what is described as the 'background' population (Simeon et al. 2003). In recent years there have been key treatment advances in the medical management of people with SSc, particularly in the area of pulmonary artery hypertension (Williams et al. 2005) and many more patients are surviving with this disease. This means

that there are increasing numbers of people who live with the many potentially devastating consequences of SSc.

2.2.1 Diagnostic Criteria

Scleroderma is a term used to represent a spectrum of diseases. The systemic form of the disease is called Systemic Sclerosis (SSc), and has two disease sub-types, diffuse cutaneous systemic sclerosis (dcSSc), and limited cutaneous systemic sclerosis (lcSSc) (Black 1995).

An overview of scleroderma and 'scleroderma-like diseases' is presented in Table 2.1, and illustrates the range of conditions under the umbrella term of scleroderma.

As with many rheumatological diseases, SSc has diagnostic criteria developed by the American College of Rheumatology (ACR). It is these diagnostic criteria that are the internationally accepted definition of diagnosis for SSc, used in clinical trials, research and clinical practice:

American College of Rheumatology (ACR) Diagnostic Criteria for SSc:

- Major criterion: Proximal scleroderma

- Minor criterion: Sclerodactyly, Digital pitting,

- Bibasilar pulmonary fibrosis

  (Masi et al. 1980)

For the diagnosis of SSc, the major criterion and at least two of the minor criterion should be present. Thirty years on there is recognition of the need for review of these criteria, and the American College is currently undertaking this review.

Table 2.1 Spectrum of scleroderma and scleroderma-like syndromes

Adapted from (Black 1995)

Raynauds phenomenon	Raynauds disease (secondary)
	Raynauds disease (primary)
Scleroderma: Systemic Sclerosis	Sub-types:
	Diffuse cutaneous Systemic Sclerosis (DcSSc)
	Limited cutaneous Systemic Sclerosis (LcSSc)
Spectrum of scleroderma: Scleroderma sine scleroderma (no skin involvement) Localised - Morphea (plaque, guttae, generalised) Linear - En coup de sabre Juvenile Chemically induced Environmental/occupational Drugs	
Scleroderma-like diseases:	Eosinophilic fascitis Metabolic Immunological/inflammatory Visceral diseases Eosinomyaligic syndrome Mixed connective tissue disease Overlap syndromes

2.2.2 Anti-bodies associated with SSc

An understanding of antibodies associated with SSc has evolved over the past thirty years. There is an association between particular antibodies and autoimmune diseases, including dcSSc and lcSSc (Senecal et al. 2005). The first stage of autoimmune analysis in SSc is the examination of blood samples to look for the presence of general antibodies associated with

autoimmune diseases such as anti-nuclear antibody (ANA). The presence of ANA has been described as an almost universal feature of SSc with 96% of patients testing positive for ANA (Pudifin et al. 1991). Evidence of specific antibodies strongly associated with SSc is constantly emerging (Denton et al. 2006). Key antibodies identified are anti-centromere, which is associated with lcSSc, and anti Scl 70 (or anti-topoisomerase 1), which is associated with dcSSc.

In diagnostic terms, positive findings for these antibodies are hallmarks of the SSc subtypes. However, as with many diagnostic tests, the absence of these antibodies on testing does not exclude a diagnosis of SSc, and indeed there are many patients with SSc who are ANA positive but who do not have either of these specific antibodies. Other antibodies also aid in the diagnosis of SSc in that they may be associated with differential diagnosis such as Mixed Connective Tissue Disease (MCTD). Further developments also suggest potential links between antibodies and pathologies in SSc (Senecal et al. 2005; Denton et al. 2006). Therefore, antibody testing is a key part of the diagnosis and monitoring of patients with SSc, and offers useful parts of the jigsaw that make up the diagnosis and management of SSc.

2.2.3 Classification systems for SSc and its sub-types

Current literature describing SSc identifies two sub-types of the systemic form of Scleroderma, these being diffuse cutaneous systemic sclerosis (dcSSc), and limited cutaneous systemic sclerosis (lcSSc).

The sub-types of dcSSc and lcSSc are recognised as distinct disease sub-types with different severity and survival (Wollheim 2005; Wilson and Vincent 2006; Denton 2007).

In order to understand the differences between the sub-types and their impact on the health of the individual, several sub-type classification systems have been proposed and detailed classification systems, as discussed by (Haustein 2002), have been published.

It is Le-Roy's classification (Le Roy et al. 1998) that appears to be the basis of the modern classification system. This identifies the two SSc sub-sets identifiable in modern clinical practice and published literature. Le Roy's classification is presented in table 2.2.

Table 2.2 Le Roy's classification. (Le Roy et al. 1998)

Limited Cutaneous SSc	Diffuse Cutaneous SSc
Raynauds phenomenon for years at presentation	Onset of Raynauds phenomenon within 1 year of onset of skin changes
Skin sclerosis limited to hands, feet, face and forearms or absent	Truncal and acral skin involvement
Significance incidence of pulmonary hypertension, trigeminal neuralgia, calcinosis, and telangectasia	Early and significant incidence of interstitial lung disease, oliguric renal failure, diffuse gastrointestinal disease, and myocardial involvement
Dilated nail fold capillary loops, usually without capillary dropouts	Nail fold capillary dilatation and destruction detected by wide field nail fold capilliaroscopy
	Presence of anti-DNA topoisomerase 1 (anti Scl-70)
	Absence of anticentromere antibodies

A comparison of the Le Roy et al classification and the more modern system outlined by Denton (Denton et al. 2006), shows significant similarities in the distribution of skin thickening and the Raynauds history. The earlier Le Roy classification also includes reference to antibody status. Improvements in

techniques for immunological study enabling scientists to identify antibodies has introduced an exciting new dimension to the study of SSc. Denton lends further insight into the immunological links with SSc in his 2006 review of fibrosis in SSc (Denton et al. 2006). This review references many modern discoveries and theories of the association of antibodies with SSc, which are discussed in detail later in this chapter.

The sub-types of SSc are associated with different morbidities and impacts. These are summarized in table 2.3, a more detailed description following in section 2.2.3.1 and 2.2.3.2,

Table 2.3 Differentiation of LcSSc and DcSSc and their associated morbidities - Adapted from (Denton et al. 2006)

LcSSc	DcSSc
Approximately 60% of SSc patients	Approximately 30% of SSc patients
Skin involvement spares proximal limbs and trunk	Skin involvement includes proximal limbs and trunk and may reduce after 18-24 months
Prominent vascular symptoms and Raynauds phenomenon	Prominent inflammatory symptoms at onset, including oedema, arthralgia and pruritus
Associated organ involvements include isolated pulmonary artery hypertension, severe bowel involvement and pulmonary fibrosis.	Associated organ involvement may include renal crisis, lung fibrosis and cardiac disease.
Long duration of Raynauds phenomenon	Short duration or simultaneous onset of Raynauds phenomenon

2.2.3.1 Diffuse Cutaneous Systemic Sclerosis (DcSSc)

The rarer of the two types of SSc (30% of SSc cases table 2.2), dcSSc is typically considered the sub-type with the greater degree of inflammatory disease and fibrosis, (Denton et al. 2006), although it still may have immunological and vascular involvement. As shown in table 2.3, dcSSc is

associated with major organ involvement such as heart, lung and renal disease. Key research articles such as the Steen and Medsger study of severe organ involvement in dcSSc (Steen and Medsger 2000) found that if severe organ involvement occurs early in the course of the disease, the length of patient survival is reduced. This recognition of the early organ damage in dcSSc has led to close monitoring of this patient group and early intervention to slow disease progression.

2.2.3.2 Limited Cutaneous Systemic Sclerosis (lcSSc)

As indicated in table 2.3, lcSSc is the more common of the two SSc sub-types, with over 60% of SSc patients falling into this group (Maddison 2002). lcSSc is characterised by thickening skin which may occur on the face, hands, and distal to the knees and elbows. As discussed below, lcSSc is also associated with the anti-centromere antibody on immunological blood test. Typically considered the sub-type with the greater vascular involvement (Denton et al. 2006), it may be linked with vascular complications such as renal involvement, which until recent therapeutic developments, was a key cause of death in these patients (Maddison 2002).

It may be helpful at this point to explain some historical nomenclature associated with lcSSc. LcSSc has formally been referred to as CREST both in literature and in clinical practice, CREST being an acronym for its symptoms:

C - Calcinosis (lumps of calcium typically lying just under the skin)

R – Raynauds (vasospasm)

E – Esophageal (US spelling) involvement

S – Sclerodactyly (tightened skin over the fingers)

T – Telangectasia (a flattened red spot or rash)

(Denton and Black 2004)

This disease was renamed for pragmatic reasons. Clinically many patients diagnosed with CREST did not actually have all of the five elements of the condition and so, typically, patients notes and letters would be filled with diagnoses such as CREST without calcinosis, or CREST without telangectasia, which indicated that the term was not always representative of the underlying symptoms.

It may also have been noted that lcSSc is sometimes referred to as Limited Systemic Sclerosis. These two terms are used interchangeably.

2.2.3.3 Impact of disease sub-types

The literature described earlier in this section alluded to the difference in impact between the two disease sub-types of SSc. The difference in impact between the two disease sub-types, illustrated in Table 2.2, summarised current literature describing the differences between the two sub-types. The morbidities described in Table 2.3 are explored in sections 2.7,2.8 and 2.9 of this literature review. Together with a description of the morphology itself, these sections also explore the impact of these morbidities on the individuals' activities and their ability to participate in life. Therefore, the morbidities associated with each sub-type may be linked with different impacts upon the life of the individual.

A clear message arising from this literature describing the sub-types of SSc is that disease sub-type is associated with different physical morbidities. This

message is incorporated into the review of impairments in SSc (section 2.7) and serves to inform the hypothesis development in this study which is discussed in detail in 3.5.1.

Whilst SSc research underlines the importance of the sub-types of dcSSc and lcSSc, (Denton and Black 1999; Barst and Seibold 2003), it is recognised that not all patients have their disease classified into these sub-types. A group of clinicians interested in the diagnosis, classification, assessment and treatment of scleroderma are promoting the importance of this classification (the UK scleroderma Interest Group, internationally linked with the scleroderma Clinical Trials Consortium (SCTC) and the Connective Tissue Disease International Scientific Advisory Board (Rubin et al. 2007)). There are guides for clinicians to help them make this classification (Black 1995).

2.2.4 Aetiology

The cause of SSc is unclear but there is consensus that there is a trigger to the pathological processes associated with SSc (Mattucci-Cerinic et al. 2007). There has been much discussion and laboratory research into the role of specific biological triggers of scleroderma. These potential triggers include microchimerism, oxidative stress, genetics and environment, each of which will now be explored in more detail to illustrate the many facets of possible causes of SSc.

2.2.4.1 Microchimerism

Persistent foetal DNA has been found in female patients with SSc who had been pregnant in their past (microchimerism), stimulating the theory that this may be a factor in developing SSc. There are significant questions to be

raised regarding this theory. Literature (appendix1) appears to offer compelling support to the argument to explore microchimerism as a link to SSc.

There are some key questions to answer with regard to the feasibility of the microchimerism theory. For example, how does microchimerism apply to men with SSc? There are findings of Y –chromosome DNA being found in SSc patients who had not carried a male foetus (Arlett et al. 1997) which begs the question as to the origin of this Y-chromosome DNA. These are significant questions that remain unanswered. For readers with an interest in this area, more detail of studies of the theory of microchimerism can be found in appendix 1.

2.2.4.2 Oxidative Stress

The theory that oxidative stress may play a part in SSc pathogenesis has been proposed across several research papers (see appendix 2). The theory proposed is that oxidative stress may be a key mechanism in triggering or maintaining abnormal features of cells involved in SSc pathogenesis. These abnormal features include vascular damage, immune activation, auto antibody generation or fibroblast activation (Denton and Black 1999) . There have been several studies regarding this process. A summary of these findings for the interested reader is available in appendix 2; they are not presented in the main body of this text, as pathogenesis of SSc is not central to this study.

2.2.4.3 Genetics

Patients frequently ask if the disease can be passed on to their children. The evidence here is emerging. In British based research only one family out of

60 had more than one case of scleroderma within the family (Maddison 1986 cited in (Briggs and Welsh 1991). There are case reports of two sisters with SSc (Molta et al. 1989), and identical twins with the disease (Dustoor et al. 1987).

However, there are also reports of a pair of monozygotic twins where one had the disease and the other did not (Guseva et al. 1981). The debate in this area is further illustrated with the statement that SSc is not primarily a genetic disorder (Briggs and Welsh 1991), and twin research which suggests inherited genetic factors are not sufficient to explain the development of SSc in the affected twin, but that inheritance may influence the development of serum antibodies in the non SSc twin (Feghali-Bostwick et al. 2003).

More recent reviews of the genetic factors associated with SSc (Assassi and Mayes 2003; Mayes et al. 2003; Mayes and Trojanowska 2007) present a case for a genetic component to SSc. Links with the underlying pathological processes involved in vascular damage and fibrosis in particular are proposed, although the link between these two processes remains unclear. Also of significance to our understanding of the genetics of SSc is gene profiling. Profiling of SSc skin biopsies has revealed altered expression of approximately 1,800 genes in SSc skin as opposed to 'normal skin' (Gardner et al. 2006), thus giving impetus for further exploration of these differences.

Current literature therefore suggests a genetic link with SSc, but does not yet reveal full understanding of the mechanism of this link. This field of research may yield more understanding of the genetic associations of SSc in the future.

2.2.4.4 Environment

There are several environmental factors that have been proffered as potential effectors to SSc. Environmental agents proposed for implication in scleroderma (Silman and Hochberg 1996) include:

- Silica dust: seen in coal miners, gold miners, and stonemasons.

- Organic chemicals: aromatic hydrocarbons: toluene, benzene, xlyene, aromatic mixes: white spirit, dieselene

- Alphatic hydrocarbons:

- Chlorinated: vinyl chloride, trichloroethylene, perchloroethylene

- Non-chlorinated: naphtha-n-hexane

- Toxic Oil

- Epoxy resins

- Biogenic amines: m-phenylenediamine

- Urea formaldehyde foam insulation

- Drugs: Bleomycin, carbidopa, L-5 hydroxytryptophan, pentazoacine, cocaine, appetite suppressants – e.g. diethylpropion, fenfluramine hydrochloride

- Breast augmentation: silicone – paraffin.

Silman and Hochberg, (Silman and Hochberg 1996), emphasize that no causal link has been established between this list of chemicals and SSc. Environmental exposure is suggested in some men diagnosed with SSc

(Haustein and Zeigler 1985). As early as 1914, links between silica contact and stonemasons was hypothesised (Bramwell 1914), moving through to Bleomycin, vinyl chloride monomer, epoxy resin compounds and organic solvents including toluene, benzene, xlyene and trichloroethylene in later research (Fagundus and Le Roy 1995).

Non-industrial associations have also been discussed, perhaps most significantly the potential link with breast augmentation. The suggestion of a link between breast augmentation and SSc was brought to the fore by a Japanese study (Kumagai et al. 1984). The broader literature was reviewed in 1996 (Wong 1996), including fifteen epidemiological studies on breast implants and connective tissue diseases. It was concluded that the available data did not provide evidence for a causal relationship between silicone breast implants and connective tissue disease (including SSc).

2.2.4.5 Cancer Risk

A suggestion of a link between SSc and cancer was proffered in a report which presented information of a cluster of cases of breast cancer in women with SSc (Lee et al. 1983). Whilst this was not backed up by a later, formal epidemiological study, the later study did suggest a time relation between the onset of the two diseases in a small part of their sample (Roumm and Medsger 1985). A more recent case control design study has been conducted exploring the characteristics of those people with breast cancer and scleroderma (Derk 2007). This research draws conclusions as to the demographics of those individuals with both diseases, but again, a categorical link remains unclear. What has been revealed is a link between

lung cancer in SSc patients, unrelated to smoking but related to pulmonary fibrosis (Peters-Goldern et al. 1985).

2.2.5 Pathogenesis

The underlying pathology of SSc is emerging through recent advances in cellular research. It is clear that the process consists of three processes, and that these phases are interlinked. These components are:

- Fibrotic

- Vascular

- Immunological

(Denton et al. 2006)

Whilst this is key to research into curative treatments for SSc, it is not central to the development of the SSc QoL or testing of the research hypothesis. Therefore, what follows is an overview of the pathogenesis of SSc with more detail available in appendices as referenced.

2.2.5.1 Fibrosis

Fibrosis is one of the three major interlinked pathological processes occurring in SSc, and it features excessive scarring and connective tissue remodelling. The stages of the process of fibrosis are complex and are well described in a review publication (Denton et al. 2006). Thickening and fibrosis of the skin are a key characteristic of this disease (Seibold 1993) with only 1-3 % of patients with scleroderma showing no skin changes (Clements et al. 1993; Black 1995; Silman et al. 1995).

2.2.5.2 Vascular involvement

It is acknowledged that vascular involvement is a central mechanism involved in SSc (Riemekasten and Sunderkotter 2006). Publication of research into the vascular aspect of SSc increased in the 1980s, and has continued to grow as an area of research. SSc vascular research has evolved in many areas such as Pulmonary Artery Hypertension (PAH) and Renal involvement, adding to the body of knowledge about vascular involvement in SSc.

Therefore, in order to present these diverse areas associated with the vascular involvement in SSc, specific areas of research will be presented in section 2.7, described as impairments associated with SSc. These specific areas are PAH, Renal disease, Cardiac disease, and Raynauds Phenomenon. More information on vascular involvement in scleroderma can be found in appendix 3.

2.2.5.3 Immunological component

Immunological involvement is a recognised component of the pathology of SSc (Le Roy 1992; Black 1995; Senecal et al. 2005; Denton et al. 2006), however knowledge of the area continues to emerge. Clinically, immunological evidence has played a helpful role in the diagnosis or sub-typing of SSc since the discovery of antibodies related to SSc, and laboratory methods of testing for them have been developed (Denton and Black 2004). It is proposed by these authors that not only are these autoantibodies useful in diagnosis, but that some of them have a pathogenic role in SSc. It is proposed that anti-topo1 can react with the cell surface in SSc patients. The argument is developed by considering other auto

antibodies such as anti-RNA polymerase 1/111 which is associated with renal crisis in SSc, but not for instance, with fibrosis. The authors also argue that as auto antibodies are often present very early on in the disease and in large numbers that they may be involved in the pathology of SSc; a point further made by the link between the serum concentration of these auto antibodies and SSc severity (Naparstek and Plotz 1993). In contrast, this view of a primary pathogenic role for auto antibodies in SSc has since been questioned (Denton et al. 2006).

The presence of T cells in SSc skin lesions demonstrates immunological associations with SSc. This presence of T cells may vary in intensity and distribution, but the location of these infiltrates around blood vessels and at sites of active deposition of connective tissue re-enforce the link between the immune system and the pathogenesis of SSc (Grand round 1996).

Emerging research is showing cellular moderators involved in SSc. These cellular pathways include:

- Transforming Growth Factor Beta (TGF beta)

- Connective Tissue Growth Factor (CTGF)

- Endothelin (ET)

- Platelet Derived Growth Factor (PDGF)

- Tumour Necrosis Factor (TNF)

(Le Roy 1992; Denton et al. 2006; Abraham and Distler 2007)

2.3 Epidemiology

Fortunately SSc is relatively rare, with an estimated UK prevalence ranging from 20 to 100 per million (Silman 1997). In the USA figures of 276 cases per million adults have been reported (Mayes et al. 2003). This range in estimates of prevalence illustrates the limited data on this small patient group. Its effects are potentially devastating with data from the 1990's showing approximately 50% of patients dying in the first ten years (Silman 1997). Other reports of mortality from SSc found 26% of women and 32% of men to have died within five years of presentation (Bryan et al. 1999). Despite the success of treatments for renal failure (Maddison 2002) and a new era of treatments for pulmonary hypertension, fatal complications are still seen (Black 2005).

2.3.1 Incidence of SSc by age group, gender and ethnic group

The peak incidence of this disease is 45-55 years of age, and it is three to eight times more frequent in women than in men (Silman 1991). The time between onset of symptoms and diagnosis of SSc can range from days to years. Typically there is a long lapse time before diagnosis due to the heterogeneous nature of SSc (Denton and Black 1999), and its many presenting symptoms (Wilson and Vincent 2006). For instance, fatigue and joint pains are common symptoms seen by General Practitioners and it is often only the addition of further pieces of the jigsaw, frequently that of skin thickening, which prompts referral. Therefore, it may take many years for people to be referred into specialist services. Logically this infers that there may be more people living with SSc than currently diagnosed.

A study of a defined SSc female American population reports a survival rate at 7 years from diagnosis as being 81% for those with limited disease, and 72% for those with diffuse disease (Laing et al. 1997). Age adjusted survival was lower in black women than white; this was hypothesised to be because of increased diffuse disease at a rate of 49.6% in black women and 24.9 % in white women in the retrospective study.

A review of the epidemiology of scleroderma found there to be no difference between the distributions of SSc in rural or urban locations (Medsger 1978 cited in (Silman 1991). SSc is found in many non-Western countries such as Japan, USSR, Nigeria, Mexico and in Polynesians in New Zealand (Medsger and Masi 1971). In the UK, higher incidences of SSc were found in small pockets of the population, and these areas were found to be adjacent to international airports (Silman et al. 1990).

2.4 A Patients Experience of SSc

The diagnostic process of SSc can be a long and complex route for many patients (Vincent and Wilson 2006). For others, diagnosis may result from a single acute medical event. The disease is classically defined as heterogeneous (Denton et al. 2006), underlining that its path varies for each individual. Heterogeneity of presenting symptoms may be a key factor in a long lapse time from symptoms to diagnosis. People may present with the consequence of any of the underlying pathologies associated with SSc, namely vascular damage, immunological involvement or fibrosis. In clinical terms, this means there can be a huge range of apparently unrelated symptoms which only amalgamate the diagnostic jigsaw to give the picture of SSc. In many cases, the diagnosis of SSc is finally made when the classic

symptom of skin thickening is noted. A further complication in this diagnostic process is the existence of a group of 'scleroderma-like' syndromes as outlined in appendix 4.

2.4.1 How does SSc affect the individual? – A case study

In order to illustrate SSc and how it may affect the individual, a case study of a person with SSc follows. This case study aims not only to illustrate the pathological effects of the disease, but also to give a sense of the impact of this disease on those who live with it.

Case study – Sylvia.

Sylvia is a 42-year-old woman who is married with two children, Peter aged 13 and Becca aged 11. She is married to John who works as a building labourer and Sylvia works part-time as a nurse. Six years ago Sylvia noticed her fingers swelling which was making some tasks at work difficult. She also felt increasingly tired and noticed that she had some flattened red spots appearing on her skin.

On visiting her GP, she was initially told that she may have some arthritis through 'wear and tear', and to take simple painkillers such as paracetamol. After three months of doing this, she described to her husband that she "felt terrible and she had to do something". She was now unable to perform many of the essential everyday activities such as driving, handling cooking pans, and her fatigue was such that she could no longer concentrate at work and needed to go straight to bed as soon as they had had their evening meal.

Sylvia felt she was losing control over her life and felt too ill to do anything about it.

Her husband had become increasingly worried by Sylvia's symptoms, she had lost her sparkle for life and he saw that she was just getting worse. He made a further doctors appointment and saw a different doctor. This GP felt that Sylvia may have an underlying condition giving rise to these symptoms and contacted her local rheumatology consultant for telephone advice and an urgent out-patient appointment.

Initial out-patient appointment

At this appointment, the rheumatology consultant asked a lot of questions about how long these symptoms had been present, and how they had developed. The consultant also asked if she had any symptoms of breathlessness, ulcers on her fingers, hypertension or kidney problems, or if Sylvia had noticed any changes in her skin. The consultant pinched Sylvia's skin on the back of her hands and on her face and asked if she had any problems with swallowing, heartburn, or with her bowels.

Sylvia told her of colour changes in her finger tips when they were cold, and the pain of the change of colour from white to red when they warmed up.

Blood tests were ordered comprising of:

- A full blood count (red cells, white cells and platelets – testing for signs of anaemia, infection or abnormal platelets)

- Urea and Electrolyte levels – testing for abnormalities in kidney function shown in altered electrolyte levels

- Immunology tests - ANA, and ENA. Testing specifically for double stranded DNA, Anti-centromere, Anti Scl70 (indicators of Limited SSc, Diffuse SSc, Systemic Lupus Erythramatosus)

Other tests

The consultant also requested:

- A chest x ray

- An ECG

- A test of kidney function

Sylvia was also asked to complete a questionnaire outlining her physical function and difficulties (a Health Assessment Questionnaire – HAQ).

A follow up appointment was made for one month's time.

Follow up outpatient appointment

Sylvia and John both attended this appointment as they were anxious to hear the results of the test and desperate for some treatment to make Sylvia feel better. The consultant explained the blood test results and told them that there was some indication of auto-immune disease. By looking at the complete picture from her symptoms such as the rash, the colour changes in her fingers (which she called 'Raynauds'), her fatigue, and the swelling in her fingers a diagnosis of an autoimmune disease was indicated. The question of which auto-immune disease was also a key part of the conversation. Sylvia had heard of a condition called lupus as a work colleague of hers had been diagnosed with this several years ago, and she knew that these symptoms sounded similar.

The consultant agreed that some of these symptoms were similar to lupus, however, there were two elements of her clinical picture which suggested another disease: scleroderma (Systemic Sclerosis). These two elements were a positive anti-centromere immunology blood test, and the flattened red rash (telangectasia) on her face. The consultant seemed to place particular importance to the anti-centromere blood test. It was explained that some symptoms varied, and it was possible to have symptoms which overlapped between autoimmune diseases. A preliminary diagnosis of limited cutaneous Systemic Sclerosis (lcSSc) was made.

Treatment from her consultant

Sylvia and John had never heard of lcSSc. The consultant explained this was a condition that involved the immune system. The doctor said that Sylvia would need close monitoring of her condition for the foreseeable future, in order to monitor any changes in her condition and instigate appropriate treatment at the earliest opportunity.

More investigations were ordered including a CT scan of Sylvia's lungs to check for any signs of fibrosis, and an echocardiogram to check for any indication of pulmonary artery hypertension. It was explained that there was another, more accurate test of this, known as a cardiac catheterisation, however, this was not available locally but was available at the regional specialist centre if indicated. Treatment was instigated for Sylvia's Raynauds in the form of medication and advice. The medication was 10mg of Nifedipine MR (modified release) twice a day in order to improve her underlying circulation. She was told that the specialist nurse would give her

advice on how to manage her Raynauds. Sylvia and John then went to see the scleroderma specialist nurse.

Treatment from the scleroderma specialist nurse

The nurse took Sylvia and John into a room in the clinic and asked how they were feeling and if they had any questions. They said they felt relieved that they had a name for the condition: Sylvia had been worried that she had cancer and felt relieved that it wasn't. However, neither of them had heard of LcSSc or scleroderma.

The nurse explained that this was a condition known as 'autoimmune', referring to the persons own immune system and that it was one of a group of conditions collectively called 'scleroderma'. She explained that it involved a collection of potential symptoms including the flattened, reddened rash called 'telangectasia', fatigue, skin thickening, swollen puffy fingers (in the initial phases of the disease), Raynauds (described as a spasm of the blood vessels), and other symptoms which Sylvia didn't have signs of. These were not listed at this point in order not to overload them with information, but it was explained that this information would be included in a booklet they could have to take home, which came from one of the two patient charities who provided support and information.

The nurse then asked them several further questions about how they were coping with the symptoms. She talked about fatigue and its association with LSSc, and about pacing and grouping of activities in order to preserve Sylvia's energy. She gave them this initial information but said this would be something she would go into in more detail at their next visit. This session was then brought to a close, with a further appointment being made. Sylvia

was given the telephone number of the 'helpline' to ring if she had any queries and to write down any questions they had for their next appointment. The nurse also said that just to be aware that if they sought further information on the disease, many sources of data were out of date or very individual, suggesting scleroderma charity websites if they wanted to seek extra information.

Follow up appointment

The appointment was the following week. Sylvia came on her own as John had already taken a lot of time off work and was concerned that his employers would not like him to be off again. They had talked together about the information they had been given, and about the questions they wanted to ask. When Sylvia came in she had a lot of questions, she said she was really worried as John had looked at the literature and websites and it looked as though she may lose her fingers if the Raynauds was bad, and that people had said their relatives had died of kidney failure or lung or heart disease. The first question Sylvia had was 'can this kill me?'

The specialist nurse explained LSSc had a different path for different people, that it was individual. However, it was known that for a small number of people this condition would be life shortening, but that the treatments for SSc were continually improving. For many people it was a case of treating symptoms as they were identified, hence the need for lifelong monitoring.

This answer was further explained then Sylvia asked about the treatments which were available for the management of SSc. The specialist nurse explained that there were treatments available for many of the complications of SSc, and that although there was no one single drug to cure the disease,

there were many treatments in use for its potential complications. It was also stated that not everyone with SSc had every complication, that it was very much an individual journey and a matter of finding out how it affected her, and developing strategies to cope with it.

The nurse then went on to explain why Sylvia had been commenced on medication for her Raynauds, that it was modified release to widen (dilate) the blood vessels continually in order to minimise the effects of the vasospasm. The nurse asked Sylvia what sort of things or situations triggered these colour changes in her fingers and together they created a list of the situations which triggered these attacks. This list included such things as going out of the house first thing on a cold morning, walking through the freezer section of the supermarket, and standing on the touchline while watching her son play football. They talked about ways of ensuring that Sylvia kept her hands constantly warm, avoiding these changes in temperature for example with the use of layers of gloves and hand warmers.

A plan of care was then developed with Sylvia by identifying the key issues for her and a strategy of self-care to manage these symptoms. The nurse explained key symptoms which required urgent notification, for example: ulcers which wouldn't heal or appeared infected; prolonged Raynauds attacks lasting hours; symptoms of high blood pressure (such as headaches); or prolonged nausea which may be a symptom of kidney disease.

The nurse also referred Sylvia to the occupational therapist, physiotherapist and podiatrist in order for them to make baseline assessments of Sylvia's health and to help her with elements of her self-care such as exercise

therapy, adaptation to any difficulties with her daily activities (such as cooking), problems with her work role and pacing of activities to cope with her fatigue, and how to manage foot care and identify any potential for foot ulceration. Follow up appointments were given for both the specialist nurse and the rheumatology consultant.

Complications of SSc

Two years following diagnosis Sylvia developed sudden onset of breathlessness. She rang the scleroderma helpline run by the specialist nurse and received an urgent outpatient appointment. PAH was suspected and Sylvia was referred to her specialist tertiary centre for cardiac catheterisation that would diagnose this condition if elevated pressures were found within the chambers of the heart.

Treatment for Sylvia's pulmonary artery hypertension

Upon referral to a tertiary referral centre Sylvia had a cardiac catheter examination, this revealed a pulmonary artery pressure of 57mmhg, diagnostic of PAH. She was counselled about these results and her diagnosis. John was with her and they were both alarmed by this diagnosis as they were aware that this a potentially life threatening complication of her LcSSc. They were reassured by the consultant that there was treatment for this condition, and an anti-endothelial drug, (Bosentan), was commenced. This was a tablet to be taken daily which was designed to control the PAH. Sylvia was relieved about this as she had read about people having lines into their heart through which drugs were infused 24hrs a day (Iloprost), and she was relieved she didn't need to have a line in her chest. She had heard

of the associated risk of infection and thought the line might also alter the way John saw her.

Monitoring of treatment

Sylvia had to have her blood taken regularly to ensure that there were no effects on her blood chemistry which the Bosentan could potentially cause.

The Future

Sylvia faces an uncertain future. For as long as the Bosentan continues to be effective and she doesn't have any side effects, she continues to be able to do most of the activities she needs to do, although walking up hills or running with the children is still out of the question. She enjoys each day and just hopes that she will see her children through their school years to adulthood.

Sylvia's story gives a sense of how many people experience SSc and the potentially devastating effect it can have on their lives and the lives of those around them.

2.5 A Framework to Classify the Impacts of SSc

SSc is clearly a complex disease and, as illustrated by the previous case study, its impact on the individual can be just as complex. In order to describe the impact of the disease, an internationally recognised classification system, the World Health Organisational International Classification of Functioning, Disability and Health (ICF), (WHO. 2001) will be used. The ICF classification offers a useful biopsychosocial framework for classifying the complex consequences of SSc.

First published in 1980 and known as the International Classification of Impairments, Disabilities, and Handicaps (ICIDH), it was revised in 2001 in response to criticism of its conceptual limitations, and renamed the International Classification of Functioning, Disability and Health (ICF).

The International Classification of Diseases (ICD) is considered to be complementary to the ICF. The ICD is primarily a classification of health conditions (diseases, disorders, injuries etc), providing what is described as 'an etiological framework' (WHO. 2001). The 'ICD-10' is the version currently used, the '10' referring to the 10th edition. The ICD-10 presents the condition in a numerical form. SSc is classified as a systemic connective tissue disease identified as M 34 (systemic sclerosis) with subdivisions of M 34.0 (progressive systemic sclerosis), M 34.1 (CREST syndrome), M34.2 (systemic sclerosis induced by drugs and chemicals), M34.8 (other forms of systemic sclerosis) and M34.9 (systemic sclerosis, unspecified).

In a move to make the ICF easier for use in clinical practice, the concept of ICF core sets has been developed. This involves working groups developing a set of ICF components which are considered core to a specific condition. Core sets are not in existence for all conditions, but an ICF core set represents some of the more prevalent rheumatological conditions (Scheumringer et al. 2005; Scheuringer et al. 2005; Stamm et al. 2005).

The ICF has developed considerably from its predecessor, the ICDH (Marijke and Vrakrijker. 2003). The ICF now aims to provide classification of components of health which are considered from a body, person and societal level. It is described in its documentation as the conceptual basis for the definition, measurement and policy formulations for health and disability

(WHO website 2002) and is intended for use across five areas: research, clinical practice, statistics, education and social policy. Written with the intent to provide a positive emphasis, more traditional terms such as handicap are replaced to recognise the need for incorporation of the social as well as medical model. It is the intention of the WHO by development of the ICF, to move away from being a consequence of disease classification and become a classification of components of health (WHO. 2001). The ICF therefore classifies the position of the person or population, rather than the disease.

The diagrammatic representation of the ICF which follows (Figure 2.1) is important as it visually displays the ICF and its base in a biopsychosocial model of disability. A key element is that the ICF is based upon a biopsychosocial model of disability, and not a purely medical model (Cardol et al. 2002; WHO website 2002; Sibley et al. 2006).

Figure 2.1 Biopsychosocial model of the ICF

(WHO website 2002)
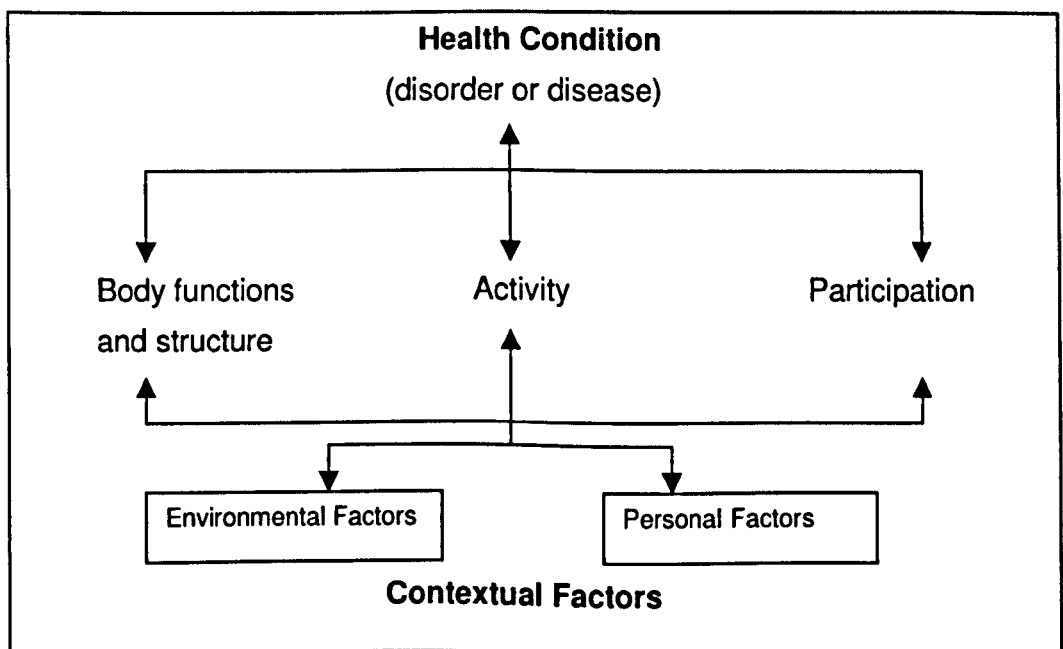
This illustrates the ICF as a dynamic model where there is interplay between the key aspects of body function and structure, activities and participation. The contextual factors identified by the ICF have sparse description, which has led to further explorations of this element of the ICF (Badley 2006).

2.5.1 Definition of terms

A wider description of the ICF is included in appendix 5, however a summary of each key term (WHO 2001) is now given.

Part 1 - Functioning and Disability

Within the ICF, the term 'functioning' refers to all body functions, activity and participation, and 'disability' refers to impairments, activity limitations and participation restrictions.

2.5.1.1 Impairment

Definition: Impairments are problems in body function or structure as a significant deviation or loss.

Impairments represent deviations away from certain generally accepted population standards in the biomedical status of the body and its functions.

2.5.1.2 Activity

Definition: Activity is the execution of a task or action by an individual.

Activity limitations are difficulties an individual may experience in involvement in executing activities

2.5.1.3 Participation

Definition: Participation is involvement in a life situation.

Part 2 - Contextual factors

2.5.2 Environmental and Personal Factors

In an effort to recognise factors which lie outside of the patients control, such as social support, work, laws etc, the ICF addresses contextual influences with the description of personal and environmental factors (WHO 2001). Whilst the ICF does not go any further than recognition of the potential influence of personal factors due to its diversity, environment factors are explored in more detail.

Environmental factors are considered to make up the physical, social and attitudinal environment in which people live and conduct their lives. These factors are external to the individual and their influence on the performance of the individual as a member of society, on the individual's capacity to execute actions or tasks or on the individual's body function or structure, may be positive or negative (Wang et al. 2006). There is some debate regarding the success of this incorporation of environmental factors, (Cardol et al. 2002; Nordenfelt 2003), with the ICF described as a disability model which fails to adequately explore the relationship of external factors to the disability pathway.

2.6 Impact of SSc using the ICF

The ICF presents a framework in which disabilities or health conditions can be associated with all three elements of the ICF, impairment, activity limitation and participation (WHO website 2002). Mapping the impacts of

SSc across the ICF structure of impairment, activity limitation and participation, clarifies the biopsychosocial impacts of this complex disease.

2.6.1 SSc in terms of the ICF

The picture of SSc revealed so far in this study is one of a disease which has both diverse and potentially devastating effects. These effects include impact on the individual's skin, gut (gastrointestinal tract), kidneys (renal involvement), energy levels (fatigue), lung, heart, circulation and psychological profile. Whilst differences between the two sub-types of SSc have been illustrated (2.2.3), there is insufficient literature to discuss their impacts as separated entities. Therefore, the impacts of SSc as a whole will be presented using the structure of the ICF.

2.7 Impairments of SSc

Key aspects of SSc are now presented in relation to their impairment. This will be followed by description of their relation to activity limitation, and then to participation.

2.7.1 The skin

SSc usually effects the skin of the fingers and face (Balbir-Gurman et al. 2002). People who have had this disease for a while say that they look in the mirror and see a stranger looking back at them. Some facial affects of this disease are thinning of lips, beaking of the nose, reduction in lines and for some, small, flattened red spots called telangectasia which can manifest themselves in other areas of the skin.

Sclerodactyly, or tightness of skin over the fingers, is a common skin symptom leading to both reduced function and altered appearance. The skin over fingers appears shiny, taut and often oedematous (puffy and swollen). Oedema and infiltration of inflammatory cells around the blood vessels of the dermis are part of the underlying pathological process within the skin (Denton et al. 2006).

Figure 2.2 – Photographs of skin involvement in SSc

Later phases in the disease often see this oedema settle, but the fingers often remain contracted by the tightness of the skin and tendon contractures (Mayes 1999). This can lead to severe reduction in the range of movement and practical use of fingers with all associated problems with activities of daily living, work and household tasks. The face is also frequently affected leading to characteristic visual symptoms of the disease such as microstomia, and a beaked nose. Patients frequently experience the functional impact of microstomia (DiMarinao et al. 1973) where the ability to open the mouth is reduced.

This aspect of SSc is classified to both lcSSc and dcSSc (table 2.2), what differs is its distribution in each sub-type; in dcSSc the skin can be affected

anywhere on the body whereas in lcSSc it is restricted to the face, arms distal to the elbow and legs distal to the knee.

Therefore, skin impact in hands and face is common across sub-types. However, the impact of skin thickening on the upper arms, legs and on the trunk, and the impact associated with this thickening, is specific to those with dcSSc.

2.7.2 Gastrointestinal (GI) effects

Patients with SSc frequently suffer from symptoms of both upper and lower GI involvement with the majority, 85%, of complaints being linked to dysphasia (difficulty swallowing) and oesophageal hypomotility (Fagundus and Le Roy 1995). Effects on motility (movement of the gut to pass food down through the GI tract) may be found throughout the GI tract with an abnormal response to neurogenic signals being noted in both the large and small intestine (Heyt et al. 2004). In a study of thirty-five patients with SSc twenty-five, (74.1%), demonstrated an impaired or absent rectoanal inhibitory response. This is closely correlated with faecal incontinence. No relation was found between this finding and the disease duration. In relation to this finding and disease sub-type, no link was found (Mayes 1999). However, in the summary of disease sub-type in table 2.2, diffuse bowel disease is associated with dcSSc.

Reduced downward pressure within the oesophagus allows acid to reflux back through the cardiac sphincter of the stomach leading to profoundly painful 'heartburn' symptoms, particularly at night (Denton and Black 1999).

Other associated complications are that of primary biliary cirrhosis and wide mouth diverticular in the large intestine (Fagundus and Le Roy 1995) and effects on the lower bowel such as the rectal sphincter.

2.7.3 Renal involvement

Renal crisis occurs typically early on in the disease process with estimates ranging from the first 3 years of diagnosis (Fagundus and Le Roy) to the first 5 years (Denton and Black 1999) and possibly in association with worsening skin involvement (Steen and Medsger 1998). Early symptoms of renal disease are described as malaise and headache. Until recent years, renal crisis was the main cause of death in patients with SSc, occurring in 20% of patients with dcSSc (Steen et al 1990 cited in (Maddison 2002)). This is a significant finding, and supports the for the difference in impact between the two disease sub-body of evidence that there is a different disease impact between sub-types

The cause of renal disease in SSc is vascular damage, thought to be endothelial injury. Intimal thickening of renal arteries leads to decreased renal perfusion affecting the juxtaglomerular apparatus which in turn leads to increased rennin production causing hypertension (Maddison 2002). SSc renal disease is thought to be marked by RNA polymerases (Okanao 1993 cited in (Denton and Black 1999).

2.7.4 Fatigue

Fatigue has been recognised as a major debilitating problem for patients with rheumatic illness (White 1998; McKinley et al. 2005; Hewlett et al. 2007). Fatigue is described as having far-reaching impacts on the life of the individual, and an appropriate outcome measure for fatigue in rheumatoid

arthritis is currently being investigated (Hewlett et al. 2007). Within the field of SSc, fatigue is mentioned as a key symptom on patient organisation websites, but is markedly absent from healthcare publications.

This review found no literature describing the impacts of fatigue in SSc by sub-type.

2.7.5 Interstitial Lung Disease (ILD)

The pathogenesis of ILD has several components such as alveolar inflammations, interstitial fibrosis and vascular abnormalities, with the hypothesis that there may be another event or process as yet unclear (Silver and Clements 2003). Survival for those with SSc and interstitial lung disease is inversely proportional to the amount of restriction present for that individual: 10 year survival ranging from 87% for those with no ILD, to 75% with moderate ILD, and 58% 10 year survival in those with severe ILD as cited (Khanna et al. 2007).

ILD has been associated with the diffuse sub-type of SSc (table 2.2). The most recent, large, randomised control trial of the treatment of ILD in those with SSc (Khanna et al. 2007) did not identify the sub-type of its study participants and therefore no conclusions can be drawn as to the incidence or impacts of disease sub-type and SSc from that work.

There is a strong case for early detection and early treatment of ILD because for those with severe ILD, their loss in lung function occurs more significantly in the earlier years of the ILD diagnosis, therefore commencing early treatment may help to preserve more lung function. Treatments for ILD in SSc are being reviewed. A recent study of oral cyclophosphamide showed the requirement to treat six to seven patients in order to achieve a clinically

meaningful improvement in one persons functional ability above that of a placebo drug (Khanna and Merkel 2007).

2.7.6 Cardiac Involvement and Pulmonary Artery Hypertension

Cardiac involvement in SSc includes pericardial effusion, myocardial inflammation or fibrosis and conduction (Kahan and Allanore 2006) with cardiac complications seen in 10% of SSc patients (Denton and Black 2004). Described as a pathology which has silently killed people with SSc, cardiac disease is a key issue, however there is still much to learn of the pathology of myocardial ischaemia in SSc (Mattucci-Cerinic and Seferovic 2006).

PAH is associated with cardiology as it requires right heart catheterisation for accurate diagnosis and therefore patients are frequently referred into cardiac services for their diagnosis and treatment. PAH is defined as a mean pulmonary artery pressure (pap) exceeding 25mmHg at rest, or 30mmHg during exercise (Faber and Loscalzo 2004; Black 2005). It may be classified as a stand-alone condition (Primary PAH) and as such has a mortality of 45-60% within the first two years from diagnosis (Magliano et al. 2002). However, there is a known association of PAH with autoimmune rheumatic disease (Mukerjee et al. 2003) and when associated with SSc (SSc PAH), the survival is suggested to be 55% (Kawut et al. 2003) although an element of this perception may be accounted for by research design and clinical technique (Black 2005). PAH is the most prevalent complication of SSc, affecting approximately 15% of SSc patients (Black 2005). SSc PAH is of prime concern for clinicians and their patients.

PAH is diagnosed clinically by use of cardiac ultrasound, or more accurately by cardiac catheterisation to estimate the pressure within the right ventricle.

Its cause is associated with the vascular impact of SSc or secondary to interstitial lung disease (Hachulla and Coghlan 2004). Until recent years there was little treatment for SSc PAH. However pharmacological developments have meant that treatments are available (Riemekasten and Sunderkotter 2006). These treatments include drugs such as prostacyclins (such as Iloprost), which may be administered via continuous intravenous infusion and more recently by inhalation. Iloprost has been the stalwart of therapy until the evolution of the current new era of therapies. The use of an endothelin receptor antagonist (ERA) is revolutionising therapy (Veale and Belch 1993; Hachulla and Coghlan 2004).

2.7.8 Raynauds phenomenon (RP)

First described by Maurice Raynaud in the 19th century, RP is a spasm of the blood vessels. RP presents in 'attacks' where the blood vessels are stimulated to constrict, commonly referred to as a spasm of the blood vessels. These attacks are commonly triggered by a change in temperature, stress or in some circumstances emotional stress (Belch 1991; Hennes and Wigley 2007). The areas affected by this vasospasm are commonly the extremities such as the fingers, ears, feet and end of the nose with affected areas undergoing a characteristic tri-phasic colour change. In the ischaemic phase the affected area appears white, then blue (cyanotic phase), then red (reperfusion) (Herrick 2005). There is increasing evidence to suggest that RP may affect internal organs such as the cerebral, coronary, pulmonary and mesenteric circulations (Marq et al. 1986).

RP is sub-divided into primary and secondary. Primary Raynauds is a stand-alone condition being found in approximately 10% of the population (Olsen

and Neilson 1978). Secondary Raynauds is where the RP accompanies a disease such as SSc, rheumatoid arthritis, and systemic lupus erythmatosus. RP links are seen at a clinical level in RP secondary to SSc. The time of onset of RP may also give diagnostic clues in SSc with a sudden onset of RP in middle age or later life being a warning sign of the potential association with a secondary condition such as SSc.

The pathogenesis of Raynauds phenomenon is outlined in a review of this subject (Herrick 2005), where the vascular, neural and intravascular elements of pathogenesis are explored.

2.7.9 Ulceration

People with SSc may also be affected by the secondary consequences of the disease as may be seen in the lower limb with vascular pathology (Wan et al. 2001) which lead to reduced blood flow manifesting in reduced Ankle brachial pressure index or ABPI (La Montagna et al. 2002). The foot may be affected by this vascular insufficiency leading to ulceration which in turn affects mobility (Milio et al. 2006). Ulceration may be painful and this can lead to insomnia, the inability to carry out paid or unpaid work, and the inability to participate in social and family activities. At it's worst ulceration may lead to amputation of part of the foot, or even the lower limb.

Ulcers of the extremities are often linked with prolonged or profound RP attacks. Digital ulceration is frequently sited on the fingertips and over the interphalangeal joints. They are often painful and limit the activities of the patient. If infected, they can lead to osteomyelitis and soft tissue infection (Korn et al. 2004). Treatment for digital ulceration should be prompt in order to avoid amputation. A mainstay of hospital based treatment is intravenous

Iloprost (Denton and Black 2004), with more modern treatments such as

Bosentan offering promise of prevention of new ulceration (Korn et al. 2004).

2.7.10 Pain in SSc

Research into pain in SSc patients has not been widespread but is

documented in the typically small studies seen in the SSc population often

documented as a comparison measure amongst others (Faber and Loscalzo

2004). Pain (measured by visual analogue scale reported in a value of 0-3),

is reported as correlated with both the physical and mental components of

the SF36 Health related QoL measure (Georges et al. 2006). A 'bodily pain'

question is one of the eight questions within the SF 36, however the authors

report pain as a high correlation across several aspects of the SF 36.

2.8 Activity Limitation

The impairments of SSc are now shown in their impact upon activity

limitation. The literature in this area is less abundant than that published

around impairment. There is little information available on the activity

limitation associated with renal disease, Raynauds phenomenon, ulceration

and fatigue in SSc. More general information on these impacts is given

where available.

2.8.1 Physical function

Physical function is a key feature of much research in SSc, as measures of

function such as the Health Assessment Questionnaire (HAQ) (Fries et al.

1980), and its derivation, the Scleroderma Health Assessment Questionnaire

(SHAQ) (Steen and Medsger 1997) are frequently used as outcome

measures in SSc studies. The importance of this is the Disability index

element of the HAQ and SHAQ which provides a body of evidence of the effect of SSc on physical function.

Impairment of physical function have been shown in many SSc studies (Steen and Medsger 1997; Khanna et al. 2005). Research has illustrated that those with dcSSc report poorer physical function that those with lcSSc (Steen and Medsger 1997; Benrud-Larson et al. 2002).

2.8.2 Skin involvement

Microstomia frequently leads to difficulties with day activities such as eating (those with SSc often struggling with the cold remains of a meal while those around them have finished), dental care, and kissing. Whilst this information may be recounted by individuals on SSc websites, no publications were found in this area. The effect of skin thickening on fingers, sclerodactyly has been mentioned in relation to its pathology, and there are wider SSc studies using function as a comparison, (Benrud-Larson et al. 2002; Richards et al. 2003; Johnson et al. 2006). However, there is little mention of the direct effect of skin involvement on activity limitation save a mention that it can make day to day functioning difficult (Vincent and Wilson 2006).

2.8.3 Gastrointestinal involvement

The activity limitation associated with GI tract involvement in SSc include the requirement to alter eating habits (not eating late at night, avoiding spicy food) and sleeping position in combination (Mayes 1999). In a qualitative study of disease and symptom burden in SSc, (Suarez-Almazor et al. 2007), patients identified difficulty swallowing and digesting some foods, constipation and diarrhoea, pain and bloating.

The use of medication such as Proton Pump inhibitors is frequently required to control these symptoms (Khanna et al. 2007). Symptoms found in the lower GI tract include altered bowel habit such as constipation (Mayes 1999), combined with reduced responsiveness of the rectal sphincter which may lead to faecal incontinence (Heyt et al. 2004). The activity limitation associated with this, or the fear of incontinence is not documented.

2.8.4 Pulmonary Artery Hypertension (PAH)

The pathological mechanisms of PAH have been described (Faber and Loscalzo 2004). Clinically the disease may present with symptoms of breathlessness on exercise or a reduced ability to exercise, this may lead to breathlessness on climbing a hill or the stairs and at later stages also occurs at rest. Other symptoms, which occur at the later stages of the disease, include chest pain or syncope (faint) on exercise.

2.8.5 Interstitial Lung Disease (ILD)

Activity limitation in SSc patients with ILD is focused around outcome measures of disability such as the Health Assessment Questionnaire, Short Form 36 and dyspnoea scores such as Mahler's dyspnoea index (Khanna et al. 2007). Unfortunately detail on the activity limitations found in SSc populations with ILD is not explicit, however breathlessness and a cough are characterised as common symptoms of lung disease in SSc (Mayes 1999).

2.9 Participation

The body of literature relating the impact of SSc on participation is minimal. This is in contrast to the growing literature regarding impairment in SSc and the associated links made with activity limitation. Minimal information is

however available in some areas of participation, much information arising from a single qualitative article, (Suarez-Almazor et al. 2007), which explores potential effects on the participation of the individual. This body of literature is now described.

2.9.1 Skin involvement

There are potential psychological associations with these skin manifestations such as altered body image (Benrud-Larson et al. 2003), and reduced self-esteem (van Lankveld et al. 2007). Each of these has a potential effect on the individual and their desire or ability to participate in life as they would wish. No explicit evidence in available in this area but appearance self-esteem appears to be linked to acceptance and anxiety (Benrud-Larson et al. 2003), and body image is a significant factor for women with SSc (van Lankveld et al. 2007). A qualitative study exploring the experience of living with scleroderma (Joachim and Acorn 2003), explicitly explored the effect of the rarity of the disease and its visible signs. This research revealed that patients with visible signs of scleroderma were conscious of being different from others.

2.9.2 GI effects on Participation

The symptoms of GI involvement have been documented. It is logical to assume that these symptoms lead to problems in participation, and this is supported by a qualitative study of the disease and symptom burden in SSc where GI symptoms were identified as the most prevalent and disruptive physical symptoms (Suarez-Almazor et al. 2007).

2.9.3 Renal impact on participation

Whilst there is little information on the renal impact upon participation in SSc patients, more general renal literature suggests that patients with chronic kidney disease experience fatigue, nausea and vomiting, headaches, the need to urinate frequently, numbness in hands and feet amongst other impacts (Foundation 2006).

The effects on the individual's ability to participate in life can only be surmised but the breadth of the effects of renal disease indicate significant potential effects upon the individual's ability to participate as they would wish.

2.9.4 Fatigue

The implications of fatigue extend far beyond the more common experience of tiredness that cannot be compared, with SSc patients reporting both mental and physical fatigue. Patients with SSc have stated that due to their fatigue they don't feel like going out, and they had become a 'couch potato' (Suarez-Almazor et al. 2007). This links with the social life aspect of participation described in the ICF (WHO 2001), illustrating this impact of SSc.

2.9.5 Work

Work is a participation listed within the ICF structure (WHO 2001) where aspects of work such as work preparation, training, acquiring, keeping and terminating a job, remuneration and types of employment are outlined. Work disability has been described as a common outcome in other rheumatological conditions (De Croon et al. 2004), with impact on both the individual and societal level. There is little research into work participation in

SSc, however a study of pain and depression in SSc found that those who were unemployed reported poorer social adjustment than those who were not (Benrud-Larson et al. 2002).

2.10 Mapping of SSc Outcomes against the ICF

Having seen how some of the symptoms of SSc relate to the ICF, it is important to see how outcome measures used to assess these symptoms and their treatments map against this framework. The rheumatology outcome measures group, OMERACT (Outcome Measures in Rheumatology) 2002, considered outcome measures for SSc and applied the OMERACT filter (a set of criteria of validity which outcome measures must match) to SSc outcome measures (Merkel et al. 2003).

The measures identified by OMERACT are presented below in Table 2.4, together with additional mapping of the measures against the ICF. This illustrates that participation and QoL are not represented.

Patient-perceived QoL

Patient-perceived QoL refers to QoL measures which have been developed using the patient as the expert informant, providing the items which will form the measure. These differ from measures which have been developed with healthcare professionals in the role as expert informant providing their items to form the measure.

Despite further publication in the area of measures of response, or outcome in SSc, (Khanna and Merkel 2007; Valentini and Mattucci-Cerinic 2007; Khanna 2008), the gap in the availability of participation and patient-perceived outcomes of QoL in SSc perpetuates.

The OMERACT outcomes do not include a measure of patient-perceived QoL in SSc.

Table 2.4 Mapping of OMERACT outcomes in SSc outcomes against the ICF

Domain	Validated Response Variable	ICF Classification
Cardiopulmonary	Right heart catheterisation. Vital Capacity	Impairment
HRQoL/Function	The 20 item disability index of the Health Assessment Questionnaire (HAQ)	Activity
Raynauds	Raynauds Condition Score (RCS) MD Global for Raynauds. Digital ulcer derived VAS.	Impairment
Renal	Serum Creatinine. Complete blood count (fragmentation of RBC, haemolytic anaemia) in Renal crisis.	Impairment
Skin	Modified Rodnan Skin (thickness) score	Impairment
Gastrointestinal	Need for total parenteral nutrition (tpn). Pseudo obstruction.	Impairment
Global	Death Cumulative survival rate.	Impairment

2.10.1 Disease specific outcome measures in SSc

There is evidence that patient questionnaire scores are able to predict mortality more effectively that other traditional methods (Carreira 2006). Therefore, literature beyond OMERACT was reviewed to identify further

disease specific measures for use in SSc using key databases such as Medline, Embase, Cinhal and key author searches. Once identified from the literature, the measures were subjected to a process of critical appraisal. This appraisal aimed to identify any measure which was a patient-perceived measure of quality of life developed with SSc patients as the expert informant. This appraisal took the form of a checklist of key elements:

1. Was the measure developed specifically for use in the SSc population?

2. Were patients/participants with SSc acknowledged as the expert informants in the development and testing process?

3. Was the measure based on a taxonomy of QoL? If a QoL taxonomy, which approach to QoL, such as Subjective Well Being (SWB)?

The measures identified in the literature are outlined in table 2.5, together with their appraisal. To describe this appraisal in more detail, each measure is now explored.

The Self-administered Systemic Sclerosis questionnaire (SySQ) (Ruof et al. 1999), is based on a disability taxonomy and therefore measures a range of physical symptoms such as pain, stiffness, coldness, complex functions, strength of hands and rising. Whilst it was developed from patient input, it is a measure of disability, not a measure of QoL.

The UK Functional Index is an eleven-item questionnaire focused around physical function in scleroderma whilst developed specifically for use in SSc; again it is not a QoL measure

The SHAQ has already been mentioned (2.8.1), this being a measure based upon the Health Assessment Questionnaire (Fries et al. 1980), but with the addition of five visual analogue scales to measure Raynauds phenomenon, digital ulcers, gastrointestinal symptoms, lung symptoms and overall scleroderma respectively. Interestingly, the disability index of the HAQ/SHAQ has been referred to as a Quality of Life measure in one study, (Johnson et al. 2006), although it consists purely of physical activity questions. Therefore, the SHAQ, whilst including a vas of QoL is not designed as a QoL measure, and its sole QoL question does not have a stated QoL approach.

Table 2.5   Analysis of SSc specific measures

Measure Identified	Developed specifically for use in the SSc population	Patients with SSc acknowledged as expert Informants	Taxonomy of QoL	Approach to QoL e.g. HRQoL, SWB
Scleroderma Health Assessment Questionnaire (SHAQ)	Core HAQ measure for Rheumatoid arthritis with later additions for SSc	No, additions developed by clinicians	No – Measures disability but with an additional single VAS of QoL.	No approach identified
SSc Self-administered questionnaire (SScSQ)	Yes, developed for SSc population	Yes	Based on Nagis disability taxonomy	N/A
UK Functional Index (Score) (UKFI)	Yes, developed for Scleroderma SSc population	No – Delphi technique with healthcare professionals	No – disability	N/A

A small study in SSc utilizing the World Health Organisation QoL

(WHOQOL) measure was identified, which revealed there was no significant

difference between the HRQoL (as described in Chapter 3) of people with

dcSSc, and lcSSc (Hyphantis et al. 2007). This was not included in table 2.5

as it is not a disease specific measure.

The analysis of disease specific measures for use in SSc presented in table

2.5 found no measures which met the criteria as a patient-perceived

measure based on a QoL taxonomy. Therefore, this presents a gap in the

toolkit available to assess the impact of SSc on the individual.

2.11 Psychological burden of SSc

Having demonstrated the physical impact of SSc, the area yet to explore is

the psychological impact of the disease. Studies published about the

psychological aspects of SSc appear to come from a mixture of two

methodological backgrounds. Firstly there are papers which present an

exploration of the personality or psychological characteristics of the

individual with SSc such as depression and body image. Secondly are

papers which explore the association between the physical and

psychological impact of the disease. The effect of disease sub-type on

psychological burden in SSc is discussed in some papers, but has not been

addressed as the focus of research.

2.11.1 Psychological characteristics of people with SSc

Publications which have explored the psychological characteristics of people

with SSc, frequently use a methodology where patient reported outcome

measures (PROMs) are administered to patients supplemented by

occasional physician led assessment of their psychological characteristics (Straszecka et al. 1996; Angelopoulos et al. 2001). The rationale for the choice of each PROM is frequently based on literature from existing research in other medical conditions, rather than an existing theoretical framework. The volume of literature exploring the psychological associations of SSc is far outweighed by that focusing on the physical aspect of the disease. This is despite broader medical evidence of the relationship of emotion and psychological issues to patient outcome (Sireling et al. 1985; Dorian and Garfinkel 1987).

However, various aspects of psychology have been studied in SSc patients for example Angelopoulos, (Angelopoulos et al. 2001), who found significantly increased levels of depression, anxiety, somatization, interpersonal sensitivity and obsessive-compulsiveness in females with scleroderma, in comparison with a healthy female population. Hostility, in particular guilt, was also significantly higher in the scleroderma group. Whilst this was a small study (thirty women with scleroderma, not specifically SSc), and thirty-five healthy women, these results generate initial information suggesting the psychological impacts in SSc.

Several aspects of the psychological burden of SSc have been studied in more detail, including depression, body image and adaptation.

2.11.2 Depression in SSc

A systematic review of depression in SSc (Thombs et al. 2007), concludes that symptoms of depression are common in those living with SSc and suggest routine screening for depression in these patients. A body of evidence has been growing regarding the impact of depression in SSc.

Studies in SSc focusing on depression or including depression as an outcome measure have supported the evidence that depression (and often anxiety), are present at significant levels in those living with SSc (Roca et al. 1996; Straszecka et al. 1996; Matsuura et al. 2003; Legendre et al. 2005)

2.11.3 Body image

SSc is associated with classic changes in appearance previously discussed in section 2.7.1. In addition, there may also be effects on how people feel about their sexuality, or their physical ability to have a full sexual relationship (Mayes 1999). The impact of this can be broad. In terms of SSc research this has been presented as 'body image dissatisfaction' (Benrud-Larson et al. 2003) or 'appearance self-esteem' (Malcarne et al. 1999). This latter work focused on the effect of skin thickening distribution and its associated impact on self-esteem and psychological distress. Body image is an aspect of SSc that is not commonly addressed in clinical care, other than by provision of limited voluntary services providing 'camouflage' make-up. The fact that only two studies were identified around this area of SSc illustrates the low priority this is given within health provision. For individuals living with SSc this may well be a key issue for which they can find little support or help.

2.11.4 Adaptation in SSc

Adaptation or adjustment emerges as a theme from the literature regarding psychological aspects of SSc. Demographic variables have been found to explain little of the variation seen in patient adjustment to SSc (Moser et al. 1993); with this study of ninety four SSc patients showing educational level, functional ability, illness-related uncertainty, hardiness and social support as significant predictors of adjustment in SSc. A larger study of two hundred

and forty two people with SSc in the same year, (Malcarne and Greenbergs 1996), found wishful thinking, blaming self, and problem-focused coping appearing as predictors of psychosocial adjustment in SSc.

From the perspective of research into QoL in DcSSc and LcSSc, it is of particular interest that disease sub-type whilst related to distress, was not a predictor of distress, (Malcarne and Greenbergs 1996), nor indeed were demographics. In a later, UK based study of forty nine patients with SSc, it was found that physical elements such as disease sub-type, skin score and functional ability did not determine the beliefs and symptoms of those with SSc (Richards et al. 2003).

2.11.5 The relationship between physical and psychological impacts of SSc

Several studies have been conducted exploring relationships between psychological and physical measures in SSc populations. In line with the ethos of linking the physical and the psychological, many authors use the HRQoL model of QoL (explained in chapter 3). These studies, including (Moser et al. 1993; Malcarne and Greenbergs 1996; Roca et al. 1996; Benrud-Larson et al. 2002; Richards et al. 2003; Danieli et al. 2005; Legendre et al. 2005; Eklund and Sandqvist 2006; Malcarne et al. 2006), use a wide range of measures of disease impact. Findings from such studies appear mixed, but many present some level of association between the physical and psychological impacts of SSc. For example, a strong correlation with disability and depressive symptoms was found in SSc (Danieli et al. 2005), and reduced physical function and abnormal GI function were found to be significantly correlated with depression (Nietert et al. 2005).

There appears to be variation in the literature as to the strength of links between the physical and psychological impacts of SSc, with findings that psychological characteristics seen in SSc patients, such as anxiety and depression, are not directly related to the physical impact of the disease (Roca et al. 1996). Also, beliefs of SSc patients about their disease, are not ruled by disease sub-type, skin score, functional ability or severity of digital ischaemia (Richards et al. 2003).

In conclusion, evidence of links between the psychological and physical characteristics of those with SSc is varied and remains an area of research which requires further development.

2.12 Current Treatments for SSc.

Treatments for SSc have broadened due to an increased focus in this clinical area over the last five years. This is reflected in the formation of groups of interested clinicians such as the Scleroderma Clinical Trials Consortium (SCTC) and the UK Systemic Sclerosis Interest Group. Treatment strategy consists of regular assessment of organs which may become affected, combined with early treatment of disease once it has been identified. SSc affecting a single organ may trigger drug therapies, but treatments often take the form a systemic therapy.

Whilst in the past there have been some broad treatments used to reduce underlying inflammation, currently treatments are usually focused around the organ or symptom affected in each individual patient. The new generation of therapies for symptoms associated with SSc include drugs such as the endothelial inhibitor Bosentan, used in people with PAH. A key issue in the

treatment of PAH is its diagnosis. It has been an issue that the most commonly used screening tool for PAH, echocardiogram, may not be accurate enough to detect PAH (Mukerjee et al. 2003).

In SSc renal disease angiotensin converting enzyme (ACE) inhibition has been a focus for research and clinical practice. The search for therapies which can protect injured endothelial cells, which in turn prevent platelet aggregation and the release of platelet and endothelial derived mediators continues (Maddison 2002).

Until recent years, the mainstay of treatment for PAH has been continuous infusion of prostacyclins, such as Iloprost. However, there are issues with their administration, as they are frequently administered through a central venous line in-situ, entering the patient through an incision in the chest wall. These lines are a potential risk of infection and also may become blocked. Researchers have sought other routes of delivery for prostacyclins (Wigley et al. 1998) and also for development of new therapies such as endothelial receptor blockers. Such drugs are now commercially available. These endothelial antagonist drugs such as Bosentan are in tablet form making them much more flexible to a patients lifestyle. Their administration by daily tablet is a major breakthrough in the treatment of SSc PAH (Hachulla and Coghlan 2004).

2.13 Future treatments for SSc

The focus for future therapies in SSc is to address the key pathological pathways, (Table 2.6), which if investigated may prove to be successful in

producing a targeted therapy that addresses the underlying pathogenesis of SSc.

Table 2.6 - Attenuation of key pathways in systemic sclerosis: agents for evaluation (Denton 2007)

Candidate therapy (drug)	Target pathway
Bosentan	E T a/ E T b pathway (Endothelin)
Imatinib	PDGF receptor signalling
Infliximab	TNF – alpha
Adalimumab	TNF – alpha
Etanercept	TNF – alpha
CAT – 192	TGF beta
GC- 1008	TGF beta 1, 2, 3
FG-3019	CTGF ligand
Alefacept	LFA3/CD2
Basiliximab	IL-2Ralpha
MLM – 1202	CCR2
Efalizumab	LFA/ICAM-1

Key:

Transforming Growth Factor Beta (TGF beta); Connective Tissue Growth Factor (CTGF); Endothelin (ET); Platelet Derived Growth Factor (PDGF);Tumour Necrosis Factor (TNF);Lymphocyte Function Associated (LFA);Chemokine Receptor (CCR);Intracellular Adhesion Molecule (ICAM)

2.14 Summary of Chapter 2

This chapter has presented a review of the literature around SSc and used both a case study, and the framework of the ICF, to illustrate its profound physical and psychological impacts. There appears to be a lack of clarity in the evidence regarding links between the psychological and physical impacts of SSc, and a paucity of qualitative literature regarding patient-perceived effects of SSc was revealed.

The disease sub-types of dcSSc and lcSSc have been described together with emerging evidence of their individual associated morbities. The physical impact of disease sub-type on the individual has been identified, raising the question as to the wider potential impact of disease sub-type.

The chapter has concluded with a summary of current treatments for SSc together with a description of future treatments under development.

3. Quality of Life

This chapter discusses the concept of Quality of Life (QoL). The history of QoL is outlined and the two underpinning contexts of QoL assessment, the societal and individual, are discussed. In relation to assessment of QoL within healthcare, the concepts of health related quality of life (HRQoL), and Subjective Well-being (SWB) are discussed in more detail.

The rationale for selection of a conceptual model of QoL for use in the development of the SSc QoL is explored. The chapter concludes with exploration of the needs-based model of QoL as the model of choice for the SSc QoL.

3.1 QoL

It is customary to begin exploration of a concept with a definition. In relation to QoL, definition is perhaps one of the most challenging aspects of this exploration. There is no one commonly accepted definition of QoL, rather a variety of definitions, their use based upon the ideology of each author. Therefore, this section will begin with an exploration of the history of the concept of QoL and some key approaches to QoL before returning to the issue of definition and the definition to be adopted for this research.

It has been commented that:

'The quality of life construct has a complex composition, so it is perhaps not surprising that there is neither an agreed definition nor a standard form of measurement'.

(Cummins 1997)

The lack of consensus around a definition of QoL illustrates the many different ways in which this construct is interpreted. In turn, this has led to many different conceptual bodies of thought within the field of QoL research, each passionate about their own view. A commonly agreed definition of QoL for reference and use seems beyond our current grasp. However, definitions of QoL are not difficult to find (Bowling 2001; Rapley 2003). Definitions range from those that acknowledge the individual nature of QoL to those that focus on specific areas of the range of things that can influence QoL. They vary so much that a review has proposed a taxonomy of the definitions of QoL. This taxonomy divides definitions into:

- Global definitions (general and all-encompassing)

- Component definitions (definitions which break QoL down into components or dimensions)

- Focused definitions (definitions referring to one or a small number of the components of QoL)

- Combined definitions (as the name suggests, a definition which combines the over-arching and component elements of QoL)

    (Farquhar 1995)

This taxonomy works well in illustrating the complexities and volume of definitions which populate QoL literature. It also makes some very clear and pragmatic points about QoL research. For example, it underlines the need for researchers to clearly define their own interpretation or definition of QoL for the reader. There is in fact a long history of QoL, and it is often defined differently. There may be several reasons behind this lack of consensus,

which may become clearer with an understanding of the history of QoL development.

3.2 History of QoL

Our modern day views of QoL have evolved over many years. A summary of this development is given in Figure 3.1 which presents a timeline of the prominence of QoL models over the past fifty years.

Figure 3.1 A timeline of the prominence of QoL conceptual models in the mid to late 20th century. Abstracted from conference presentation (Tennant 2006).

1950	1960	1970	1980	1990	2000
Subjective Well Being ---					
Health Status ---					
Health Related QoL ---					
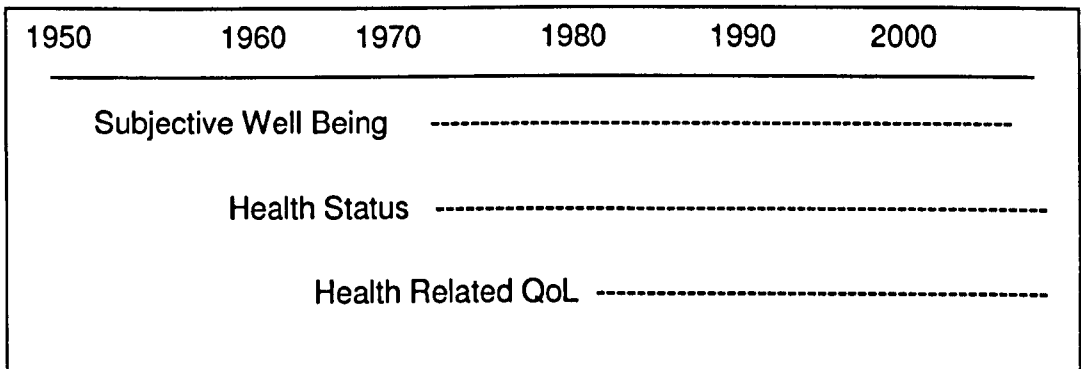
QoL has historically developed along two lines, firstly the social construct (Bowling 2001) which measures of the state of whole populations such as the social indicators movement of the 1960's. Secondly, QoL measures have developed along the micro level, looking at QoL on an individual, subjective level. On a conceptual level, QoL publications appear to divide into health related and non-health related models, and on an application level they divide into those models applicable to populations and those applicable at an individual level (Wilson and Cleary 1995; Spilker and Revicki 1996; Rapley 2003).

These can be represented in a simple diagram (Fig 3.2) below, which is the author's summary of the literature in this area.

Figure 3.2 QoL levels of assessment
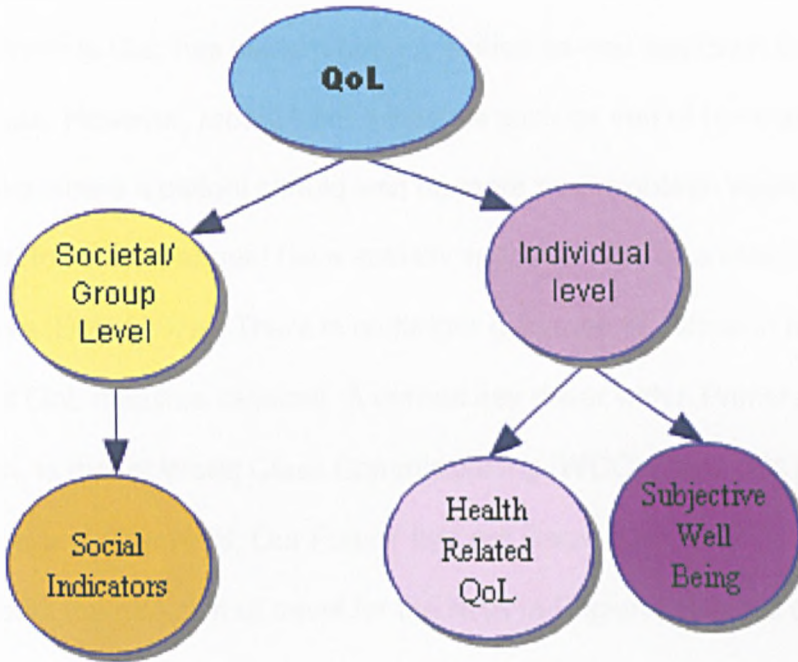
This diagram illustrates the two key levels for the study of QoL, that is at the population or the individual level, and the conceptual approaches to QoL of Societal indicators, Health Related QoL and Subjective Well Being.

3.2.1 NHS healthcare and QoL

In some ways, this has been seen within the healthcare agenda for sometime. From a governmental viewpoint, quality of healthcare services have been measured in terms of accessibility, with mention of involvement of patients and the public in the development of services. The requirement of

NHS healthcare services to ask the question of the effect of healthcare on the individual's quality of life is a much more recent one.

Current NHS guidance for healthcare provision requires patient and public involvement in service planning and evaluation. This involvement should be on both an organisational and an individual level. Interestingly, individual or patient group QoL has seldom been specified as one approach to gathering this input. However, recent NHS initiatives such as that of the eighteen week initiative where a patient should wait no more than eighteen weeks from referral to initial treatment have actually specified QoL as a measure for this initiative (DoH 2007a). There is no further guidance or definition as to the type of QoL measure required. A current key driver within Primary care in the UK, is that of World Class Commissioning (WCC) (DoH. 2007b), and the NHS review, 'Our NHS, Our Future' by Lord Darzi, (Darzi 2007). These represent the direction of travel for the NHS in England over the coming years, and both documents contain drivers for the development and use of Patient Reported Outcome Measures (PROMs). The term 'PROMs' and 'Patient Reported Outcomes' (PRO's) are used interchangeably within this study.

As there are such pressures within NHS healthcare delivery, and indeed within private healthcare provision, requirements to show measures of 'success' such as improved QoL are increasing. This has meant in some cases that, as previously mentioned, there may be a tendency to measure that which is easy to measure, hence the use in many cases of a health status measure of QoL such as disability. Also, it cannot be underestimated that the conceptual definitions of QoL may not be at the forefront of the

clinicians or managers mind when considering the definition or tool to meet their QoL reporting requirements (as seen in the lack of specification in NHS guidance (Dazi 2007; DoH 2007a). Whilst this may address aspects of the drive for healthcare professionals to obtain information labelled as quality of life, it underlines that there is a huge potential for difference in perspective between those evaluating these measures. This point is illustrated by studies such as an interview-based study of people with chronic obstructive pulmonary disease (Leidy and Hasse 1999). The authors propose that what they term 'personal integrity', (interpreted as quality of life by Rapley commenting on their findings), is not an isolated assessment but related to the lived experience of the individual.

The Department of Health commissioned a large study, (Johnston and Pollard 1996), into outcome measurement in chronic disease incorporating the older WHO classification of emotional, impairment, disability and handicap (ICDH). This study examined several outcome measures used within chronic disease management and assessed if they should be used separately or brought together to represent a construct of Quality of Life. The research findings found little support for the WHO model of the time, the ICIDH (see section 2.5), and found that emotional outcomes and impairment were distinct constructs from the others studied.

3.2.2 Pharmacological drivers for QoL assessment

The US Food and Drugs Agency (FDA) exerts significant influence over current priorities within pharmaceutical companies wishing to use QoL as an outcome for their produce. The FDA controls the licensing of new drug therapies within the US, including setting criteria as to the outcomes

expected for each pharmaceutical trial and in turn the claims which can be made with regard to the drugs researched. Therefore the outcomes selected by the FDA become core outcomes for pharmaceutical research which then spread across national boundaries. There is a history of debate regarding QoL and FDA guidance (Lewis 2001). In 2006 the FDA published an online paper 'The Importance of Patient-Reported Outcomes... Its all about the Patients' (FDA 2007), there was discussion by the FDA describing patient reported outcomes as 'any aspect of a patient's health status that comes directly from the patient, without the interpretation of the patient's responses by a physician or anyone else'

Not surprisingly, this FDA publication discusses the push from pharmaceutical companies to claim an improvement in patients quality of life, and its own stance in seldom allowing these claims to be made in pharmaceutical literature.

3.3 Assessment of QoL

The development of QoL illustrated two levels of QoL assessment, (figure 3.2), that is the societal level and the individual level. These are explored in more detail together with a description of some of the models used to operationalise them within healthcare.

3.3.1 Societal Indicators

To explore these in a little more depth, the rapid development of what were to be termed 'social indicators' during the 20th century can be traced through a series of historical events and conceptual movements. Such a conceptual movement, commonly referred to as the 'Chicago school', (Rapley 2003),

was at its height in1930s and 40s America. A commentator on the developments of social indicators, (Noll 2000), offers further insight into the social indicators movement.

For example, in the 1950s, the work of Drenowski (United Nations) was notable in its focus on 'identifying components of welfare and by constructing retrospective indicators (Noll 2000). The political and social climate of the 1960s and 70s was considered conducive to the rapid adoption of social indicators at a population level. Intellectual drive of the time also focused on social indicators. Social indicators remain a key focus of national information such as the UK Social Trends report, and indeed form a key part of much of the information gathered at census and in a wide range of other government data around health and social care in the UK on which health priorities such as National Service Frameworks (NSF's) are based (DoH. 2008).

However, whilst the 1960s and 70s were a time of economic development, this brought with it a questioning of money and material status as the measure of success at a population level. It has been suggested that this questioning brought with it a much more complex concept of QoL which emerged as an alternative to the view of the societal goal being directly related to affluence (Noll 1996). This was known as the Individual QoL movement.

3.3.2 Individual QoL movement

The multi-dimensional view of QoL, which arose at this time, has been referred to as the American quality of life (Rapley 2003). This model moved away from the concept of societal indicators at a population level, but rather

looked toward the individual level of QoL. In the 'German' approach described by Noll, individual welfare of QoL is defined as:

'good living conditions which go together with positive subjective well-being'

(Noll 2000)

3.3.3 Health Related Quality of Life (HRQoL)

HRQoL is a model of QoL. It is stated to measure impairment and activity limitation and, until recently, HRQoL was referred to as 'Health Status' (Tennant 2006). It is possible to see both terms in contemporary healthcare literature. The term HRQoL was introduced to restrict consideration to outcomes considered to be easily assessed. Akin to the broader term QoL, HRQoL suffers from a plethora of definitions. Perhaps the neatest definition offered is that of Carr and colleagues who conclude that health related quality of life is the gap between our expectations of health and our experience of it (Carr et al. 2001). Other definitions of HRQoL offer that common theme that this aspect of QoL is related to health or the experience of health.

There is some confusion regarding the terms of HRQoL and QoL within healthcare publications. Attempts to define Quality of Life have used the term QoL and HRQoL interchangeably to mean 'the patients' personal morbidity – that is various effects that illnesses and treatments have on daily life and satisfaction' (Muldoon et al. 1998).

HRQoL is focused around physical health and disability, assuming that they are the key factors influencing QoL. There have been two major drives towards the development of outcome measures based on HRQoL. The first

of these was Karnofsky and Burchenal 1949 (cited in (Bowling 2001) .

HRQoL measures are commonly seen both in clinical practice and research

as assessments of clinical outcome such as the Stanford Health

Assessment Questionnaire HAQ (Fries et al. 1980), or the EuroQoL (Group

1990). They are based on the premise that QoL in the context of health is

directly related to the physical or physiological impact of the disease on the

individual.

Domains considered integral to HRQoL vary greatly depending upon the

model of HRQoL being used. Medical practice in the UK traditionally favours

a concept of HRQoL which focuses upon four main domains as described in

a lengthy article published in the BMJ (Muldoon et al. 1998). These four

domains are described as:

- Physical functioning

- Mental functioning

- Mental well-being

- Physical well-being

The proposed domains of HRQoL range from the simple model presented by

Muldoon and colleagues, to more complex models such as that offered by

Fayers and Machin who describe the following elements:

- General health

- Physical functioning

- Physical symptoms

- Toxicity

- Emotional functioning

- Cognitive functioning

- Role Functioning

- Social well-being and functioning

- Sexual functioning

- Existential issues

(Fayers and Machin 2000)

Whilst there appears no definitive list of the domains covered by these terms, the literature does appear to agree on a mixture of physical and emotional elements, and the ability to differentiate between domains.

3.3.4 Quality Adjusted Life Years (QALYs)

QALY measures are those where years of life are balanced with the QoL of those years, giving a statistic as a result. The work of Nord (Nord 1992a) offers a good description to the development of QALY measures. For health economists, these tools provide a method of comparison across medical interventions by giving a scale of 1.0 for healthy to 0.0 for dead through mathematical calculation of the respondents answers. The QoL information required for this calculation comes from measures of HRQoL such as the WHOQoL (WHOQOL 1998), or the EuroQoL questionnaire (Group 1990).

QALYs have been described as a common currency with which to assess the sustained benefits from interventions (Phillips and Thompson 1998), however their use presents an area of contention.

This contention arises from the apparent application of a value to an individual's life, with concerns that these may lead to interpretation that death is preferable to a low quality of life as related to euthanasia, and that QALYs may also be used to justify rationing of healthcare: debates presented in Rapleys review of QoL research (Rapley 2003).

3.3.5 Health Utilities

Utility measures are rated by the individual in response to individual goals, risk taking and preferences given set hypothetical states (Rapley 2003). Similar to the QUALYs, utility measures also give a numerical scale of 1.0 for perfect health to 0.0 for death.

Three main techniques fall under the umbrella of utilities: time trade off; standard gamble; and direct rating scales all sharing a common element, that is that the respondent is given options which they have to rate. Health utilities receive similar critique as that presented for QALYs (Rapley 2003).

3.3.6 Subjective well-being (SWB)

SWB is an individual measure of QoL, considering life satisfaction: why and how people experience their lives in positive ways (Deiner 1984). It is associated with three key elements. Firstly, as suggested in the name, it is subjective and individual and has been described as residing within the experience of the individual (Campbell 1976 cited in (Deiner 1984). Secondly, SWB contains positive measures and does not focus on the absence of the negative, and thirdly, SWB measures include assessment of all aspects of the persons life, usually with the use of an integrated or global assessment of the individuals life (Deiner 1984).

3.3.6.1 Domains of SWB

As seen in the previous section, a dominant author in the area of SWB

research is Ed Diener. His publications are at the fore of the literature in this

area and the model of SWB he describes is based on domains of happiness,

pleasant emotions, life satisfaction, and a relative absence of unpleasant

moods and emotions (Deiner and Biswas-Diener 2000).

There is some challenge to this model. A seven domain model of SWB

consisting of Productivity, Intimacy, Safety, Community and Health has also

been proposed (Cummins 1996). Whilst these domains could be seen to be

in line with the twelve domains, Cumming's key variation is that of QoL as a

biologically determined brain state.

This conceptual exploration presents us with two basic conceptual

viewpoints underpinning SWB, one being temperament and personality as

key influences on peoples happiness, the other that of adaptation, where

over time people adapt to both the good and bad and therefore these have

less or no affect on their SWB (Brickman and Campbell 1971). However, the

reality of the wider literature around SWB is that these two basic viewpoints

are expressed through a variety of proposed models. Examples of these

models of SWB are presented in table 3.1.

The range of models of SWB described in Table 3.1 show not only the

variety of thoughts on the influences underpinning SWB, but also reveal

several other aspects of this view of QoL, and more debate in this area is

seen in review publications (Deiner and Biswas-Diener 2000).

Table 3.1 Examples of Models/theoretical approaches to SWB

Example of Authors	Description of model	Description analysis of model
(Costa and McCrae 1988)	Temperament and personality as underpinnings to whether people are happy	Considers extraversion and neuroticism as the personality traits important to peoples propensity to react to events.
(Brickman and Campbell 1971)	Adaptation model based on the 'Hedonic treadmill'	This model principally states that over time people habituate to both good and bad events so that these circumstances will no longer influence SWB. This is further supported with research into lottery winners in particular (Brickman et al. 1978) and seriously disabled people (Silver 1982 as cited in (Deiner and Biswas-Diener 2000)
(McKenna 2004a)	Goal theory	People have more positive effect if they succeed at their particular goals, and indeed if they have important goals. This is supported by (Oishi et al. 1999) who found students valued good results as a predictor of their satisfaction.
Csikszentmihalyi 1997 cited in (Deiner and Biswas-Diener 2000)	Theory of Flow	In this model, the key to happy life is seen as engagement in interesting activities, with interesting being seen as a balance of challenge and skill.

3.3.6.2 Schedule for the Evaluation of Individual QoL (SEIQoL)

Emerging in the early 1990s, an individual QoL measure tool was developed known as the Schedule for the Evaluation of Individual QoL (SEIQoL) (McGee et al. 1991). This is a QoL tool where the individual outlines the areas of their QoL they wish to address by means of a semi-structured interview with a health care professional. Evolution of the initial SEIQoL measure led to the Direct weighting procedure for Quality of Life Domains (SEIQoL-DW), the use of which is outlined in the schedule administration

manual (Boyle et al. 1993). SEIQoL offers an individual measure of QoL. It does however have its limitations. For example it may be difficult to use in a cognitively impaired individual or one who cannot participate in the required interview process.

3.3.6.3 Needs based QoL

The needs based model of QoL is based on a theory of human need expressed in 1954, and reviewed in 1970 and 1987 (Maslow 1970) . Abraham Maslow, an American psychologist, was considered radical in his time for his belief in theories based on the concept that the individual is an integrated organized whole. In the context of Maslow's motivational theory and the needs based model applied to QoL assessment, need is a construct.

This construct forms the basis of Maslow's motivational theory, where needs are seen in a hierarchical design. The 'push and pull' of human motivation are described by Maslow as 'drivers and needs'.

Motivational theories refer to those theories which seek to explain why people do what they do. For Maslow, his implicit belief in the wholeness of the individual influenced his motivation theory with the belief that the whole individual is motivated rather than just a part. His motivational theory also looked at what he called the 'means to the end' where he uses the example of buying a new car (Maslow 1970). Maslow describes a situation where we want a new car because our neighbour has a new car and we don't want to feel inferior to them. The new car maintains our self-respect and so we can be loved and respected by others. There are however needs which are an end in themselves, for example the respect and love previously mentioned. These needs tend not be instantly obvious, but are described as a

conceptual derivation of those things we desire. This leads to the conclusion that motivation must consider human desires or needs. Maslow's motivation theory states that our human motivation is dependent on the need to fulfill need at various levels (Maslow 1970).

Maslow's motivation theory and exploration of needs has been translated into the 'needs based theory' of QoL through the work of Hunt and McKenna. Their adaptation of this theory for the development of a needs based QoL measure was that of the QLDs or Quality of Life in Depression measure (Hunt and McKenna 1992). Hunt and McKenna identified that there was frequently a lack of theoretical base for QoL measures: their work looked to models of human motivation to provide this theoretical basis. This theoretical basis, that of Maslow's motivational theory that we are motivated or driven by needs, forms the basis of the needs based QoL. Hunt expresses the premise of this model to be that:

'life gains its quality from the ability and capacity of the individual to satisfy certain human needs'

(Hunt and McKenna 1992)

In the needs based model, QoL is high when most human needs are fulfilled and low when few needs are satisfied. The needs based model clearly links directly with the individual and their subjective view of QoL and the disability paradox. The model has been used in the development of several condition-specific QoL instruments which include measures of adult growth hormone deficiency (Homes et al 1995), recurrent genital herpes (McKenna and Doward 1995), migraine (McKenna and Patrick 1995), rheumatoid arthritis (RAQoL) (De Jong et al. 1997), and ankylosing spondylitis (Doward et al.

2003). The model therefore has shown to be applicable across a range of chronic conditions.

Key to the needs based methodology, as developed from the literature review of Hunt and McKenna, is a list of 'needs crucial to quality of life'.

These needs are described as:

- Food, drink, sleep, activity, sex, pain avoidance.

- Warmth, shelter, security, safety, freedom from fear, stability

- Affection, love, physical contact, intimacy, attachment, communication, sharing experiences, sharing goals, affiliation

- Curiosity, exploration, play, stimulation, enjoyment, creativity, meaningfulness

- Identity, status, recognition, approval, appreciation, usefulness to others, respect, competence, self-esteem, mastery, achievement, power, independence, freedom

- Time, structure

- Self-actualisation

(Hunt and McKenna 1992) p.312)

These were translated into a topic list for qualitative interviews required for the QoL development which is discussed in Chapter 4.2.

3.4 Adaptation and response shift

Whilst it is not the focus of this research, the concept of adaptation to disease, reflected in research terms as a Response shift, is a key consideration in outcome measurement.

Literature around adaptation specifically in SSc, has already been presented (see section 2.11), demonstrating the many manifestations of adaptation. Wider theories of adaptation to changing health exist, suggesting that as people adapt to their disease and its consequences, they re-orientate their expectations of life (Schwartz and Sprangers 2000). Therefore, people who have adapted may assess their QoL differently due to their adaptation rather than to any fundamental physical change in the effects of their disease. In terms of measurement of QoL, this concept is proposed to relate to response shift.

3.4.1 The Disability paradox

The disability paradox focuses on the fact that many people with physical disability would judge themselves to have a good QoL and are not necessarily constrained by their physical handicap. It is based on a 'salutogensis' theory of Sol Lavine (cited in (Albrecht and Devlieger 1999), who sought explanation of how people may manage well despite poor health.

The research of Albrecht and colleagues presents results of semi-structured interviews with 153 people with disabilities, showing 54.3% of their respondents with moderate to serious disabilities reporting a good or excellent QoL (Albrecht and Devlieger 1999), thus presenting a clear

argument against direct relationship between physical disability and poor QoL, hence the disability paradox.

For those reporting a poor QoL in this study, interviews revealed QoL was dependent upon establishing a balance between body, mind and spirit in the self, and harmonious relationships in a social and environmental context (Albrecht and Devlieger 1999). This clearly illustrates that in this study, QoL was dependent upon much wider aspects of life than the purely physical.

An individual example of this paradox is that of Stephen Hawkins. A scientist of worldwide eminence, a husband and father, his disability leaves him wheelchair bound and unable to speak independently, but appears to have little effect on his perception of QoL (Hawking 2008). Here is distinct evidence that QoL is not directly related to the severity of the disease.

3.5 Impact of SSc and the needs based model of QoL

The impacts of SSc and its sub-types have shown to be diverse, with a biopsychosocial model of disability, (the ICF), being selected as the framework for classification of its impacts (section 2.5). A model of QoL, which accommodates this diversity, is required as the conceptual base for this study of QoL in SSc.

The needs-based model of QoL (discussed in section 3.3.2.3), has been shown to be applicable to a range of chronic diseases and precedence for its use is seen in a variety of publications (McKenna et al. 2004). It demonstrates a wider view of QoL than HRQoL, recognizing the internal interactions of need within the individual. It fits with the patient-perception

model of QoL required for this study. Therefore, the needs-based model of QoL has been identified as the model of choice for this study.

3.5.1 The Hypothesis

The research hypothesis of this study has been drawn from the evidence presented in the literature review presented in this study (chapters two and three). This review has revealed the diverse and potentially devastating effect of SSc, particularly emphasizing the different morbidities associated with each of its sub-types, dcSSc and lcSSc.

The differences in impact of SSc by sub-types have been illustrated throughout the literature review described in chapter 2; specifically in section 2.2.3, which explains the differences between the physical impacts of the disease sub-types. This literature gave a clear message that the sub-types of SSc have different physical impacts and therefore leads to ask the question does disease sub-type influence other impacts of the disease. Section 2.11 illustrated the psychological associations with SSc, but there were confused messages regarding links with disease sub-type and psychological impacts.

Literature exploring the conceptual basis for QoL revealed two key approaches, subjective well-being (SWB), and health related QoL (HRQoL). This review illustrated that the viewpoints differ, HRQoL associating QoL directly to health status, and SWB focusing on the patients perspective of their QoL. No studies of QoL led from the patient perspective of SWB were found, despite studies interviewing patients directly (Joachim and Acorn 2003; Suarez-Almazor et al. 2007). No tool for measuring SWB in people with SSc was identified.

In summary, the literature review has given three key messages. Firstly, there is little known about the impact of SSc on QoL from the patient perspective. Secondly, there is no tool available to measure QoL in SSc from the patients' perspective; and thirdly dcSSc and lcSSc are associated with different physical morbidities but how this impacts on patient perceptions of QoL is not known.

Based on the findings of this literature review, the study will seek to fill this knowledge gap by setting three study aims:

1. Develop a framework to describe and understand the impact of systemic sclerosis (SSc) on QoL.

2. Develop a questionnaire to measure patient-perceived QoL in people with SSc

3. Use the questionnaire to test the hypothesis that there will be differences in the level of QoL between people with different subtypes of SSc.

3.5.2 Summary of Chapter 3

Chapter three has summarised concepts of QoL, and the key drivers for QoL measurement in healthcare. Two models of QoL have been explored in detail: Health Related Quality of Life (HRQoL) and Subjective Well-Being (SWB). The concepts of adaptation in healthcare, and the disability paradox have been described.

The QoL model of choice for this study has been identified as a patient-perceived model of QoL, that is, the needs-based model. The study will have three components. Firstly, there will be an exploration of patient-perceived

QoL in order to develop a descriptive framework of SSc QoL, secondly development of the SSc QoL measure, and thirdly testing of the research hypothesis that disease sub-type is reflected in levels of patient-perceived QoL in SSc.

4. Methods

This chapter outlines the methods used to meet the three study aims which were outlined in the introduction to this thesis. The study aims to:

1. Develop a framework to describe and understand the impact of SSc on quality of life

2. Develop a questionnaire to measure quality of life in people with SSc

3. Use the questionnaire to test the hypothesis that there will be differences in the level of quality of life between people with different subtypes of SSc.

The study will use both qualitative and quantitative methods as appropriate as outlined in a summary diagram in Fig 4.1 below. Figure 4.1 outlines the methods used within this study. Whilst these are presented as three separate processes, there were many actions which were carried out in parallel or were inter-dependent for example Figure 4.1 outlines the methods used within this study.

4.1 Developing the descriptive framework of QoL in SSc

The descriptive framework of QoL in SSc will provide insight into the impact of SSc from the patient perspective. The methodology selected to develop the descriptive framework of QoL in SSc is based on qualitative data gathered from those living with SSc. Methods of gathering qualitative data, and for its analysis, are now described together with the rationale for selection of the methods employed within this study.

Fig 4.1 Summary of study methods

Column 1 (red boxes):

Study Aim: Develop a framework to describe and understand the impact of SSc on QoL

↓

Qualitative data gathered by interviews and focus group (data also used for item selection in SSc QoL development)

↓

First stage of thematic analysis - familiarisation with the transcripts

↓

Second stage of thematic analysis. Second researcher review

↓

Third stage of thematic analysis

Refine definitions

↓

Use of themes to identify overarching themes

Second researcher review

↓

Use of overarching themes and themes to develop the descriptive framework of QoL in people with SSc

Column 2 (blue boxes):

Study aim: Develop a questionnaire to measure QoL in people with SSc

↓

Identification of DcSSc and LcSSc sample populations via the National Scleroderma database

↓

Data base cleansing: by disease subtype, deceased status, address and cross check with PAS system

↓

Anonymisation of data for computerised randomisation into two study sample groups– First postal and Test/retest

↓

Item selection process (detail in 4.2.1

↓

Development and post out of first postal questionnaire (90 item SSc QoL)

↓

Rasch analysis of the first postal questionnaire. Revised version of questionnaire postal out for Test/retest analysis

↓

Rasch analysis of test/retest data.

SSc QoL 29 items

Column 3 (green boxes):

Study aim; Test the hypothesis that there are differences in levels of QoL between difference sub-types of SSc

↓

Data entry from the postal questionnaires used in the development of the SSc QoL

↓

Non-parametric testing of SSc QoL against disease sub-type

Structural Equation Modelling of QoL in SSc using the SSc QoL measure and comparator measures to explore the link between disease sub-type and QoL in SSc

↓

Conclusions of the hypothesis testing based on parametric and SEM analysis

Figure 4.1 presents three separate processes, however, there were many actions which were carried out in parallel or were inter-dependent such as the SEM process was dependent upon data gathered during SSc QoL (this inter-dependency indicated by use of an arrowed line from one process to another).

4.1.1 Methods for gathering qualitative data

As outlined in figure 4.1, the qualitative data gathered in this research will be used in two ways. Firstly, thematic analysis of the data will provide a descriptive framework for QoL in SSc. Secondly, an established approach for development of a needs based QoL measure, (Hunt and McKenna 1992; Tennant et al. 2004), will be applied, involving identification of statements which will become items for use in the SSc QoL. This later analysis is outlined in Figure 4.2.

There are many strategies available to gather qualitative data, (Morse and Field 1998). These range from one to one interviews between a researcher and participant to observation of situations or people by a researcher external to the experience (Miles and Huberman 1994).

The data collection methods within this study are based on recognition that the patient is the expert informant. Therefore, the qualitative data required for development of the descriptive framework of SSc QoL, and the SSc QoL measure, are gathered directly from patients living with this disease. This was carried out by one to one interviews and a focus group. The data collected from these interviews also formed the descriptive framework on which further data collection was based.

4.1.1.1 Sample technique

Sample sizes in qualitative research do not apply rules of quantitative sample size calculation (Holloway and Wheeler 2002). This is because sample size within qualitative research is dictated by other factors such as feasibility and the depth and duration of interviews (Britten 1995).

This topic is discussed in more detail (Holloway and Wheeler 2002), where issues such as people, context and time, and description of access to the sample are identified through review of the literature in this area. To summarise, the purpose of this qualitative research is to explore the experience of QoL for those with SSc. Three things will therefore dictate the size of the sample based on:

- population traits considered potentially relevant to QoL in SSc

- data saturation

- resources of the researcher.

4.1.1.2 Qualitative Sample Frame.

The conceptual base for the needs based QoL is focused around the holistic needs of the individual. This would suggest that it is unnecessary for a sample frame based around purely physical characteristics of the population. However, the elements of the sample frame were adapted to account for the expectations of clinicians caring for these patients and precedent in selecting representative subjects for needs base QoL interviews (Doward et al. 2003). The sample frame for this study includes patients of both disease sub-types, of young and older patients, of those who have had their disease for a short or long time and, as far as possible, a mixture of men and women.

The rationale for these groupings is closely related to literature review of SSc. SSc affects many more women than men (Silman 1991; Mayes 1997), therefore, it was recognised from the distribution of SSc, that there would be few males with SSc to approach.

There is evidence of the different paths of SSc, and that for some people the first few years of the disease may be aggressive and lead to poor outcome (Steen and Medsger 2000). This presents the rationale for including participants with both short and long disease duration within the sample frame. As Steen and Medsgers' work used five-year criteria, a division of disease duration into above and below five years was used. With regard to age, the sample frame aims to represent age groups of younger and older people to include a sample representing the younger and older SSc population. Disease sub-type is included as an element as the sample frame to allow exploration of the effects of disease sub-type.

The population of SSc nationally is small (approximately three thousand patients being recorded on the UK National Scleroderma database). This means there are not enough potential participants to divide the sample into any more detailed grid squares. The sample frame used to identify patients for the qualitative interviews is presented in Table 4.1. It was aimed to fill each cell in this sample frame with at least one interviewee. Data saturation would then determine when recruitment ended.

4.1.1.2.1 Data Saturation

The question of how many interviews are enough is encapsulated in the concept of data saturation. In qualitative data this has been described as the point at which no new information is observed in the data (Guest 2006). In

research using sixty in-depth interviews, saturation was reported to be seen in as little as twelve interviews (Guest 2006). Within the field of needs based QoL development a standard amount of qualitative interviews appears to be around thirty interviews (Hunt and McKenna 1992).

However, in development of needs based measures intended for use in different countries, sixty two to sixty five interviews were required in order to include interviewees from each of the countries involved (McKenna et al. 2004)

Key issues for debate surround data saturation. For example, is the data saturation affected by the order in which data is collected from respondents, or the ability of the respondents to provide data. For example, if the first participants to be interviewed were people who were able to express themselves eloquently more data could be generated than from participants who were unable to express themselves. The order of participant interviews is arbitrary, and therefore this element of data saturation in qualitative research must be open to a large degree to chance.

In order to study data saturation in more detail, this study proposes an innovation to the standard QoL development protocol by tracking items (statements/items in the QoL questionnaire). This research will track items through from the interview transcript to the QoL measure itself. This process of item tracking will provide a new aspect to needs based QoL research that is identification of the point of data saturation required for the items of the QoL measure itself.

4.1.1.3 Exclusion and Inclusion Criteria for the sample

Interview participants were required to be aged 18 or over, to have an American College of Rheumatology diagnosis of dcSSc or lcSSc (as seen in Chapter two), and be to able to participate in a verbal interview conducted in English. Participants were required to give written informed consent as per ethics approval.

Potential participants who did not fit these criteria were excluded. The criteria for English speaking interviewees were used for three reasons. Firstly, the SSc population of the rheumatology centre was solely English speaking. Secondly is the need to interpret closely not just the word but the intonation of the words expressed within the interview process. And finally, this was due to the cost, both in time and money, of advertising and conducting this research in multiple languages when there was no evidence of non-English speakers with SSc in the recruitment site.

Table 4.1 - Sample frame for qualitative data collection

	DcSSc	LcSSc
Age 18 -50 female disease duration (dd) of < 5 years		
Age 18-50 male dd < 5 years		
Age 18-50 female dd > 5 years		
Age 18-50 male dd > 5 years		
Age 50 + female dd < 5 years		
Age 50+ male dd < 5 years		
Age 50+ female dd > 5 years		
Age 50 + male dd > 5 years		

4.1.1.4 Research management and governance approvals

In line with the Research Governance Framework 2001, 2005, ethical and research and development (R&D) approval was sought for this study. This approval was obtained from the Leeds West Ethics committee, and the Leeds Teaching hospitals R&D in 2003. A protocol amendment was received for methodological developments, which were the additional focus group, and extension to a multi-site study to enable the researcher to access the Royal Free Hospital in London. The Royal Free Hospital is the base for the National Scleroderma Database. R&D approval was sought and gained from the R&D department at the Royal Free Hospital London (2006), in order to access this database and send out the postal questionnaire required for development of the SSc QoL.

4.1.1.5 Sample recruitment

The aim of the recruitment process was to recruit at least one interviewee from each sample grid cell. Options for patient recruitment considered were:

- Advertisement in areas where patients congregate such as out-patient waiting rooms

- SSc Patient organisations

- Patient SSc events

- Advertising in sites of healthcare provision such as GP surgeries

Due to the rareness of SSc and the potentially wide geographical spread of patients who were members of SSc patient organisations, these options were not followed. Interviewees for this study were recruited by advertising

the research project amongst SSc patients attending a hospital based

rheumatology outpatients department. Those who expressed an interest in

participating were given study patient information in accordance with the

inclusion/exclusion criteria. As the demographics within SSc patients are

heavily weighted towards older females, it was accepted that the amount of

participants in each cell may reflect these demographics, although every

effort was made to recruit participants in each of the sample grid cells.

Participants who were given the Patient Information sheet (as approved by

the ethics committee) had a minimum of 24 hours in which to consider their

consent. If they wished to participate, an appointment was made at a venue

of their choice, normally hospital or home. Informed consent was obtained at

the time of interview.

4.1.2 Qualitative Interviews

Implicit in the needs based model of QoL is recognition of the patient or

respondent as the expert informant of their own QoL. This recognition is

consistent with the grounded theory approach to qualitative research (Glaser

and Strauss 1967), but the methodology in this study is overlaid by the

needs based concept of QoL. The patient is also viewed to be the expert

informant in the generation of items for potential inclusion in the QoL

measure itself (Hunt and McKenna 1992; Doward et al. 2003; Gilworth et al.

2004; McKenna et al. 2004).

Interviews are traditionally an interaction between two people, with one

person as the interviewer, the other the interviewee. The focus of the

interview is usually pre-determined in that there is usually a reason for the

interview, but the structure of the interview may vary. There are three key

types of research interview: structured; semi-structured; and unstructured,
(Parahoo 1997).

The interviews in this methodology are described in some publications as
unstructured (Doward et al. 2003), and by the original methodological
authors as taking a 'conversational' approach (Hunt and McKenna 1992).
The interviews use a topic list (Hunt and McKenna 1992; Doward et al. 2003;
Doward et al. 2004). The topic list is based that used by Hunt and McKenna
in their original research, and is outlined in Figure 4.2.

Figure 4.2 Topic list

- Activities around the home

- Personal and occupational relationships

- Social life

- Cognition

- Personal hygiene

- Leisure pursuits and hobbies

- Sleep and rest

(Hunt and McKenna 1992)

The topic list does not suggest an order for direct questioning, but rather a
checklist for the researcher to work with during the interview to prompt
participants if they do not introduce these topics independently. This is
required to address all aspects of the needs based model of quality of life
selected by the researcher. It does not, however, exclude any additional
topics the interviewee wishes to introduce. The emphasis of the interview is

that the patient leads the interview with their own experiences of how their condition has affected their ability or capacity to meet their needs. The structure of each interview may vary according to the participant and what they want to bring to the interview, but the core elements of the needs based QoL will always discussed.

4.1.2.1 Researcher bias

The researcher has been acknowledged as an instrument in qualitative research whose skills are reflected in the quality of data collected and the data analysis carried out (Morse and Field 1998). The researcher's skills were key to the development of a rapport with participants during the interview and focus group: their facilitation skills were essential to eliciting information within the interviews, and to ensure equality of access for those participating in the focus group. The researcher in this study had a clinical relationship with the interviewees. The decision to invite a second researcher, who did not have previous knowledge of the interviewees, was made, and evaluated at the mid-point review of the interviews by both researchers. The researcher's previous knowledge of the interviewees appeared to have no effect on the length of the interviews, or the emerging themes. Therefore, it would seem that the clinical relationship of the researcher to the interviewees was not a negative bias.

4.1.2.2 Ground rules

Ground rules are agreed protocols between participants in qualitative data gathering (Holloway and Wheeler 2002). They cover aspects of the interview such as confidentiality, recording, what happens if the interviewee wishes to end the interview or if they become upset. Within the interviews for the SSc

QoL the researcher re-enforced the patient information leaflet by saying that the interview will be tape recorded and then transcribed at a later date by a transcriber. It was made clear that the tape will be numbered and would not contain the interviewee name as their name would not be used during the interview. It was stated that if the interviewee wished to stop they were free to do so at any time, and they did not have to talk about anything they didn't want to. It was also explained that there would be opportunity at the end of the interview to discuss any issues which may arise from the interview with the researcher or with outside organisations such as the scleroderma charities.

The researcher encouraged the participant to lead the interview following an introductory discussion about how the interview would be recorded. No time length was explicitly stated for the interviews but previous experience in this established methodology suggests interviews ranging from thirty minutes to two hours (Hunt and McKenna 1992; Doward et al. 2003). In practice the interview length varied from 45 – 60 minutes until the participants felt they had no more they wished to discuss. The second interviewer, who interviewed one third of the participants, reported that the average time span of her interviews was also 45 - 60 minutes.

4.1.2.3 Transcription

In order to analyze the data generated at interview, each interview was recorded on audio-tape. The use of the recorder was explained to the participant, and an initial trial of recording was made prior to each interview. Brief observation notes were also made of each interview to serve as a prompt to the memory of the researcher. Each audio recording was then

transcribed 'verbatim' by an external transcriber, verbatim transcription being described as giving the 'fullest and richest data' (Holloway and Wheeler 2002). No annotations were used.

The researcher then read the transcripts alongside listening to the tapes to ensure the accuracy of the transcripts. There were some aspects of the transcriptions that were ambiguous in their meaning and therefore the researcher needed to listen to the tape in order to understand the intonation behind some statements in the transcript. The researcher annotated the transcript with their interpretation of the meaning behind the statement in order to retain that information to aid later analysis.

4.1.2.4 Interim review of qualitative data

A hiatus in data gathering was planned in order to review the quality of the data being produced. This allowed the two interviewers to collaborate and exchange experiences mid point through the research. This was to allow reflection between the two researchers to consider any practical issues arising from the interviews, to make a preliminary assessment of the quality of data being generated, and to make adjustments to the method if required.

It appeared that interviews from both researchers were approximately 45 to 60 minutes in length. This allayed concerns that interviewees may give substantially more, less or different information to the interviewer they had met previously in clinical practice.

The participants did not raise any issues or concerns regarding consent to the research, and the majority of the interviews were conducted in the participant's home at a time of their choice. The interviewees appeared

comfortable with the interview structure. Some interviewees required prompts; others were spontaneous with their information.

The use of a focus group was explored as another forum for participants to express their views. The rationale for this was firstly to compare a focus group setting with the one to one interview as a data gathering method. This was to be tested by comparison of the themes generated. A focus group was selected for this, as it provided a setting for people to discuss with each other, which may trigger off more information sharing. An example of a similar methodology is seen in a later qualitative SSc study (Suarez-Almazor et al. 2007), where both interviews and focus groups were used as data collection methods.

4.1.2.5 The Focus group

Focus groups offer the opportunity for interaction between participants that, if well facilitated, may stimulate discussion amongst the participants (Bloor et al. 2002). In order to see if this method promoted more discussion amongst participants, a pilot focus group was arranged following submission and approval was gained from the Leeds West Ethics committee for this protocol amendment (2006).

The pilot focus group was held to answer the following question:

- Does the focus group format bring up new data not previously mentioned in one to one interviews?

The structure and facilitation of focus groups is well documented in qualitative research literature (Miles and Huberman 1994; Parahoo 1997). The number of participants varies, but it is considered to be between six and eight (Bloor et al. 2002). In order to answer the question which was the

purpose of the focus group, the ideal participants were those who had most recently taken part in the one to one interviews and whose life had remained stable since their interview, thus allowing some comparison between the data brought up at focus group with the data brought up in a one to one interview.

The most recent eight participants of one to one interviews were contacted by telephone and details of the focus group were explained. In all, five of the eight participants approached consented to participate in the focus group.

It has been stated that focus groups should have both a facilitator who undertakes the running of the group, and an observer who takes no role in the group but who observes the verbal and non-verbal interactions of the group, making field notes on their observations (Bloor et al. 2002). An experienced, independent observer was used for this focus group and their observational notes can be seen in appendix 6.

4.1.3 Analysis of the qualitative data to form the descriptive framework of SSc QoL.

Choice of analytical approach

There are several approaches to the gathering and analysis of qualitative data including grounded theory, phenomenological analysis and thematic analysis.

Grounded theory was developed from a sociological perspective to understand human behaviour. It is based on a quantitative paradigm and statistically average behaviour, and its analytical technique is based on constant comparison (Holloway and Wheeler 2002).

The objective of a phenomenological approach is to describe the essence of behaviour; it has been described as both a method and a philosophy. In practical terms it identifies meta-themes and interrelationships between data.

Thematic analysis seeks to identify common threads in qualitative data, typically interviews. Themes may be 'indicated' by the data rather than being directly observed by the participants (Morse and Field 1998).

Of these three methods of qualitative analysis, the rationale for selection for use in this study was made by matching the method to the study aim which in this case was the development of a descriptive framework of QoL. Grounded theory and phenomenology were not selected as they seek to explore relationships between data, which whilst it this is of interest, would extend beyond both the study aim and the study resource.

Therefore, thematic analysis was identified as the qualitative analytical tool of choice as it identifies the common threads in the data which enables clear description of the interview content. The themes can then be brought together to form a descriptive framework of these common threads (themes).

Initial coding into themes

Thematic analysis is a process of identification of key codes or themes by an iterative process. Themes (or codes) are tags or labels for assigning units of meaning to the descriptive or inferential information compiled during a study. Themes or codes are usually attached to chunks of varying size, words, phrases, sentences or whole paragraphs, connected or unconnected to a specific setting (Miles and Huberman 1994). This process identifies the key themes of the data.

4.1.3.1 Multiple coding or data and counting occurrence of themes

There may be certain blocks of text that contain a mixture of themes. Coding a statement under multiple themes becomes of debate if there is a plan to count the frequency of a theme as it occurs during transcripts. Counting of how many times a theme occurred during the data gathering may be suggested to intimate the 'strength' of the theme in terms of how often a theme is mentioned in the data. Therefore, if the researcher is counting the frequency of themes, coding a statement under several themes will ensure that each theme is fully represented.

Counting frequencies of statements relating to a theme was not employed during this research for two reasons. Firstly, the frequency of a statement was not relevant to this methodology as the items selected for the SSc QoL will be subjected to a wider sample of hundreds of people with SSc during the Rash analysis process. Secondly, from a qualitative research perspective, counting of code frequency is not part of the coding guidance commonly found in qualitative data analysis texts (Miles and Huberman 1994; Silverman 2003).

Coding and thematic analysis may be done manually but many researchers use a computer software package to help them to organise their data.

4.1.3.2 Computer analysis techniques

The availability of computer analysis software has revolutionized the ease with which qualitative researchers can handle large amounts of qualitative data such as that generated by interviews or focus groups.

These software packages such as NVIVO, provide an alternative to the traditional method of coding each transcript with a pen, cutting each coded

section into a slip and putting each slip with the coded quote into piles of quotes representing each code, or alternatively using reference cards documenting the place or actual quote representing each code (Pope et al. 2000). The enormity of this process can only be imagined when dealing with multiple lengthy transcripts. Compounded with the difficulty of sections of text which fit into more than one code, is the problem of maintaining the context of the quote. In many cases this is imperative to ensure the correct interpretation of each statement.

Such software packages are a tool with which to manage large amounts of qualitative data. Whilst they can be set to search for terms, they do not aim to interpret or reflect upon the data (Morison and Moir 1998; Pope et al. 2000). Computer analysis software was explored for use within this research, however a combination of manual coding and thematic analysis was selected for use, supported by data storage and item tracking using a Microsoft Excel spreadsheet. This spreadsheet offered the flexibility to record both themes and items through each stage of analysis and item selection. The spreadsheet then supported data analysis of thematic analysis and item tracking.

4.1.3.3 Second stage of thematic analysis, coding of sub-themes

It is important to avoid 'premature closure', that is leaping to a theme early on in the data analysis prior to full understanding of the text. In this study initial themes were identified on the second reading of the transcripts. Preliminary theme definitions were compiled at this stage. Constant reference was made back to the transcripts to check against these inferential leaps (Holloway and Wheeler 2002).

At this stage, the data and themes were reviewed by a second researcher

(supervisor) to ensure there was agreement with the themes.

4.1.3.4 Third stage of thematic analysis

At this point, themes and theme definitions were revisited and refined.

4.1.3.5. Identification of overarching themes

The third stage of the thematic analysis process was identification of

overarching themes. This involved the researcher grouping together the

themes identified into groups that shared an overarching higher construct.

For example, all those themes that related to an aspect of physical limitation

were grouped into an overarching theme of 'Physical Restrictions'. Again,

these overarching themes were analysed by a second researcher

(supervisor) and consensus achieved.

4.1.3.5 Formation of the descriptive framework of QoL in SSc

The descriptive framework of SSc QoL will be developed from results of

thematic analysis of the interview transcripts exploring peoples' experience

of SSc and its effect on their QoL. The themes are presented in chapter five.

4.2 Attributes required in the development of the SSc QoL

It is suggested that a measure of QoL has certain key attributes (Medical

Outcomes Trust 2002). This key article, written by the Scientific Advisory

Committee of the Medical Outcomes Trust, suggests eight key attributes of a

QoL instrument. Figure 4.1 (p.82) presented the methods used to develop

the SSc QoL, Table 4.2, relates the eight attributes of a QoL measure and

how they are addressed within the development of the SSc QoL.

Table 4.2 – The Medical Outcomes Trust attributes of a QoL measure (Medical Outcomes Trust 2002) - Summary of how these are met in the SSc QoL

Attribute of QoL measure	How this is achieved in the SSc QoL
Conceptual and measurement model	The concept to be measured is patient-perceived QoL in those with SSc. The Needs based model of QoL forms the conceptual basis of the SSc QoL. The SSc QoL will be developed for use with people who have limited or diffuse SSc. The Rasch measurement model is the standard method of validity testing in order to produce an interval scale.
Reliability	Data to allow test-retest reliability testing will be gathered by administration of the SSc QoL over two time points (section 4.2.6) to the same population. Reliability of the SSc QoL will be assessed using Rasch analysis and parametric testing. In Rasch analysis Differential Item Functioning of the two time points was used; parametric testing using Spearmans correlation of results over the two time points was also used.
Validity	Face validity as patient is the expert informant (4.2.1) and cognitive debriefing process (4.2.3)
Responsiveness	Person separation index of Rasch analysis is designed to show the function of a scale across groups. Longitudinal study of the SSc QoL was not a requirement of the study hypothesis
Interpretability	The SSc QoL will produce a simple sum score; the higher the score the higher the impact of SSc on QoL.
Respondent and administrative burden	Feedback from Cognitive debriefing will inform the respondent burden of the SSc QoL. The administrative burden of the SSc QoL is small as it is a sum score that can be added in the clinical setting.
Alternate forms	The study aim is to produce one form of the SSc QoL at this stage that is a paper based measure written in English.
Cultural and language adaptations	This falls beyond the requirements of this study but the needs based QoL methodology provides a clear protocol for cultural and language adaptations of the SSc when required

4.2.1 Item Selection

Items are the questions or statements that make up the QoL measure. The

process of selecting these items for the SSc QoL measure follows an

established in previous needs-based QoL measures (Doward et al. 2003; Gilworth et al. 2004). The process of item selection in the development of the SSc QoL was summarised in Figure 4.1 and is expressed in more detail in Figure 4.3 as follows.

Figure 4.3 Development of the SSc QoL measure – Item selection

```
┌─────────────────────────────────────────────────────────────┐
│              Item Selection from transcripts                  │
│   (Researcher, Independent assessor, application of criteria) │
│                            ↓                                  │
│      Item Reduction – through the Rasch analysis process      │
│                            ↓                                  │
│         Item Reduction – Rasch (test/retest analysis)         │
│                            ↓                                  │
│                Items in the QoL questionnaire                 │
└─────────────────────────────────────────────────────────────┘
```
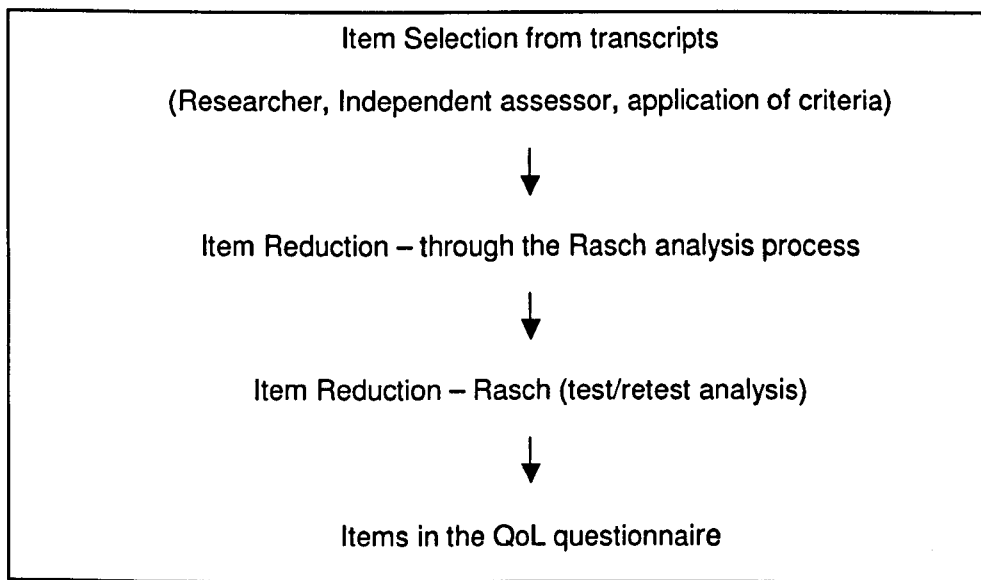
Key statements were identified by the researcher and mapped onto the Microsoft Excel database used for item tracking. A copy of each interview transcript was divided between a group of three researchers and healthcare professionals with experience of working with the needs based model of QoL. Each transcript was analysed by both the main researcher and one other member of this group.

The role of these independent researchers was to comment on the operational definition of each theme and following discussion, and identify needs based items from the key statements. Consensus was also achieved on each themes operational definition. This is a similar process as described

for development of previous needs based QoL measures (McKenna et al. 2004).

The next stage of item selection consisted of each researcher applying the item selection criteria. This criteria was based upon that used in needs based QoL development (Galen 2006).

Characteristics of items:

- Consonant with the needs-based model of quality of life

- Expressive of a single idea

- Applicable to all potential responders (i.e. not gender or age biased)

- Capable for being expressed in the first person

- Capable of being expressed in the respondent's own words

- Is unambiguous

- Is short and simple

- Does not duplicate other items

- Appear suitable for future translation.

The researchers applied these criteria to the potential needs based items. In the majority of cases the application of the characteristics enabled a clear exclusion of items, however, there were some items that required group debate as to their suitability for selection. Each item was debated and a consensus obtained as to its selection. Following this item selection process, ninety items were selected to be included in the first postal questionnaire of the Rasch analysis process.

4.2.1.1 Incorporation of the item bank into the SSc QoL

An item bank is a central place for the storage of items. These items may come from a range of measures, but it is essential that they share a conceptual base (McHorney 2003). In the case of the SSc QoL, the item bank needed to be one of 'needs based' items. Such an item bank has been developed and held by the Psychometric testing laboratory at the University of Leeds.

The use of item banks has been expressed as a key development in Patient Reported Outcome Measures (PROM's) (McHorney 2003).

The items in existing QoL measures form a needs-based 'item bank' (Lai et al. 2003; Tennant and Conaghan 2008). One of the purposes of an item bank is to find out which items are common across chronic diseases, and which are disease-specific. Any items in the ninety SSc QoL list which were the same or very similar to an item in these existing measures (item bank) were replaced with the item from the item bank.

An example of this includes:

Control:

SSc interviewee – "It's difficult to take control of my condition"

Item bank   – "I feel that I am unable to control my condition" (RA QoL)

This process was undertaken for each of the SSc items selected from interview, with any items of the same meaning being replaced with an item from the item bank. Each of the final ninety items has been tracked back to

its original source (e.g. table of item origins of the SSc QoL, Chapter 6) and this information was stored on the Microsoft Excel database.

4.2.1.2 Response format

The item statements must have the same response pattern, that is that they are all either dichotomous or polytomous (Bond and Fox 2001). This involves two processes. Firstly, a decision is made as to the response pattern for the items: this choice is between dichotomous responses (that is Yes or No), or polytomous responses (where there is a wider range of possible responses).

The SSc QoL uses a dichotomous (two options) response choice, that is 'True' and 'Not True' to each item statement (appendix 7). It was necessary to ensure that each item response was in the same response pattern. This means that each type of response (True/Not True) represents the higher impact of the disease on the patients QoL. The higher impact should receive the higher numerical score. This ensures that when calculating the end score of the measures, it is possible to allocate a score of '1' to the 'True' responses and '0' to the 'Not true' responses, with the higher score indicating the higher impact of the disease on the patients QoL. Each item was checked for the pattern of its response, that is which type of response (True or Not True) is a positive response. For example, if the question was phrased 'Going out for a meal is difficult' 'True/ Not True' – here a 'True' answer would mean there was a problem with eating out.

4.2.2 Construction of Draft Questionnaire

A draft questionnaire was constructed to go forward for validity testing. The questionnaire was an A4 size ten-paged booklet. It consisted of the ninety

items (statements) derived from item selection together with demographic questions and comparator measures. This draft questionnaire was developed on a small scale for use in the following scale development processes prior to post out of the First Postal Questionnaire (4.2.4).

4.2.3 Cognitive De-briefing in the SSc QoL Scale development

The development of needs based QoL measures has precedent for how issues of validity are addressed. Validity, the extent to which data collection methods measure the phenomenon under investigation, consists of several elements (LoBiondo-Wood and Haber 1994). Content validity is the degree to which the questionnaire or scale can adequately explore the phenomenon being studied. Face validity is a form of Content validity. It is the process of asking those not necessarily an expert in the area, to assess whether the questionnaire or measure reflects what is being studied (Parahoo 1997; Doward et al. 2004). In this case, the phenomenon being studied is QoL in SSc. The method chosen within the QoL development methodology is referred to as cognitive de-briefing (Doward et al. 2007). This process is described in development of QoL measures such as the Ankylosing Spondylitis QoL (Doward et al. 2003; Doward et al. 2007).

Within this study, cognitive de-briefing consisted of taking a draft of the QoL questionnaire booklet and introduction letter to people with SSc. Eight people were approached. Each person completed the questionnaire with the researcher present. They were asked to comment aloud to the researcher on issues such as understanding of the statements, applicability of the items, the relevance of the items and if there are any key statements/items that were felt to be missing. Participants were also asked to comment on the

instructions for completion and appearance of the questionnaire to inform any changes prior to the first postal send out. The researcher noted these comments and as far as possible adapted the questionnaire booklet instructions and format accordingly.

4.2.4 First Postal Questionnaire

4.2.4.1 Sample

The population sample for the quantitative data gathering, that is administration of postal questionnaires, required two randomly selected groups with SSc. The first group received the initial booklet of questionnaires, that is the first postal. The second group received the test and retest booklets of the questionnaire.

Sample size

The UK National Scleroderma database was the source of the population sample for this study. Sample size reflected the population documented on the UK National Scleroderma Database (held at the Royal Free Hospital, London). The sample size was guided by the total population sample of whichever disease sub-type was the smallest, in this case dcSSc. This number was then matched by an equivalent number of patients with lcSSc.

Identification of the population from the National Scleroderma database

The process of sample identification is see in Table 4.3 which illustrates that the National Scleroderma database held information for 2932 patients with SSc; 1046 of those on the database did not have a disease sub-type identified. Of the remaining 1886 who had an identified disease sub-type, 618 were patients with DcSSc, 1268 with LcSSc. Of these, 177 with LcSSc

and 169 with DcSSc were deceased; therefore 11.67% of the database patients were deceased.

As there is no electronic link between the UK National Scleroderma Database and the patient administration system (PAS) of the Royal Free Hospital, a manual cross-check was made by the researcher. This was done to ensure firstly that questionnaire booklets were not sent out to those who were deceased, and secondly that the patients identified had the key demographic data required for later data analysis. A further 71 patients had to be removed due to lack of a complete postal address.

The remaining sample was then anonymised and randomised into two postal groups; each containing similar numbers of people with each disease sub-type. Following this randomisation (stage 5 in Table 4.3), those lcSSc with were checked against the PAS system against the same criteria as the dcSSc sample. This was not done at the same time as the dcSSc sample (pre-randomisation), due to the much larger lcSSc sample that would be reduced through randomisation to a number similar to that of the dcSSc sample.

Records management guidance

Due to records management guidance (DoH 2006), data was anonymised prior to electronic transfer to the statistician for computer randomisation. Due to this, the date of birth was removed from the data therefore sample age is not available for the sample group, and therefore for the non-responder group also. Disease duration, or date of diagnosis, was largely absent from entries on the National Scleroderma database, therefore disease duration is also not available for the sample group or the non-responder group.

Table 4.3 Sample identification for the postal questionnaires used in development of the SSc QoL measure

Stage of sample identification	Numbers in database	Remaining sample available
1	Total in database - 2932	2932
2	1046 identified as having no disease sub-type documented	1886 remaining: 618 with dcSSc;1268 with lcSSc
3	Identified as deceased: 169 with dcSSc 177 with lcSSc	Total sample remaining: 449 – dcSSc 1091 - lcSSc
4	Diffuse sample checked against the hospital Patient Administration System (PAS): deceased; insufficient postal details; outside of the UK -83 cases removed	366 dSSc patients 1091 lcSSc patients
5	Cases anonymised and sent for randomisation	383 patients for group 1 (183 dSSc, 200 lcSSc) 383 patients for group 2 (183 dcSSc, 200 lcSSc)
6	PAS checking of those anonymised to leave final sample groups for the development of the SSc QoL Group 1 – First postal questionnaire for the draft SSc QoL Group 2 – Test/Retest of the draft SSc QoL	**Group 1 (n= 336)** 177 with dcSSc (36 Male, 141 Female) 159 with lcSSc (22 Male, 137 Female) **Group 2 (n=369)** 182 with dcSSc (33 Male, 157 Female) 187 with lcSSc (63 Male, 149 Female)

Randomisation of the sample into sample groups

Two groups (first postal questionnaire and test/retest sample) were to be identified from the remaining sample. Each group should have a comparable

number of patients with dcSSc and lcSSc. There are various processes available for selection, randomisation presenting the option least susceptible to bias (LoBiondo-Wood and Haber 1994). Of the methods available for randomisation of data, randomisation by computer offers a system that is quick and transparent (Parahoo 1997). Therefore, randomisation of the population into two sample groups was carried out using computer software. Data of patients from the national database was anonymised in line with NHS Records management guidance (DoH 2006), and presented for randomisation in separate dcSSc and lcSSc Microsoft Word folders. These were sent electronically to the departmental statistician who randomised each folder into two groups, group1 for the first postal questionnaire, and group 2 for the test/retest data collection.

4.2.4.2 Potential measures identified for hypothesis testing

The descriptive framework of this study identified several key themes which participants associated with QoL in SSc. These themes were used to identify a range of measures or outcomes for incorporation into the postal questionnaires, results of which were then available for use in later modelling of QoL in SSc.

This modelling takes the form of Structural Equation Modelling (Schumacker and Lomax 2004), and is described in more detail in section 4.3.

Where available, themes within the descriptive framework were represented by a corresponding comparator measure. These are summarised in table 4.4. For example disability, was part of the theoretical framework of SSc QoL, therefore the Scleroderma Health Assessment Questionnaire

(Disability Index) and the UK Functional Index were included as a

comparator measure in order to reflect disability in SSc.

Table 4.4 Comparator measures used and their link to theme of the descriptive framework, and element of the ICF

Comparator measure	Element of the ICF	Theme from the descriptive framework
Scleroderma Health Assessment Questionnaire (SHAQ)	Disability	Physical restriction
London Handicap Scale	Participation	Finance, social impact, hobbies, hygiene, work
Euro QoL EQ 5D	Health status	Physical restriction
UK Functional Index	Disability	Physical restriction
General Perceived Self-Efficacy	Not assigned	Control, Family (role)
Rosenberg's Self-Esteem questionnaire	Not assigned	View of self
Hospital Anxiety and Depression questionnaire	Anxiety – 'Emotional factor' covers all elements Depression is not assigned in the ICF	Depression, anxiety, Emotion
Fatigue Severity Score	'Fatigueability' – covers all elements	Fatigue

Selection of measures

Five criteria were used to select the measures for potential use in later

modelling.

- The measure represented an aspect of the descriptive

  framework of SSc QoL developed from the SSc participant

  interviews

- The measure had some evidence of previous reliability and/or

  validity testing, preferably within SSc patients

- The measure was available for use with sufficient information of its content and scoring methods

- The measure was considered user friendly at the cognitive debrief stage

- The measure was not excessively long or complex

The measures which were explored, but not included in the questionnaire, are identified in detail in an appendix to this study (appendix 8).

Following the return of the first postal booklet, several changes were made to the booklet for use in the test-retest analysis stage. The rationale for these changes was two-fold. Firstly, some additions were made such as questions around pain and sexual activity due to reflections on the theoretical framework generated from the qualitative interviews. Secondly, changes were made to some response categories in order to simplify or clarify data analysis.

Changes made to the booklet for the test/retest analysis:

- Age and disease duration to years not categories to allow more precision.

- Removal of the question if the respondent had been 'told their disease sub-type', as this was felt to be open to response error due to the time elapsed since that information may have been given.

- 'Not applicable' option considered for removal but kept in for the 5 Visual Analogue Scales of the SHAQ, despite the potential for analytical issues, as this is it's original format.

- Added 'S' questions which were original QoL items removed during the Rasch process of internal validity testing. They were included as they appeared conceptually meaningful to the interviewees, and may have represented a sub-scale.

- A marital status question for some indication of social network in the home.

- Pain Visual Analogue Scale (VAS) - this was not included in first postal data collection as not a 'strong' theme, but included in test/retest version of the booklet, as both pain items had been retained by Rasch analysis illustrating the relevance of pain to the first postal sample group.

- Sexuality single question added as this seemed to have a potential link with items which had been retained by Rasch, such as those around confidence, relationships, self-esteem.

4.2.4.3 Process of Questionnaire production, mail-out and data entry

A postal questionnaire booklet was the tool identified to gather the quantitative information required for the development of the SSc QoL, in line with previous needs based QoL development methodologies (Doward et al. 2003; Gilworth et al. 2004). The booklet contained demographic questions, the items generated by the item selection process and comparator measures of the key elements of the SSc QoL theoretical framework.

In order to encourage competition and return of the questionnaire booklet several issues were considered. Firstly, the length of the booklet was reviewed with the aim to minimise the task of completion. It may be logical to assume that the shorter the questionnaire, the less onerous the task to complete and the higher the return rate. However, literature does not support this assumption, showing that questionnaire length does not have a direct relationship with response rate (Subar et al. 2001). The questionnaire was designed to be visually neat, with precise instructions, easily readable text and using simple language. Hand written personalisation of the research introduction letter was considered in order to engage recipients to respond. However, questionnaire design literature, (Byrom and Bennison 2000), does not support the effect of personalisation on response rates, therefore a quicker, printed form was used.

Options for production of the booklet included payment for commercial printing or internal make up of the booklets using a high-powered photocopier. Due to the financial constraints of the study, a photocopier was used. The introduction letter for each stage of the postal administration included a formal departmental heading to show the academic support of the research. It also included an invitation to contact the researcher for discussion or question and information of financial support and academic role of the project. The postal questionnaire booklet had an estimated completion time (based on the construct validity testing process) of 20 – 30 minutes.

The questionnaire booklets were colour coded to allow easy differentiation between disease sub-types and study stages. Each booklet was identified

with numbers taken directly from the SSc database and a D/L added at the

end of the number. The D/L label reflects the disease sub-type of the

respondent as dcSSc or lcSSc. This ensured the researcher could identify

diffuse or limited disease when responses were entered into the database.

This identification number was hand written on each questionnaire to allow

identification on return and inform the reminder list for non-respondents. A

letter franking account was established with the university together with a

Freepost address for return of the questionnaire booklets. Each envelope

contained an introductory letter, a questionnaire booklet, an open sheet for

respondent's comments and a return pre-paid envelope.

4.2.5 Construct Validity Analysis (Rasch)

Validity, when related to research, has many definitions. Perhaps the most

cited of these definitions is 'An account is valid or true if it represents

accurately those features of the phenomena that it is intended to describe,

explain or theorize' (Hammersely 1987 cited in (Winter 2000). The view that

validity is not a single or universal concept has been explored during a

comparison of validity issues between qualitative and quantitative research

(Winter 2000). Validity is often linked with the concept of reliability, reliability

being described as 'the consistency of a particular method in measuring or

observing the same phenomena' (Hoyle and Smith 1994).

Construct validity refers to the level to which the questionnaire or scale

reflects the construct which is being assessed (LoBiondo-Wood and Haber

1994). The method for assessing internal construct validity within the needs-

based QoL methodology is that of Item Response Theory, namely Rasch

analysis (Tennant et al. 2004). This 2004 article describes the use of Rasch

analysis in the development and application of QoL instruments, illustrating

the benefits of the Rasch model. These benefits including the ability of

Rasch analysis to transform ordinal scores in interval level measurement

and provision of a means of assessing a range of measurement properties.

4.2.5.1 Item Response Theory and the Rasch model

Item Response Theory (IRT) is a statistical approach to data used to test a

measure's precision in measuring a latent (hidden) construct, (Wilson 2005).

This is done by testing the responses of individuals to the measure against

the latent construct (US National Cancer 2006). A construct is the idea or

concept that is the theoretical object of our interest (Wilson 2005). A

construct map reflects the underlying construct being measured, in this case

QoL. The items selected for use within the QoL measure represent this

latent construct. Whilst Rasch analysis cannot itself make this direct link to

identify the latent construct, the link is drawn from the conceptual basis of

the qualitative data from which the SSc QoL is developed, and the cognitive

debrief process described in section 4.2.3.

The structure of the qualitative data collection (interviews and a focus

group), was supported by a topic list drawn from a conceptual approach to

QoL, need based QoL. Also, it was explained prior to each interview that the

focus of the interview was how SSc had impacted upon the individuals' QoL.

Therefore, the data from these interviews and focus group represents the

view of QoL from people living with SSc.

Relating this to the latent construct of the SSc QoL, it can been seen that

there is a direct relationship between the qualitative data gathered from

those with SSc, through the item selection process, to the SSc QoL measure

itself. The process of IRT (Rasch analysis) is designed to identify those items which represent other dimensions or latent constructs. This is explained further in section 4.2.5.2, which discusses the concept of unidimensionality in the Rasch process.

Precedent for a choice of IRT model is found in previous needs based QoL measures such as the Betchets QoL (Gilworth et al. 2004) and the Ankylosing Spondylitis QoL (Doward et al. 2003). This precedent is the Rasch model.

The Rasch model

George Rasch, a mathematician, developed a model of Item Response Theory, (Rasch 1960), initially based within education. Rasch analysis sets out a mathematical model against which new or existing scales can be tested for psychometric (measurement) properties and therefore acts as a test of internal construct validity (Pallant and Tennant 2007). In short, Rasch analysis provides a statistical way of transforming the qualitative statements (ordinal data) into an interval scale measure (Rasch 1960; Tennant and Conaghan 2008). Measures that attain the requirements of the Rasch model are independent of variables such as the age, gender or disease sub-set of the respondent.

The Rasch model is based on an assumption that the probability (ρ) of a person affirming an item or statement is a logistic function of the difference between the respondents actual level (θ) of, for example QoL, and the level of QoL expressed by the item (β), and only a function of that difference (Pallant and Tennant 2007; Tennant and Conaghan 2008). To put this into mathematical language, the Rasch model would appear as follows:

$$p(X_{ni} = 1 \mid \theta_n, \beta_i) = \frac{\exp(\theta_n - \beta_i)}{1 + \exp(\theta_n - \beta_i)}$$

(Wright and Panchapakesan 1969)

The equation contains two key components; the person's probability of affirming the item, and the item itself. The Rasch analysis process is carried out using software such as Rumm 2020 (Andrich et al. 2003), ConQuest (Wu et al. 1998), or WINSTEPS (Linacre 2007), which uses information gathered from the responses to the items. This means that the items to be tested are given to groups of respondents (usually in a questionnaire form) and the answers provide the information required to compare against the Rasch statistical model. In picture form, the end result of the Rasch analysis places the item along the ruler (Figure 4.4) at equal distances ranging from the item most easy to affirm to the item most difficult to affirm, the latter indicating a worse state of QoL.

Figure 4. 4 The Rash Ruler – Interval scale

Best |___|___|___|___|___|___|___|___| Worst

Possible   **QoL**   Possible
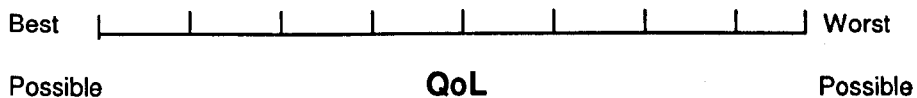
The Rash model places the items tested along this linear scale. Within the Rasch ruler or linear scale, each unit represents 'an increase in the odds of a person succeeding on an activity by 2.716 times' (Tennant et al. 2004).

Rasch analysis and Factor Analysis

Rasch has been compared with other statistical approaches, chiefly Classical Test Theory (CTT), and Factor analysis. CTT refers to statistical

models that assess the performance of an item and has been applied to QoL instruments and compared with Rasch analysis (Nijsten et al. 2006). This includes traditional statistical methods such as Factor analysis. Factor analysis is used to identify a set of factors that represent the underlining relationship between variables (Pallant 2005). Rasch analysis and Factor analysis differ in their approach to analysis, Rasch analysis approaching the data with a pre-set model, Factor using the data to create a model. Factor analysis has been stated to be 'confused by ordinal variable and highly correlated factors,' Rasch analysis however, assumes a unidimensional set of items and is able to produce a linear scale from ordinal data (Schumacker and Linacre 1996). Rasch analysis is therefore a key statistical model for use in the conversion of qualitative ordinal data, into a linear scale.

Models of Rasch analysis

The original Rasch model was dichotomous (Rasch 1960). There are two variations on the Rasch model, both of which accommodate the polytomous response, called the rating scale model (Andrich 1978), and the Partial Credit model (Masters 1982). The precedent within the needs based QoL measures are for the use of dichotomous responses, (Gilworth et al. 2004), therefore indicating use of the dichotomous Rasch model.

4.2.5.2 Unidemsionality

Unidemsionality is the concept that the data, and by implication therefore the items, are representing a single underlying higher order construct (Bond and Fox 2001). In the case of this study, the higher order construct studied is QoL. For example, if the data being analysed came from a questionnaire developed to measure depression, if an item in the questionnaire measured

a different construct such as hope, this is likely to show misfit to the unidimensional Rasch model. This would enable the analyst to recognise this different underlying construct and deal appropriately with that item. This concept is automatically assumed in measurement of things such as height and weight, but is not always questioned in social sciences (Bond and Fox 2001).

Rasch analysis assumes that the items, summed together, form a unidimensional scale. Tests of this assumption continue to develop, but the use of principal components analysis of the residuals of items is the method facilitated within Rumm 2020 software. This analysis consists of identifying subsets of the most negatively and positively correlated items and applying a t test (Smith 2002). A binominal test of proportions is calculated (again using software) and if unidimensionality is present the value should cross the 5 % expected value given (Tennant and Conaghan 2008).

4.2.5.3 Local Dependency

Local dependency of items means that there are associations between items, that is the success or failure of an item is dependent upon the success or failure of another item (Bond and Fox 2001). This has two forms, dependency of item response and multidimensionality. Response dependency as it suggests, is where responses from one item show links or will determine a response from other items. A clear example of this would be that if an item asks if you can climb 20 steps and the respondent has affirmed that item, an item asking if you can climb 5 steps will automatically be affirmed. The residual correlation matrix will identify this situation. This issue can be then be addressed by combining items (Tennant and

Conaghan 2008). Local dependence through multidimensionality will be identified and managed through the process of unidimensionality testing previously described.

4.2.5.4 Assessment of Fit and Differential Item Functioning

Rasch analysis contains several tests of 'fit'; that is a summary of how well the data fit into the Rasch model (Pallant and Tennant 2007). A summary of the key tests of fit is outlined in Table 4.5. These are the key measures of fit on which the development of the SSc QoL measure was based. More detail of each of these measures of fit are described later in section 4.2.5.4.

Table 4.5 Reference Tables of desirable levels measured during the Rasch analysis process - Summary and Individual Fit statistics

Fit statistic	Desirable level
Summary Scale Fit Statistics:	
Chi Square probability	> 0.05
Person Separation Index	>0.7 for group >0.85 for individual use
Item and Personal Residual	Mean 0, SD 1
Individual Item Fit statistics:	
Chi Sq	0.05 (Bonferonni adjusted)
Residual	+/- 2.5
DIF	> 0.05 (Bonferonni adjusted)

Figure 4.5 shows the summary analysis screen of Rumm 2020 software which was selected as the software for Rasch analysis in the development of the SSc QoL, and has been widely used for this purpose in other needs-based QoL measures (Tennant et al. 2004).

The summary fit statistics shown in Figure 4.5, together with other attributes of Rasch analysis are now described in detail.

4.2.5.4.1 Chi square probability

The Chi square probability figure is worked out on the basis of each persons observed and expected scores according to the model, and is considered to be required to be greater than 0.05 (Bland and Altman 1995). For both the summary statistics for the whole scale, as well as individual items this needs to be non-significant. Bonferonni adjustment may be required (Bland and Altman 1995).

Figure 4.5 Print screen of the summary statistics used in Rumm 2020
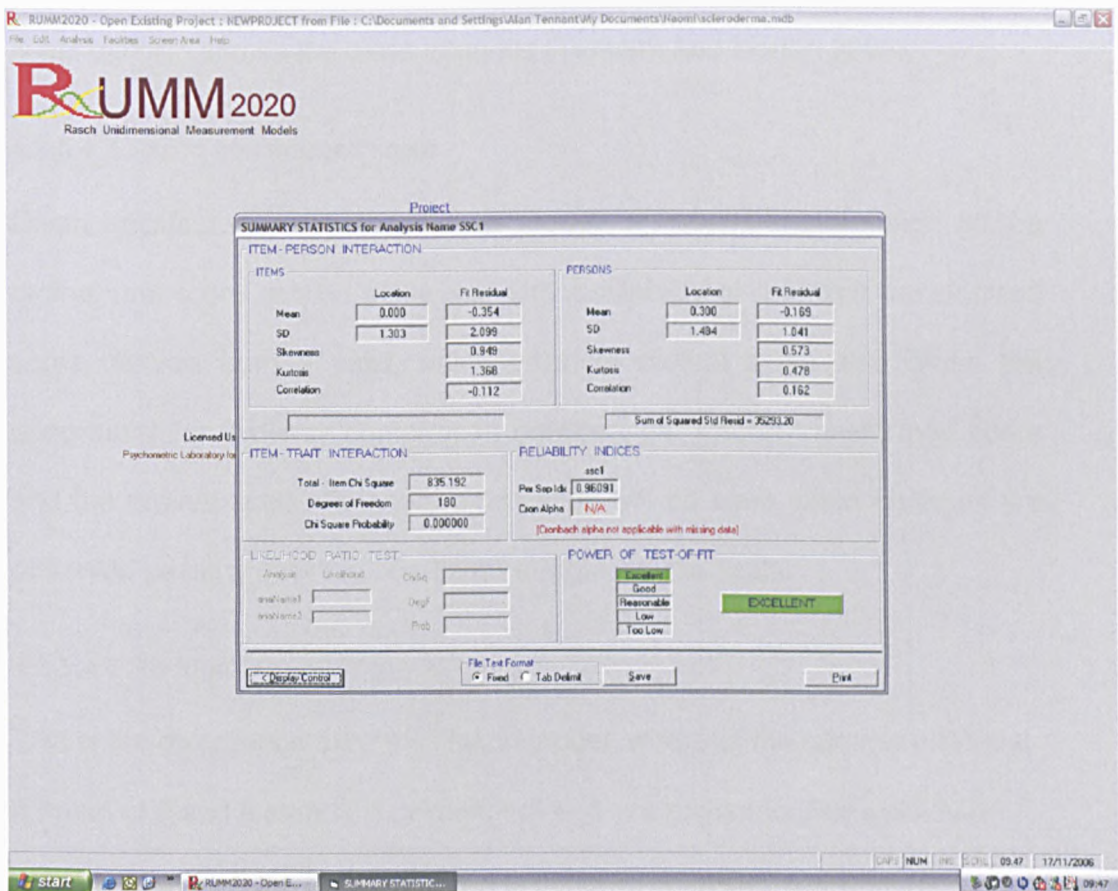
4.2.5.4.2 Differential Item Functioning (DIF)

DIF is a test of how each item works across the different groups identified in the data, evidence of DIF illustrating item bias (Bond and Fox 2001). For

example, in the case of this study the groups identified were the age,

gender, disease duration and disease sub-type of the respondents. DIF is

seen in items which produce different response functions for two or more

groups (Bhakta et al. 2005). If DIF is identified in a group for an item (that is

a level of 0.05 and below), then that item could not be used uniformly across

a population that includes that particular group. There are two types of DIF,

uniform and non-uniform. Uniform DIF is where there is uniformity amongst

the differences between the groups; that is all the men are performing

differently to all the women. Non-uniform DIF is used to describe DIF which

is not uniform across the class intervals (Tennant and Horton 2006).

4.2.5.4.3 Rasch transformed score

Given satisfactory fit to the Rasch model, a linear transformation of the

ordinal raw score can be achieved. The availability of a Rasch transformed

score derived from a valid, unidimensional ordinal scale also offers the

opportunity for two-way comparison between the Rasch transformed score

and the ordinal scale. Potential differences will be seen when changes are

observed passing over the non-linear margins of the scale.

4.2.5.4.4 Residuals

This is the divergence from the Rasch model, where at the summary fit level

a mean of 0 and a standard deviation of +- 1 are expected. For individual

items a value outside the +-2.5 level is considered misfit.

4.2.5.4.5 Class intervals

Rasch orders persons in terms of ability and then automatically splits them

up into groups of approximately equivalent size across the sample in order

to approximate ability groups. The number of the class intervals therefore depends on the sample size. It is important that there are sufficient numbers of people (cases) within each class interval.

4.2.5.4.6 Person Separation index

Power of test fit is a visual representation of the Person Separation Index (PSI), which is indicative of the power of the construct to discriminate amongst respondents. It is equivalent to classical reliability and the minimum accepted level is 0.7 meaning it can differentiate between two groups of patients, 0.9 means it can differentiate between four groups (Streiner and Norman 1995).

The PSI is also an indicator of how much we can rely on the fit statistics. If it is low then there will be an amount of error in the fit statistics, if it is high then the data is deemed to be more reliable (Fisher 1992).

4.2.5.5 Data preparation

Data from the returned postal questionnaires were coded by using a master copy of the questionnaire booklet. The questionnaires within the booklet were allocated a numerical label in order to identify missing data, not applicable responses, missing patient ID numbers etc.

Numerical labels:

QoL items - 0 – Not true, 1 - True

8 – not applicable

9 – missing data

888 – missing database number.

888/999 missing data for Visual Analogue Scales

Preparation of Data for entry into Rumm 2020

Data was checked for errors using recommended techniques (Pallant 2005). Demographic data of the responders such as male, female, age, gender, disease sub-type and disease duration were analysed using frequency analysis, checking in particular for errors in data entry and to identify key areas of missing data. This analysis was also applied to the QoL items. All person items (such as ID, age, gender etc) were moved together at the top of the SPSS spreadsheet under the ID (person factor) headings. Actual sub-type of the respondents disease (as obtained from the National Systemic Sclerosis Database) were entered with the coding of 0 – Diffuse disease and 1 – Limited disease. All column widths were adapted to fit into the Rumm 2020 software system i.e. 1 for all columns except Visual analogue responses where a width of 3 is required. This file was then saved as a 'Fixed ASCII dat file' for use in Rumm2020, and the SPSS output saved for later reference. The ASCII dat file was read into the software and ID factors entered. As a maximum of seven ID factors only are allowed, responses to the questions 'Have you been told your disease sub-type' and 'If so, what is your disease sub-type' were removed from the ID section to limit the factors to seven. The data was read in as one item block as all items were dichotomous response items. Missing data was specified as '9' and all item details were accepted. The template file was saved. A descriptor for each item was entered alongside the number of response categories. This was then saved as an Item template file. The Item template file was opened within Excel and the labels copied over from SPSS: Item a15 was given a reverse category.

Returning to the Rumm2020 programme, the Import template was selected and the data checked to ensure that the descriptors were correct and ensure item a 15 was reversed. Item numbers and headings in Rumm 2020 were checked against the master postal booklet to ensure that they were correct.

4.2.5.6 Protocols of Rasch analysis

Rasch analysis and the software used to support it is constantly developing and until recently there were no clear guidelines for the elements of the analysis which should be a standard when presenting results. However, this guidance was provided in 2008 (Tennant and Conaghan 2008). They proposed the following elements to be required in a 'good' Rasch publication:

- Model Choice

- Where polytomous, the appropriate ordering of categories and any necessary re-scoring

- Fit of items and person to the model (including any relevant summary statistics) and justification for fit levels chose, strategy for improving fit (e.g. item deletion) and subsequent fit statistics

- Test of the assumption of the local independence of items, including response dependency and unidimensionality

- The presence of DIF and any action taken to adjust

- The targeting of the scale

- The Person Separation reliability

Therefore, these form the reporting structure for the results associated with development of the SSc QoL which are presented in chapter 6.

4.2.6 Second Postal Questionnaire (Test/Retest)

The reduced item SSc QoL, together with other adjustments outlined in 4.3.4.2.1, was sent out to the second postal group. Those who returned the completed booklet were posted out a second 2 –4 weeks following return of the first 'test' booklet. Those who did not return this were sent a postal reminder. The methods used to test scale invariance of the SSc QoL across time points, were two-fold; firstly DIF testing within Rasch analysis, and correlation of time 1 and time 2 questionnaire data.

4.2.6.1 Further item reduction

Further item reduction was carried out by use of Rasch analysis. The responses used within this second stage of item reduction were only those questionnaires where the respondents had completed and returned both the first and second postal questionnaire. This gave a total 119 questionnaires for analysis. This analysis was carried out as before with the additional DIF testing across time points of the questionnaire data. The 'test' questionnaires, that is those first send out were identified as 'time point one' in the database, 'time point two' were the retest (second), identical version, of the questionnaire sent out between two to four weeks following receipt of the test questionnaire return.

4.2.6.2 Item mapping

Item mapping is a further addition to the established QoL development methodology, and was outlined in section 4.1.1.2.1 (data saturation). The rationale for this innovation was the researchers aim to relate the volume of

interviews carried out, to the actual amount of interviews required in order to produce the items which form the QoL measure. This is related conceptually to the discussion around data saturation. As previously described, data saturation is considered to be at the point where no new topics or data are generated although existing themes may be presented in different terms. Item mapping will test this concept in relation to the item development process as it will allow each item which is in the final SSc QoL measure to be tracked back to its origin. This will allow the researcher to identify how many interviews had been required to produce the items which eventually form the SSc QoL (results shown in Chapter 6).

The difference between the point of traditional data saturation in qualitative data collection, and the analysis of transcripts for items require further exploration and this innovative exploration of the concept of saturation will form an additional analytical stream to this research.

4.3 Methods for testing the research hypothesis

Methods for testing the research hypothesis have been summarised in Table 4.1 stating that this will include non-parametric testing and SEM techniques. These techniques are now described in more detail.

4.3.1 Non-parametric testing of study data to test the research hypothesis

Non-parametric statistical techniques have been described as 'ideal when you have data that are measured on ...ordinal scales' (Pallant 2005). Therefore non-parametric techniques have been applied to the data in this study. The title 'non-parametric' describes several possible tests. The Mann-

- 132

Whitney U test is a measure used to test for differences between two independent groups on a continuous measure (Pallant 2005). Therefore this was the measure of choice to test the hypothesis that there will be differences in the levels of QoL between those with dcSSc and lcSSc disease sub-types.

4.3.2 Structural Equation Modelling - a tool to test the study hypothesis

SEM is a statistical tool used to explore relationships among observed and latent variables in order to test a theoretical model or hypothesis (Schumacker and Lomax 2004). Emerging from key publications in the 1970's (Keesling 1972; Joreskog 1973), SEM explores the extent to which the data support the hypothesised model and allows the researcher to adapt the model and retest until SEM requirements are met. It uses a combination of statistical models including path analysis, regression and confirmatory factor analysis.

Selection of SEM as a tool in this study

Non- parametric testing has been identified as one tool for testing the hypothesis of this study. An alternative method of testing the hypothesis is also suggested, that being SEM. SEM has been selected for this purpose as is it considered to be a comprehensive, flexible approach to modelling relations between variables (Hoyle and Smith 1994). SEM provides a tool to facilitate modelling of several variables at once to create a model of QoL in SSc. SEM is more powerful than multiple regression as multiple regression doesn't look at the indirect effects and is therefore unable to show what is happening behind the scenes; SEM gives that ability.

Precedent for its use when exploring needs based QoL has been seen in a recent study of QoL in Osteoarthritis (Keenan 2008). SEM is considered to have four key reasons for its increasing popularity:

- Increasing realisation of the need to use multiple observed variables to increase understanding of their research. SEM facilitates this complex modelling, and is therefore becoming a method of choice for quantitative testing of theoretical models.

- Increasing recognition of the validity and reliability of observed scores from measurement instruments. SEM embraces measurement error within the statistical analysis and incorporates the use of both observed and latent variables.

- SEM provides a way of testing both main effects and indirect effects. This increases the richness of the modelling processes allowing researchers to model both direct and indirect relationships between variables.

- Development of SEM software programmes such as LISEREL and AMOS to become more user friendly providing both syntax and window based facilities and providing both a pictorial and statistical view of the model.

(Schumacker and Lomax 2004)

4.3.2.1 SEM and the SSc QoL

Modelling of QoL in SSc utilises the information gathered from measures (comparator measures) administered during the development of the SSc

QoL. The range of comparator measures used in data collection was derived from the themes identified from qualitative interviews, these being described in section 4.2.4.2. Whilst there were nine comparator measures identified for the postal questionnaire, not all of these may be required for use in the modelling process.

Selection of measures for use in the SSc QoL model

SEM encourages the development of a 'parsimonious model'; that is the simplest model which satisfies the statistical requirements of SEM. Therefore, although nine comparator measures were identified, the process of SEM modelling seeks to find a model which is the simplest possible. In order to achieve this parsimonious approach, a small group of comparator measures were selected for initial use in the model.

If it was not possible to achieve the statistical requirements of an SEM model with these comparators, then other comparator measures would be incorporated into the model.

Rationale for choice of the initial group of measures to be used in the modelling process was based on two aspects of the underlying construct they measured. Firstly, the strength of literature to evidence the relevance of the construct measured (for example the construct of depression), to people with SSc; secondly representation of each construct in the elements of the ICF. The observed variables included within the SEM modeling process are outlined in Table 4.6.

Table 4.6 Observed variables selected for SEM of the research hypothesis

Observed variable (comparator measure)	Element of the ICF
UK Function Index (UKFI)	Disability
Fatigue Severity Scale (FSS)	Covers all elements
Hospital Anxiety and Depression Scale (HAD) – Anxiety and Depression scales	Anxiety - Impairment Depression is not clearly categorised within the ICF framework but is included to its strength within the qualitative interview data

4.3.1 Measures of fit in SEM

Models developed in SEM must show adequate fit. This will require the chi-square value to be non-significant, the root mean square error of approximation, (RMSEA) to be <0.05 and the goodness of fit index (GFI) to be > 0.95 (Schumacker and Lomax 2004). These measures of fit are reported in chapter 7.

4.3.2 Summary of Chapter 4

This chapter has outlined the qualitative and quantitative methods used in this study. Interviews and a focus group were used for data collection in order to develop the descriptive framework of patient-perceived SSc QoL. Secondary analysis of the data identified the items for the needs-based SSc QoL measure which was developed using a standard methodology. This involved sending postal questionnaires to two randomly selected groups of patients with SSc, and the use of Rasch analysis to ensure internal construct validity.

The strategy for testing the research hypothesis, non-parametric testing and Structural Equation Modeling (SEM), was outlined together with details of model requirements and rationale for selection of the elements included within the model.

5. The descriptive framework of QoL in SSc

This chapter presents the results from the qualitative aspect of the SSc QoL development. This includes results from the interviews and focus group. There are two aspects to these results, firstly the descriptive framework of SSc QoL, and secondly the thematic analysis which informed its development.

Detailed analysis of the themes generated from the qualitative transcripts using examples from the transcripts to illustrate how interviewees presented the themes. Thematic analysis (as described in chapter 4), took place in three stages. Firstly, reading of the transcripts to become familiar with the data, secondly identifying emerging themes and creation of operational definitions of themes, and thirdly refinement of the themes and definitions together with description of sub-themes where present. Over-arching themes were also identified at this stage of analysis. These themes form the base of the descriptive framework of SSc QoL).

5.1 Profile of participants

The following table (Table 5.1) represents the demographic data of each of the interview participants in the format of the sample frame described in Chapter 4. Each cell contains the number of interviewees with those demographics. A '0' represents a sample demographic to which no one was recruited.

Table 5.1 Renewed sample frame with each interviewee represented in each appropriate cell

Characteristics	Diffuse disease	Limited disease
Male Disease Duration (dd)<5 years. Age <50years	1	0
Male dd <5 years Age >49 years	0	1
Male dd> 5years Age < 50 years	1	1
Male dd > 5 years Age > 49 years	0	1
Female dd < 5 years Age < 50 years	3	3
Female dd < 5 years Age > 49 years	3	2
Female dd > 5 years Age < 5 years	3	3
Female dd > 5 years Age > 49 years	5	4

5.2 Thematic analysis

5.2.1 First stage of thematic analysis

The researcher began thematic analysis by reading all transcripts in order to

form an initial appreciation of the data.

5.2.2 Second stage of data analysis - Initial identification of themes

The interview transcriptions were re- read by the researcher and underlining key statements used by the interviewees identified emerging themes. These phrases were then recorded on an excel database. On completion, the researcher read through the phrases and a second column of emerging themes was created. Emerging themes identified were:

- Adaptation
- Anger/Frustration
- Anxiety
- Attitudes
- Breathing
- Bowels/Bladder
- Control
- Confidence
- Dependence
- Depression
- Embarrassment
- Fatigue
- Finance
- Hand function (reduced)
- Hobbies
- Housework
- Hygiene
- Information
- Pain
- Relationships
- Restriction/Mobility
- Sleep
- Slow/pacing
- Social impact
- Treatment
- View of self

- Work
- Weather

At this stage, the researcher was seeking to understand the transcripts and to bring structure to the topics of the statements which had been made throughout all of the transcripts. In order to support a structure for the thematic analysis, operational definitions of the emerging themes were created.

5.2.3 Operational definitions of themes to allow consistency in statement allocation to themes

In order to ensure consistency within the thematic analysis process, operational definitions were made for each of the emerging themes. These definitions were created by the researcher, in order to define which statements should be related under which theme. This was an iterative process for the researcher throughout the analytical processes of the first and second stage of analysis.

Operational definitions of themes:

- Adaptation - A statement that refers to psychological or physical adaptation/ lack of adaptation of the interviewee to SSc or its consequences.

- Anger / Frustration - An expression of negative aggressive emotion, or the use of the words 'anger' and/or 'frustration'. This includes statements referring to the interviewee themselves or those around them.

- Anxiety - A statement that refers to worry, anxiety or stress of the interviewee.

- Attitudes - Feelings or perceptions of the interviewee or those around them, including statements referring to the understanding and sympathy of others.

- Control - A statement which mentions their control including being in control or loss of control in any aspect of their life which is related to their disease.

- Confidence - A statement that relates to the interviewees confidence which has effected any aspect of their life. Therefore it is primarily representative of self-confidence. This theme includes statements which directly uses the word confidence or self-confidence.

- Dependence - A statement referring to dependence of the interviewee including the fear of dependence or the loss of independence.

- Embarrassment - A statement which mentions embarrassment related to the consequences of SSc.

- Fatigue - A statement which refers to fatigue or tiredness related SSc or its consequences including fatigue related to breathlessness. This also includes statements that refer to methods for dealing with fatigue or psychological consequences of disease.

- Finance – This includes statements which refer to any financial effect of SSc, including that of insurance and financial planning.

- Future - A statement which relates to any expectations or feelings regarding the future, this includes the negative or positive, and denial

and the desire not to consider the future. It also considers the participants feelings for the future of those around them.

• Hand function - A statement which refers to the hand function of the interviewee. This includes deterioration of hand function related to their disease or its consequences, and may include statements which give an example relating to reduced hand function such as 'my hands are bad so I can't manage coins'

• Hobbies - A statement that refers to the individuals' interests or hobbies.

• Housework - A statement that refers to housework in relation to the interviewee. This includes the inability to carry out housework or the use of additional equipment.

• Information – A statement which refers to the desire for, use of, or witholding of information.

• Relationships- A statement which refers to the effect of the disease on the interviewee's family or close relationships. This includes the family/ partner reactions to the disease or the patient since the onset of their illness, and the participant's reaction or feelings toward them. This also includes effects on close/intimate relationships

• Restriction/Mobility - A statement that refers to limits or restrictions on the interviewees' activities or life including restrictions on their mobility.

• Sleep – Statements which referred to sleep and its impact

- Slow/pacing - A statement that refers to having to slow down, pace themselves or do things slowly. This theme is similar to the theme of Rest. The key difference in this operation definition is a longer amount of time taken to carry out an activity is 'slow/pacing', and a statement that refers to the need to break an activity sit or recline before or after an activity, or a regular rest/sleep falls under the theme of 'rest'.

- Social impact - A statement which relates to the interviewee's social activity or restriction on social activity. This also includes interviewee's feelings about social activity and specific issues such as meals and eating socially, and the social effects on relationships and the social life of others.

- Treatment - A statement which relates to medication or other therapies utilised to address symptoms or the underlying disease. This includes side-effects of these therapies and interactions with healthcare professionals and institutions.

- View of self – Statements which refer to how the individual saw themselves or felt they as people had changed.

- Work - A statement that refers to paid or voluntary work. This will include statements which mention the financial or social impact of work.

- Weather - A statement that refers to the weather and its effect on the disease or its physical or psychological symptoms.

5.2.4 Third stage of data analysis

The transcripts were re-read by the researcher and more detail was added to each of the themes in order to add a deeper layer of understanding to what is incorporated within each theme heading. The operational definitions were also adapted as required, although this was minimal. The large numbers of themes were reviewed, and a third stage of analysis conducted. This third stage of analysis was the grouping of themes into overarching themes.

5.3 Over-arching themes

The conceptual basis of each theme was considered and each theme was brought together with others of a similar conceptual background to establish the overarching themes of SSc QoL (as seen in Figure 5.1).

Figure 5.1 Overarching themes

These overarching themes represent groups of themes with a shared conceptual background. For example, those themes related to the over-arching theme of Self were selected because the researcher assessed them to have an effect on Self. These over-arching themes are now explored in more detail together with detail of the themes of which they are composed.

Each overarching theme is followed by its constituent themes. The themes are displayed diagrammatically in order to give a more complete understanding of the experience of living with SSc. The theme is presented on the left of the page, relating to the sub-themes on the right. Each theme and sub-theme is represented within an oval shape. No ranking or interpretation has been applied to the themes. Arrows linking the theme to its sub-themes are not intended to be representative of causation, as this level of analysis was not carried out.

Each diagrammatic presentation of the theme and sub themes are explained and examples of supporting quotes from the interview texts are presented. The interviews are identified by number (e.g. Int 25) with the quote following on. Quotes from the text are identified by the use of italics.

5.3.1 Physical Restrictions
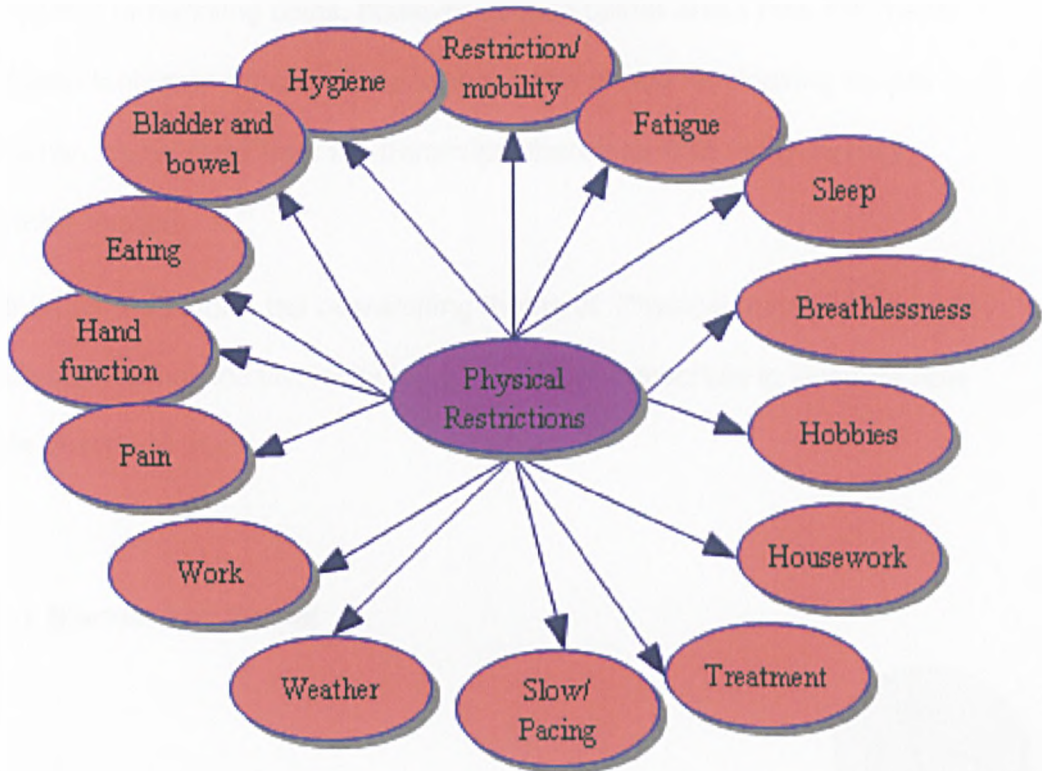
Figure 5.2 Physical Restrictions

The overarching theme of physical restriction represented a large number of the themes identified from the qualitative data of this study. Whilst many themes represented a purely physical aspect, others were much broader physical themes such as fatigue and sleep.

Many people discussed the physical restrictions SSc had placed on their lives. These were expressed both in terms of how the restriction had effected their abilities to meet their own needs in life such as in terms of housework, cooking, eating and dressing, but they were also expressed in terms of their wider implications. For example, in interview 1, the interviewee

clearly expressed the difficulties of his reduced hand function in terms of opening tins or handling coins, however he also talked about how this made him dependent upon others, and also that it had meant him leaving his job as a joiner. It was clear from the transcripts therefore, that many themes were inter-related.

The themes which form the overarching theme of 'Physical restriction' are now discussed individually, including quotes from transcripts to illustrate how people described them.

5.3.1.1 Bladder and Bowel
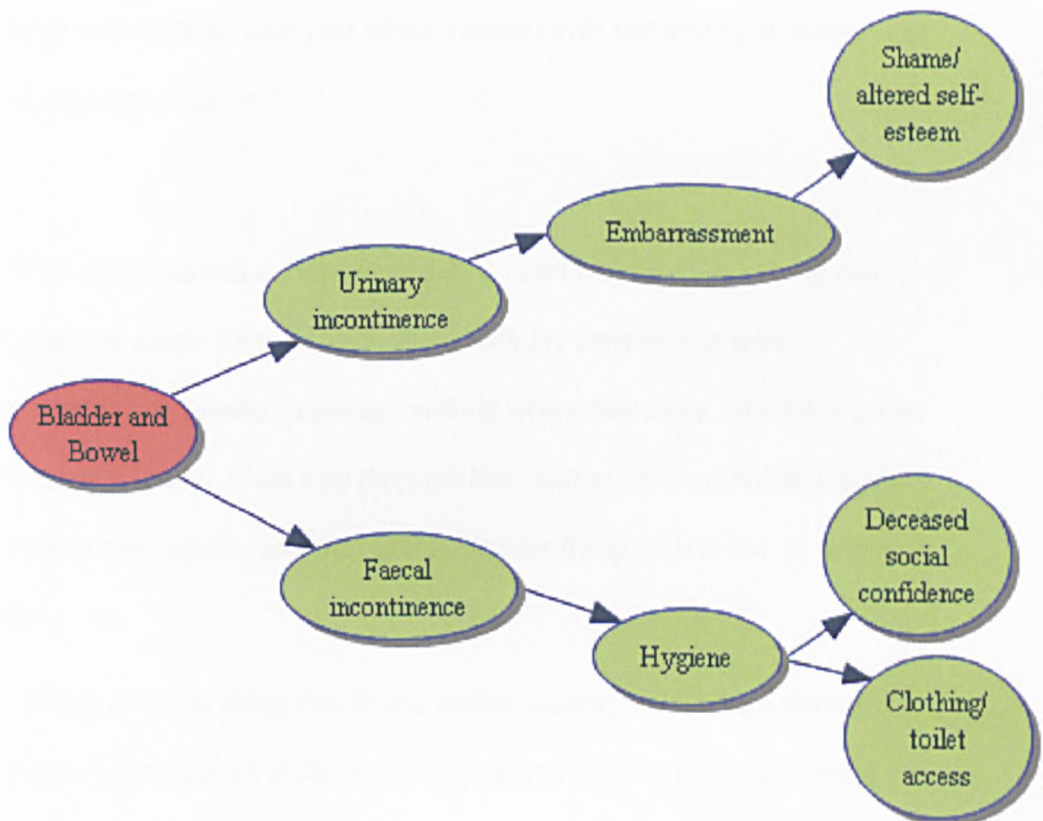
Figure 5.3 Bladder and Bowels

On initial analysis, this section had been incorporated within that of hygiene. However on further exploration of the transcripts, the effects of SSc on the bladder and bowels of individuals, and the wide-ranging effect this had on their lives, it was considered that these themes should be separated.

For example;

Int 9

" I don't feel as though I can do just what I want to do or go where I want to go or you know, eat what I want to eat or you know that way, its affects.... It's not that I want to go out all the time just that I'd like to be able to go and not have to think of taking spare knickers and pads and you know one thing and another with you which I have to do because you never now when it's gonna happen."

Int 7

"The other aspect is bowels which is I can only imagine in my own mind, that the same thing is happening with my bowels (as with oesophagus) and unless I take something every few days.. then I'm aright for a couple of days. Then I go through this next stage you know, it's the same thing over again, and that is the biggest thing, you know its affecting my life".

"That's another thing I've found embarrassing, if I do take something, I make sure I don't take it if I'm going anywhere. I like to be near a toilet so that I can go."

Whilst bowel and bladder effects were mentioned by only a small number of interviewees, the intensity of their experience is clear. This subject is not

easily revealed but the openness of some participants telling their experiences was frank. It was not possible to divide these quotes into the headings of the diagram as they are interwoven, but each aspect of the diagrammatic representation is reflected at some point in the quotes which follow

Int 10

"I can't hold me water as I used to be able to, you know that seems to have gone, that's one of the things that's happened.... Yesterday I was having a nap in the afternoon and I woke up and the family came in unexpectedly.. and I must have been asleep a long time .... I was absolutely desperate, I stood up and I thought well I didn't dare to stand up because I knew when I stood up I'd have to go but I stayed and I just said I'm going to the toilet and I was just weeing myself, it was really embarrassing. I don't think they even realised"

Int 30

"I can't control my bowels or my bladder... it doesn't keep me in the house but I've got to be very wary of thinking if its going to be a day when I know I might be going out that I need to know where the toilets are, that type of thing. Yes it is an issue (faecal incontinence) and if you really do want to go you want to go there and then and there's nothing I can do to stop it, you know you can't pull yourself back and control yourself, it doesn't work. If you're going to go you need to go and if you can't go then you do get soiling if you can't go".

"I don't like it, that's part of it that I really don't like and I don't.. I feel like I'm not in control mainly on holiday in France because toilets are few and far

between so I'm always thinking at the back of my mind perhaps maybe what

I'm eating two days before because that's perhaps when It will affect me if

we're out somewhere then I'm thinking I must make sure I've seen where

there's a toilet or there's a bar where you can go to a toilet or something like

that, that affects me quite a bit".

5.3.1.2 Breathlessness
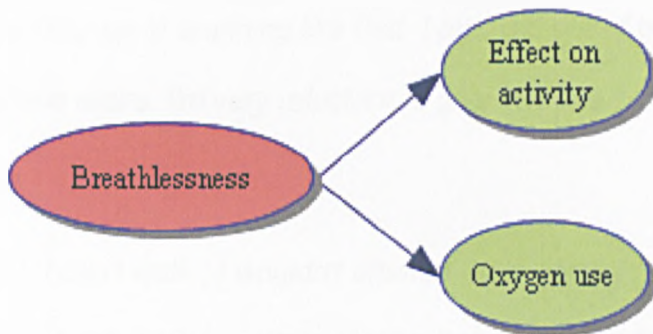
Figure 5.4 Breathlessness

Breathlessness was mentioned in various interviews, with people tending to

operationalise breathlessness; that is they usually put breathlessness into a

context within their everyday activity. This represented the impact of their

breathlessness on the everyday activities they need to undertake.

Int 27

"I do like walking and I did used to belong to a hiking club, we used to

go out. Then I realised the Scleroderma had affected my lungs, I couldn't

sort of keep up, and well, I gave up eventually but I do like to walk and I can

no longer walk... I only hope that my lungs will keep going you know, that's

the only worry I have with it really."

Int 29

"And I do get breathless as well, which I'd, I never used to do you know, like if I'm walking up hill I do get breathless there's no doubt about that, which I presume is something to do with it all."

Int 25

"I get out of breath a lot more since I've had Scleroderma.. I do get out of breath very easily when I only do little jobs around the house like dusting or washing up or anything like that. I also get out of breath very easily when I climb the stairs. I'm very reluctant to give into this."

Int 33

"..I can't walk ; I wouldn't attempt even going to walk up this hill. If I go to town I only park in certain places, hopefully on a flat and think... getting there's one things but am I doing to be able to walk back without, not dying, but coughing and spluttering and not being able to breathe."

Oxygen therapy was discussed in one interview only. It was included as a sub-theme of breathlessness in order to capture an effect of the effect of oxygen therapy. This person felt it affected their pride to be seen using oxygen therapy. People also echoed this with the use of other medication in front of their children.

Int 33

(referring to oxygen use for air travel)

"The oxygen things was a lie because you didn't have to pay it, the woman said you can have it as long as you don't have to have it all the time (on the flight). I didn't use it all the time because I just thought.. it's a pride

thing. Yes, I think it's a pride thing for me, its very difficult to use oxygen in front of people and in front of strangers and I wouldn't have sat on the plane with an oxygen mask on, I don't think I would."

5.3.1.3 Eating
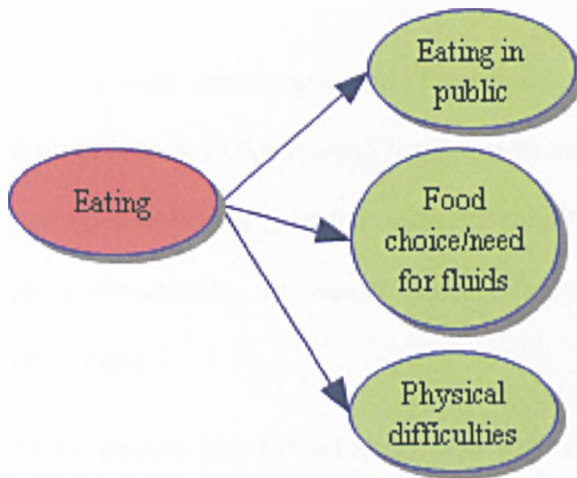
Figure 5.5 Eating

Eating was a strong theme running through interviews. This was related to the physical effects of SSc including microstomia (decreased mouth opening), oesphageal dysmotility (slowing of the passage of food through the oesophagus), and reduced hand function (leading to difficulties cutting food).

Int 7

"I developed this eating problem when I start a meal I really want to eat it, a few mouthfuls down and its stuck half way, you know between my stomach and my throat. It just won't go down, and I find that my saliva glands start working overtime and sometimes the answer to it is to leave the

table you know and then bring it back again. And then eventually after waiting a while, even drinking doesn't help, cause it all builds up its as if its stuck and guilds up on to of it and I finish up with it. So I have to go to the toilet, then I can go back, warm my dinner up and probably eat it"

Int 27

"It does affect my mouth, I get quite a lot of sores in my mouth from time to time and I've having trouble with my teeth because of the mouth getting smaller we.., I can't open my mouth very wide when they're trying to get impressions… my mouth doesn't' feel just the same or look the same I don't think."

Some people also talked about how their choice of food was affected and the need to accompany food with large amounts of water to wash down the food which feels to be stuck in their oesophagus.

Int 19

"When I'm stressed I do loose weight very easily, last year I got stressed at work and lost a stone and it was like eat all the food and I was trying, but when my oesophagus is playing up that's when I don't want to eat certain things .. the only thing (type of food)"

Int 19

" I tend to worry about in a restaurant is will I have enough water. I can eat anything as long as I have enough water to wash it down because my oesophagus is too small so the main thing is just water to wash it down with and that will get me slightly anxious and if I'm with my mum or dad they will know the first thing they do is order a jug of water… because I cant' eat

without it. I do find it uncomfortable and when it was very bad it would make

me throw up and that would just put me off eating. I just did not want to eat

in public because I couldn't guarantee what my oesophagus was going to do

no matter how much water I had and I was a university so I lost weight."

5.3.1.4 Fatigue
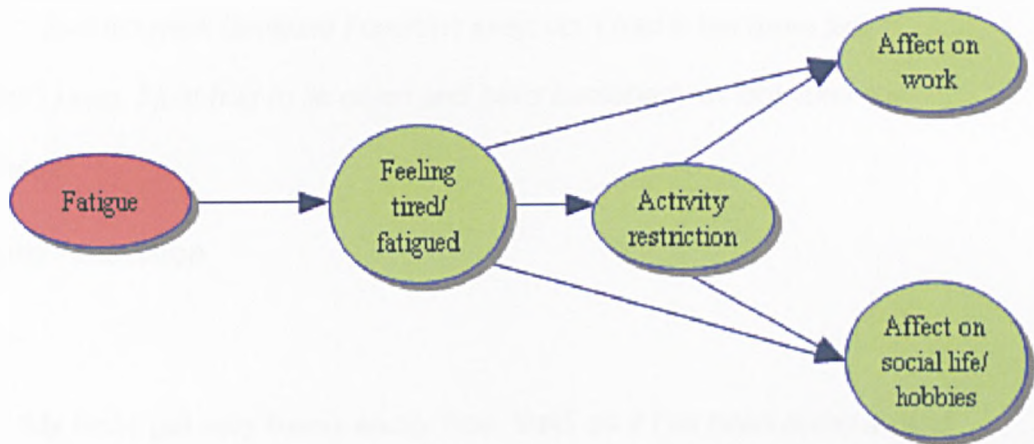
Figure 5.6 Fatigue

Fatigue was a theme that appeared to pervade into many aspect of people

lives. It affected people's physical and psychological ability to participate in

aspects of life such as their work, hobbies, and social life.

Affect on social life/hobbies

Int 14

"Well I've had a lot this week (fatigue) actually, and it's quite strange.

Last week it just, generally I'd finish work and come home and just be tired,

just the whole body seems to be tired, the mind just seems to want to shut

down and all I want to do is sleep, so I'd want to watch the soaps so I'd

watch them, have my tea and I would be in bed. And on my day off, I find that I tend to just sleep all day which I don't like to do because I've got things to do but I just find that I can't get out of my bed because I'm just literally tired."

Affect on work

Int 3

"I couldn't work because I couldn't keep up, I had a tea room and I couldn't keep, I just had to lie down and have somebody to look after the business"

Activity restriction

Int 26

"My limbs get very heavy easily now, tired, as if I've been doing a hard days work all day which I haven't, which I used to do which never used to have no effect on me. As I say this only happened this last twelve months, since I was diagnosed with Scleroderma, that this has happened and it just beggars belief .. sometimes I feel absolutely shattered and that's even when I've done nothing. I get these days where I just don't want to do anything, which isn't me... I'm exhausted when I get up in the morning because I reckon I've done too much the day before."

Int 31

"Well sometimes you have a good nights sleep and you get up and still feel tired and you think , am I tired or aren't' I, and it was difficult to explain to people but reading about it, I thought, yes, that's what I feel like. You think

you shouldn't be tired but I am and you're doing things and you soon get

weary."

5.3.1.5 Hand function (reduced)
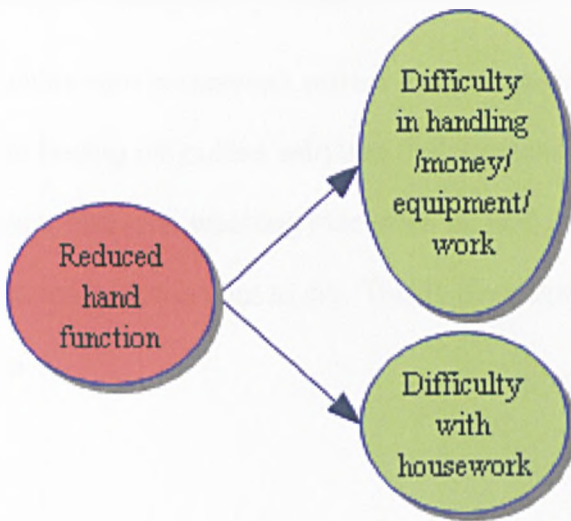
Figure 5.7   Hand function

The effects of people's hand function were diverse, but had particular effect on their abilities at work, with their housework and with hobbies. For example, this gentleman found great difficulties with the equipment required for his job as a mechanic.

Int 29

"I have a garage and its like working my fingers were all stiff, my fingers were all swollen, very badly swollen and I couldn't sort of do spanner work like I ought to be able to do. My wrists were very limited in movement and very sore..."

Or this lady whose job was as a make up artist in a high-class salon

expressed the difficulty of maintaining her job:

Int 14

"With this illness affecting my hands and I work as a make-up artist, so I

do need my hands in my everyday job which again is restricted because I

get people looking at my hands..."

Difficulties with housework were a more frequent impact of SSc, with many

people finding difficulties with use of household equipment such as tin

openers, hoovers, washing machines as well as tasks such as washing up

and hanging clothes out to dry. This is discussed in more detail in a later

theme.

5.3.1.6 Hobbies
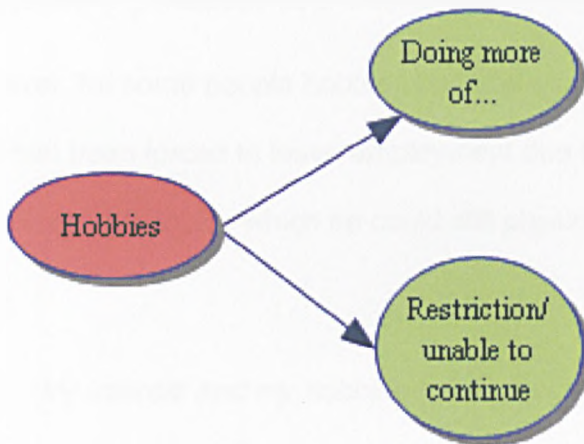
Figure 5.8   Hobbies

Many people mentioned hobbies, some people talked about how SSc had

restricted their ability to carry on with their hobbies, and some who

mentioned that their hobbies had changed or that they had more time for hobbies.

In 18

"Emotionally I've had to make massive, massive, decisions that have been heartbreaking – the selling of a young pony because I can no longer work outside with her in the winter, as a youngster she needed a lot of work being brought to saddle and she's had to be sold; and all my plans and my hopes for the future have been stopped."

Int 35

"I love bird watching and I find it very difficult to hold the binoculars anymore so we go to places that have hides, so I can rest my hands on, on the shelves in, cos if I'm stood like that Eric holds the binoculars for me you know, its you'd just cry otherwise, you just make allowances don't you... I miss gardening because I can't bend down, I can't get down."

However, for some people hobbies became a larger part of their life. This man had been forced to leave employment due to his SSc and therefore had more time for hobbies which he could still physically continue.

Int 11

"My interest and my hobbies have now become my way of life with the computer, you know so the shines gone off that a little bit but it seems like the only thing that I've really got where I can't go out and then there's that much where I can't go out that that's all I want to do is on that one thing... but sometimes I could kick it through the window... because it makes me feel like a sad head... it sometimes feel a bit pathetic."

5.3.1.7 Housework
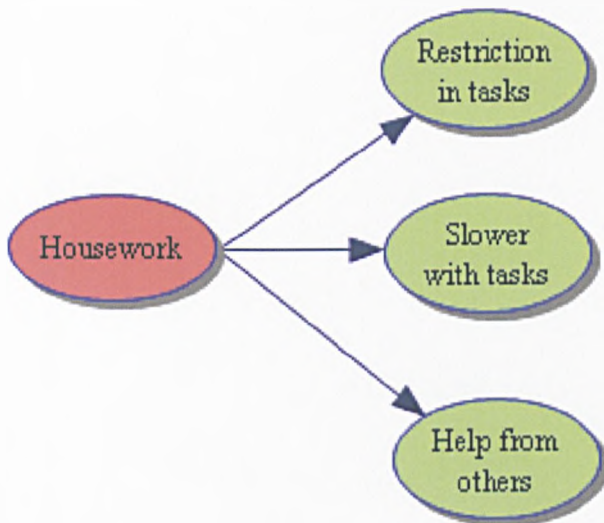
Figure 5.9 Housework

The main impact of SSc in the context of housework was difficulties with carrying out household tasks, and required adaptation or assistance in order to carry out such tasks.

Int 33

"I mean, you can't go to town, go shopping. I can't, I get out of breath hanging out washing. I get out of breath putting washing in the washing machine."

Int 31

"I think if anything its my hands that are the most trouble because they can be a bit stiff, but its probably strength, I drop things and have to pick it

up... you don't realise so I do tend to drop things and I'm slower as well, I

hadn't realised until I went on holiday with my sister and her husband self

catering and we were preparing vegetables and I was just peeling and doing

things as normal and she was doing it a lot quicker than me which I hadn't

realised until I saw her that I had slowed down."

Help from others

Int 7

"You know its gradually come on, with the use of my hands that make it

, there's quite a few jobs that aren't comfortable to do... I don't have to force

myself to do the potatoes, because I can't hold potatoes, quite a lot of jobs

really, and he (husband) goes out for instance, in the cold weather that really

does... I have a tumble dryer for days that... really you have to adapt ."

5.3.1.8 Hygiene
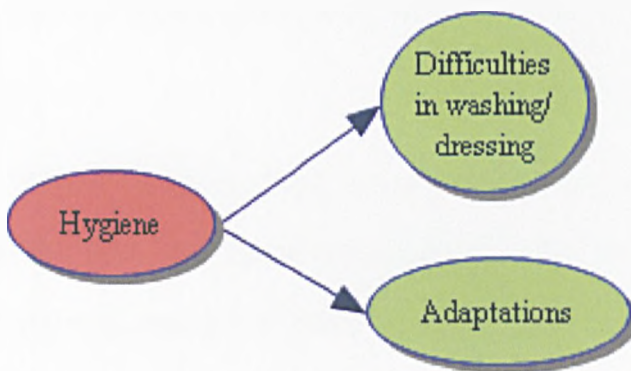
Figure 5.10 Hygiene

Hygiene was again a theme which was expressed in terms of restriction and the adaptation and assistance which may be required in order to meet the individuals needs. Adaptations for the bathroom were described:

Adaptations

Int 12

"I still can't get down on my knees, I did once because I just didn't think and I had a hell of a job getting up again, so I don't do that anymore. I've had handrails put in the bathroom and a shower put in so that I, you know, I can't sit down... I hold onto the handrails when I'm having a shower and you know...."

Further insight into the difficulties of people living with SSc is given by the following interviewee who offers a description of the difficulties they experience when washing and dressing, underlying the need for test, the time taken to complete these tasks, and the upset this can cause:

Int 32

"I had to go to the toilet.. it took me ages and I thought, oh crikey, it really did upset me. It was the breathlessness; I'd put on my dressing gown on a morning, one arm and then I'd have to sit on the bed, get up and put the other in. Sit down again and then I'd come in here and slump in here and I used to think to myself, I would have done the shopping, come back and cleaned up in the time it takes me to get dressed. It was a days job getting up getting washed, having a bit of breakfast, washing up."

5.3.1.9 Pain

Figure 5.11 Pain

When pain was expressed, it was described in terms of an experience which required them to adapt their behaviour to accommodate its effects; pain affecting many aspects of their lives. Even the most basic task, such as standing, was affected by pain.

Int 29

"I couldn't stand up for very long and the only place where I was really comfortable was when I was laid down in bed and that's the only place where I was really comfortable, where thankfully I didn't have any pain... I was in pain constantly and it were getting worse all the time. I wouldn't wish it on any... it really is a bad, you know and you can't sort of put your finger on because its all over your body sort of thing you know, it makes you feel really, really, pulled down or it did me... really, really poorly."

Int 34

"Its not very often thank God (rash on feet), touch wood, but I've had to crawl out of bed and in here and work my up the furniture because I just

cannot put them to the floor its so painful, but it only lasts two or three days if

that, and as I say sometimes it can be gone the day after."

5.3.1.10 Restriction/Mobility
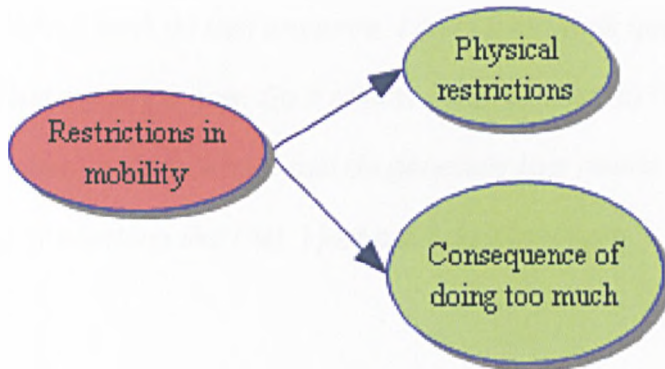
Figure 5.12 Restriction/Mobility

Restriction in mobility and the wide consequences of that restriction was clearly described by interviewees, who describe the musculoskeletal, fatigue and respiratory effects of SSc.

Int 33

"I'd say it's affected my life dramatically. I've gone from what I thought was a reasonably healthy person to being a person who takes a world of medication and can't walk long distances or flights of stairs without getting out of breath and I can't rush around. So there's lots of things that I can't do that I could do, in a very short space of time. "

Int 25

"My joints, my strength, and stamina and stuff like that. I can't do hills, I can't walk up hills.."

Int 21

"It limits because I can't do things that I want to: I used to go to aerobics regularly, I can't do that anymore. I can't even walk quickly because it's affected my lungs now. So it affects my breathing so I'm limited to walking. I'm limited really to what I can do generally that needs exertion or a lot of lifting or anything like that, I just can't do it anymore."

Int 25

"I can't do the things that I could do before."

Many people talked about bad days and good days and that sometimes they would push themselves because there was something they really wanted to do, and that there would be consequences to this:

Int 13

"I do have limits on what I can do and if I try and do too much then I just end up having a few days when I just feel really unwell."

Int 14

"You don't realise that the little things can be really big things that are actually part of your life that you don't realise because you just take it for granted every day that you can do certain things… being restricted in just doing general things, first it was probably things like opening a jar, just bending down to get something which obviously you're restricted to doing that so you don't feel normal."

5.3.1.11 Slow/pacing
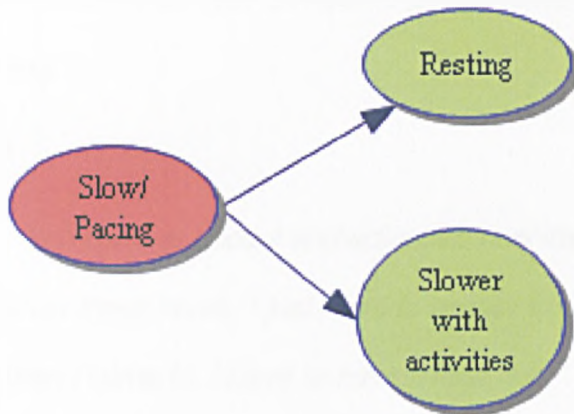
Figure 5.13 Slow/Pacing

A way of coping and adapting to SSc was slowing or pacing of activities. People described the need to rest regularly during a task in order to complete it, and also doing things at a slower pace. The following ladies describes how they use pacing and rest in order to complete their daily activity needs.

Int 29

"Like if I'm gardening, cutting grass or ought like that you know except it takes me about three or four time as long to cut all this grass than what it used to you know because I used to whiz it round with the flymo, I just sort of take it easy and do a bit of it at a time now."

Int 26

"I've got to pace myself because it does affect me if I dash and hurry things, that's when it affects me... I do try and go in the garden and do my

gardening, I do potter around the house and do things, the thing is I have to

stop and rest and then go back to it which at one time I have never had to

do.. it takes me at least an hour to get myself going and motivated in the

morning."

Int 21

"You have to accept and adjust so now instead of going out gardening

for two or three hours, I just have to accept the fact that I do half and hour

and then I come in, I have to have a little rest."

5.3.1.12 Sleep
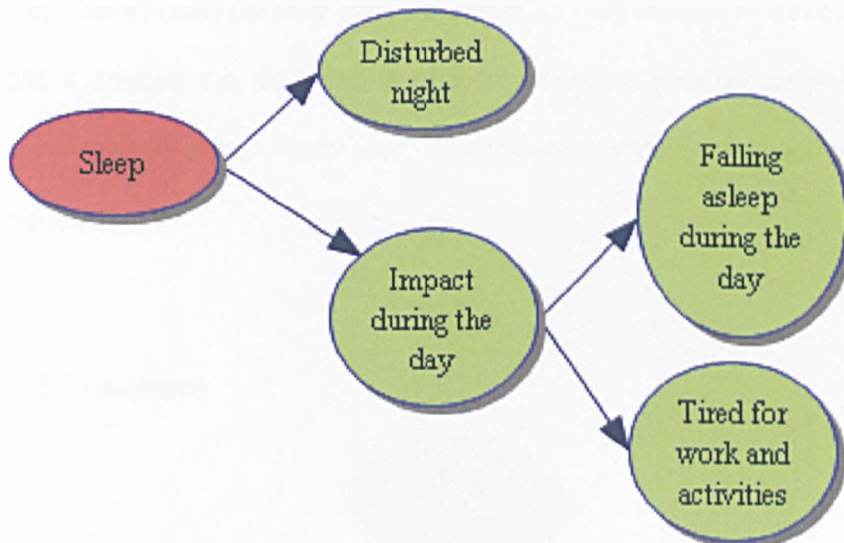
Figure 5.14 Sleep

Sleep was identified as a theme by people who described how their sleep

had been affected since living with SSc, also describing how sleep

disturbance affected them during their daily activities.

For example people described how they were sleeping during the day or how symptoms of SSc (in this example, cramp), were disturbing their nights sleep;

Int 1

"Its something to combat the terminal boredom when I can't sleep at night. I can't sleep at night. We've got to the stage where I was sleeping probably about five nights out of seven and then the five nights wouldn't be much longer than seven hours. That about as much sleep as I got"

Int 4

" my cramp disturbs my sleep and if you can't sleep them you don't operated very effectively the next day Its probably why I fall asleep in meetings, which can be very embarrassing ... I fall asleep in front of the telly at night. It annoys me, its irritating and sometimes it gets me rally wound up., I always used to sleep really well, never had any problems going to sleep, staying asleep."

5.3.1.13 Treatment
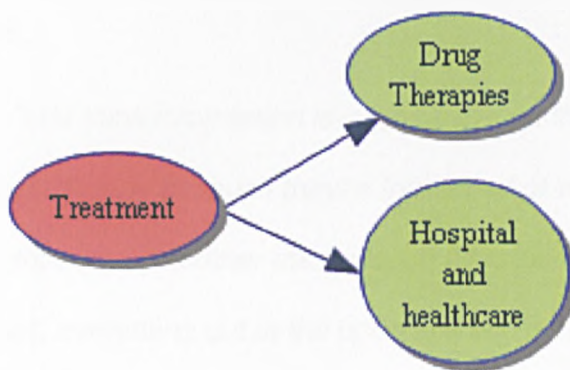
Figure 5.15 Treatment

Treatment was discussed by some interviewees, specifically talking about drug therapies or their experience of treatment delivery through hospitals or healthcare workers. For some hospital visits were an intrusion, others talked about how the drug therapy made them feel.

Int 18

"I recent, I utterly utterly resent coming to the hospital, every time the post comes and there's an appointment I hate it, I detest it because that's not me. It's, it's an intrusion. This illness has intruded into my life."

Int 20

"I get very depressed coming up to the treatment weeks, erm, knowing how poorly it makes me, but then I think OH well, its gonna make me better in the long run and how tired I am. As soon as I get out of the hospital I come home straight to bed and that's me in bed for like a day and a half until I feel up to getting out of it"

For some, information was identified as an important aspect of their treatment, this particular individual expressing the desire to have open communication and information.

Int 26

"I do think information is important and I think that's what a lot of people disregard really because they're frightened of what they're going to hear, well, that doesn't bother me because I'd rather know, I'd rather everybody be upfront, everything out in the open and laid on the tale., which they' all done up to press."

Several people valued the role of the health professional (specialist nurse) who had the time to listen to them and understand:

Int 10

"Its been really nice having someone as a supportive.. I think it's wonderful because you need somebody"

5.3.1.14 Work
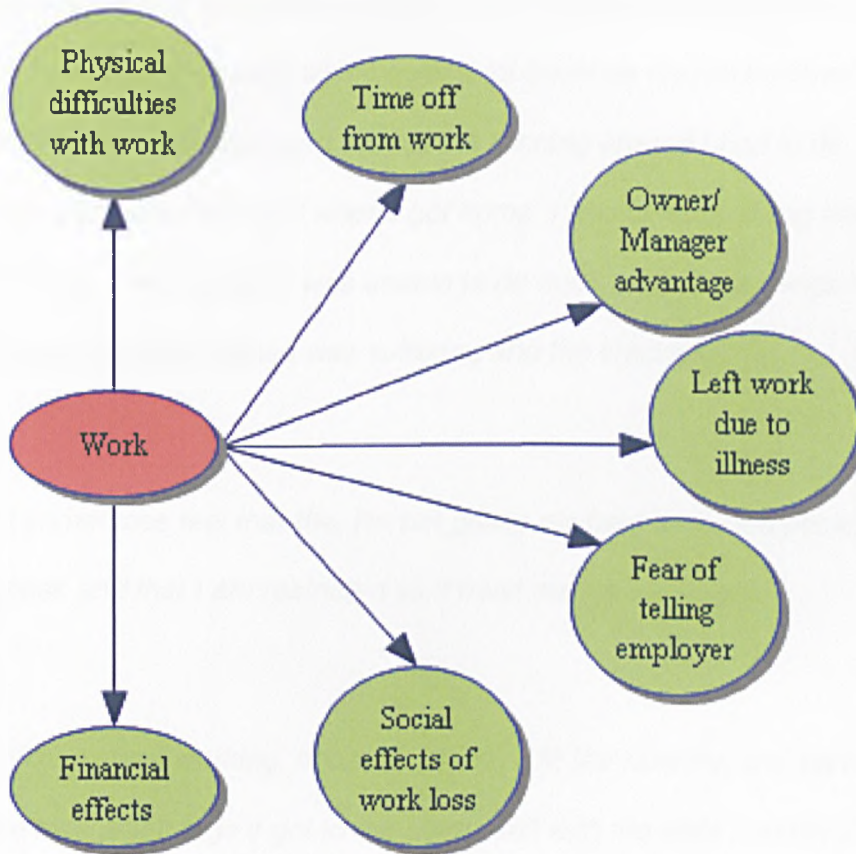
Figure 5.16 Work

Work was a complex theme, with impacts across many other themes such as finance and physical restrictions. People talked about the effect of SSc on their work in two main ways, how it affected them when still at work, and how leaving work had affected them. The effect of SSc on people at work included elements of physical restriction particularly through hand function and fatigue.

Int 28

"Whilst I was at work I suffered quite a lot of joint pains and I was finding that I wasn't having any energy to do my job. I was getting tired very quickly and breathless on walking quite a lot because my job involved supervising about 60 staff and with all the running around I had to do, I found I was exhausted every night when I got home. I had to keep sitting down quite a lot and resting and I was unable to do quite a lot of the things tat work due to the joint pains I was suffering and the tiredness."

Int 14

"I sometimes feel that the, I'm not giving my best to my job because of this illness and that I am restricted so it must makes me angry.

Int 31

"When I was working, because I worked in the nursery, and particularly outside toys and things it got to the point, well with the slide I couldn't' grip enough to life it to put it away, luckily the two people I worked with did what I couldn't do otherwise I probably couldn't have carried on working as long as I did."

There was also a concern not only about telling employers of their disease but of having time off work due to SSc.

Int 9

"I had quite a lot of time off work before it was diagnosed...then it was diagnosed I em, cut down my hours at work. So I went part time and then eventually I just had to give up work because it was too much for me.

It annoyed me; it really annoyed me because I like working .. it did annoy me because I did like working but I just couldn't do it so..I were having so much time off that it really weren't fair. You know it were like having 4 or 5 months off at a time, then I might work for 4 months and then I might need another 5 months off. You know it weren't fair really so em.. I gave up working".

Int 19

"Until about two years ago I never told work other than occupations health,... I got away with it, the last few years I've had more 'in-patient' about 5 in the last two years so I wouldn't have got away with it in the last two years, but it was about two years ago when I decided that I would tell work ... I didn't want to tell them because I was worried they would then make allowances for me and that they would then say that things were better than they were and they wouldn't judge me on my abilities but on the abilities of someone who is chronically ill, which I really didn't want."

For some, the effect of SSc became so profound that they were unable to continue with their job and described how that made them feel and the consequences which ensued:

Int 11

"I'm retired at 32 and I'm not very happy with it erm.. that's it really that's all I can say. I don't... my working and earning life's gone, it's took that away. It's took a bit of me respectability away as well you know because I like, earned what I got, and that's gone as well."

Int 28

"Eventually I had to go on sick leave and started visiting various hospitals trying to find out what was wrong with me....

I found it quite hard at first missing the people who I worked with and also keeping my brain active which whilst I was at work it was very active.. since I've been at home I've fortunately come to terms with not working which I'm very glad about it. I do miss the activity of it and meeting other people and sorting things out."

There were some interesting observations about the effect of position at work and its effect on how work could be managed. This was particularly so for those interviewees who were owners of their own business, or who were managers:

Int 29

"If I'd been working for a boss they'd have sacked me because I couldn't obviously do my job like I was, like I should have been able to do... there were five of us in the garage so I couldn't, I could sort of get through that way".

Int 34

"We're lucky we run a pub, we're pub managers so we get paid

regardless, as long as the work gets done it doesn't matter whether we're

doing it 50/50 or 90/10 or 100/0, do you know what I mean, we will get paid.

We've got staff as well so when I'm well I'll go and I'll work and I enjoy it. If

I'm not well or I'm tired or whatever, I don't have to do it and I don't do it and

it doesn't matter so we're very luck because if I worked for somebody else, if

I worked for instance for Marks and Spencer's I'd have lost my job by now

because I would have missed so much time and you know what I mean...

like I say if I had a normal job like my mother or you know, I would have lost

it."

5.3.1.15 Weather
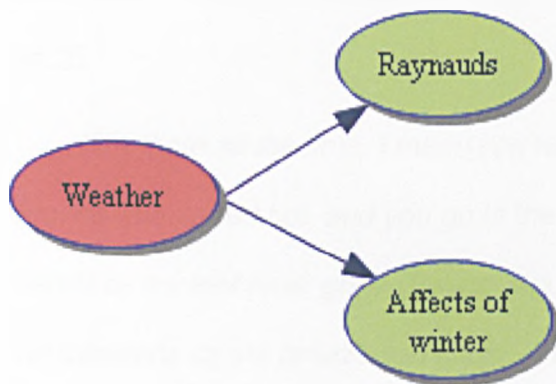
Figure 5.17 Weather

The weather and its effects on those with SSc was related in terms of the
Raynauds phenomenon (RP) experienced, and the consequences of
prevention of RP such as not going out in the cold weather.

Int 2

"The Raynauds has a big effect there's a lot of preparation you've got to make sure you've got plenty of things to keep you warm ..."

Int 30

"If I'm doing things (like driving, outside shopping) for a long time, then that affects them, more hands than feet really. I've had trouble with my feet over these last few weeks as well, which means that standing around and things like that .. I need to keep moving, once you stand around and they start going cold then I find its difficult to get going again. I've trouble walking until I get myself warmed up."

One individual relayed how this effect is present all year through, even when on holiday in warmer climates.

Int 25

"It's there all the time. I mean you're laid on a beach in the south of France and its red hot, and you go in the sea and then when I come out my hands or my feet have gone (Raynauds). It's not cold, it's just the change in temperature, or the breeze you know. I've got these black hands and I can't feel my feet and you're sort of hobbling up the beach. "

Int 31

"I go everywhere with gloves, scarf, tights in my bag in case I get cold, that's inconvenient having to take those things with you all the time."

5.3.2 Self
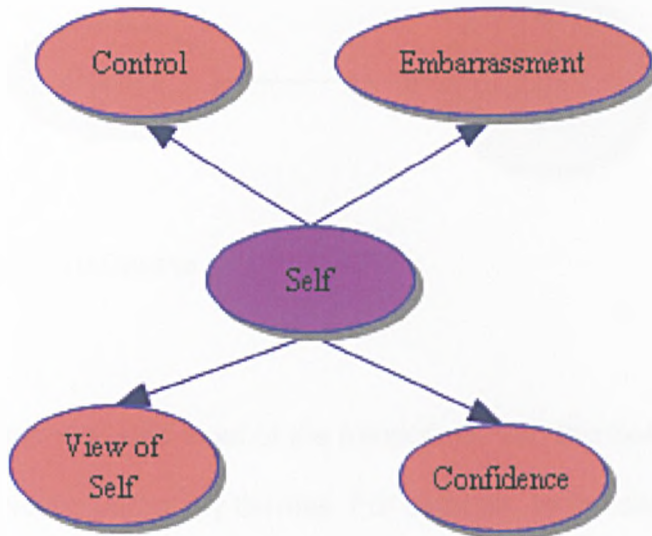
Figure 5.18 Self

The overarching theme of self was made of up those themes which represented aspects or feelings internal to the individual; and was therefore made up of psychological components. It was a difficult definition with which to work as many elements of people's discussion related to aspects of their individuality, but people expressed these feelings in a very personal way. They included aspects of control (self-efficacy), both over their lives and the disease; embarrassment which was frequently linked to symptoms; confidence which was underpinned by many aspects of the disease; and view of self which combined elements of visual appears, personality and loss of identity.

These themes are now presented in more detail.

5.3.2.1 Control

Figure 5.19 Control

Control pervaded must of the transcripts, with this being conceptual interwoven into many themes. For example, in the earlier theme of frustration, most of this arose from the lack of control over their abilities to control the limitations of SSc. This relates closely to the construct of self-efficacy which is the persons ability to exert influence over events which effect their lives (Bandura 1994).

In the following examples control is mentioned as an explicit theme. This was expressed as the lack of control over their own life to the control of SSc over their life.

Int 1

"The control bit as well. It didn't used to bother me, because I knew I could do virtually anything I wanted to, so no problem, no worries, no problems, I'd just go and do it. Now, I have to, I try to get as much control over my surroundings, or whatever's going on around me, because ultimately if it gets too bad one way or another, its going to affect me anyway. I don't mind having a day, or two days in bed coming round after doing something daft, that is that I had control over...."

Int 26

"I've always been able to do everything for myself more or less, then this Scleroderma with my hands, which is the most affected part of my body, is more or less controlling my life now."

Int 33

(in relation to assisted air travel)

"you were just under these peoples control and you felt, I don't you, I'm piled with all these bags on my lap or whatever but I actually felt quite.. I felt like disempowered, really disempowered, it was awful. It wasn't a pleasant feeling and I know it had its perk and I needed to do it but I don't know if I'd do it again. "

Int 7

"I think you've got to be the boss of the illness."

5.3.2.2 Confidence
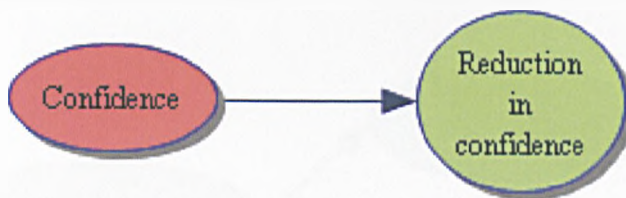
Figure 5.20 Confidence

Confidence emerged as a theme which interviewees often related to reduction in confidence. This appeared to be linked to a variety of factors.

For example, affects on their physical health, or as a consequence of others attitudes; these can be seen in the following experiences:

Int 10

"Things like shopping trips that I had on my own, going on the bus into Leeds, can't do anymore. I just can't. I've lost, I don't know if I've lost my confidence or what I've lost but I just will not do it on my own anymore. I've lost all that."

Int 14

"Well, it shows in a person if they're not confident with themselves, and I am to an extent things like my hands, just certain things, that I can't do that my friends are going to do..."

Int 5

"It started to affect me more, a lot was really, a lot more. And I became a lot less confident person than I ever was, really I think because my family fuss around me more, and don't let me.... I think I've lost my confidence an awful lot, I don't feel able to do things on my own as I once did."

5.3.2.3 Embarrassment
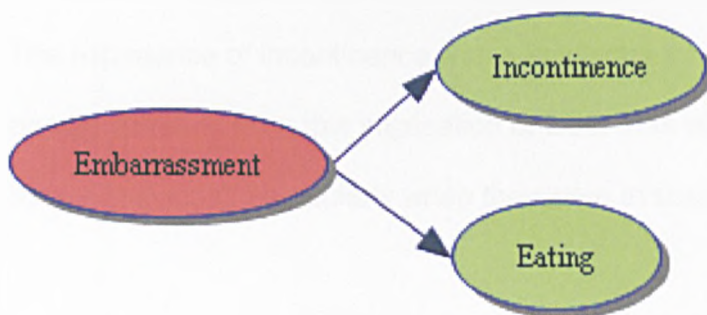
Figure 5.21 Embarrassment

Interviewees expressed a feeling of embarrassment linked to several aspects of their SSc such as eating in front of others, and the worry of incontinence.

Int 7

"Its becoming an embarrassment. We went away a short while ago and it happened then in fact then they warmed me dinner up once and I still couldn't eat it so I had for forego my dinner, its anything that seems to get into a bulk. I like my soup you know, so you know, its quite embarrassing, and sometimes a bit distressing"

This was also true for one individual who found sudden drying of her mouth which was a particular source of embarrassment when in a restaurant:

Int 30

"I don't always have it with me (mouth spray) but it does, that causes more embarrassment I think really sometimes If you start, you can start talking and then all of a sudden you can't talk because its gone dry and then you just cough and cough and cough until you get a drink or something... its embarrassing if you're out in a restaurant and things like that and start choking and coughing and things like that."

The experience of incontinence was a key focus for embarrassment in those people suffering from this implication of SSc. This was of significant concern for the individual, particularly when they were in social environments.

Int 9

"I used to go to rugby... I don't do that now because I just don't know when,

you know so I don't put me self in a position where if I'm going to have loose

bowels I'm going to be embarrassed".

5.3.2.4 View of Self
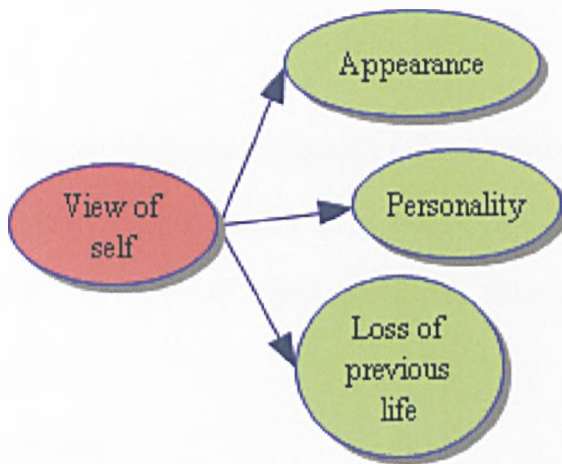
Figure 5.22 View of Self

View of self is a theme which encompasses those elements of the

interviewees where people directly mentioned impacts which were not

specific emotions, but which referred impacts of the disease on the

individuals inner self. This included elements of their personality,

appearance and feelings of isolation and loneliness.

Int 27

"I'm conscious of lumps on my knees and my arms you know, if I'm not covered up, they don't look very nice...these spots on my face, now I forget I've got them, sometimes I'm aware when I'm out that maybe children more than adults, maybe looking at me, you know, 'what are you looking at', if I haven't got my glasses on I don't notice them but I just wonder if other people notice. It would worry me."

Int 18

"I think I look old and ancient. To me the physical facial changes are horrendous yet you looking at me would probably notice no difference at all, but I do. I see it in the mirror and that is one of the work things, I see the changes."

Personality

Int 34

"You feel a lot of the time as you're missing out on things and that people think you're silly or a bit useless."

Int 18

"You've lost your personality, you've lost your privacy"

Loneliness/isolation

For some there was an experience of isolation, aptly described by one gentleman who had to give up work due to his SSc.

Int 11

"you may not like where you work, but at least you had somebody to talk to while you were there.. come winter time it gets very back, like being in prison..."

5.3.3 Impact with/from others

Figure 5.23 Impact with/from others

A theme, which ran through many interviews, was how the disease or its consequences had affected others, or how the person feared it might affect others. This was very much a social theme, including aspects of relationships and social networks. On occasion this theme was related to the direct effects of illness and particularly a fear of the future impact on family members. However, it also included interactions with the public and a

concern about the attitudes of others towards them, or how their attitudes towards others had been changed since having SSc.

Many people also expressed how the impacts of SSc had meant they were not able to meet their own needs and had become dependent upon others, or indeed that they feared this dependence in the future.

5.3.3.1 Social impact
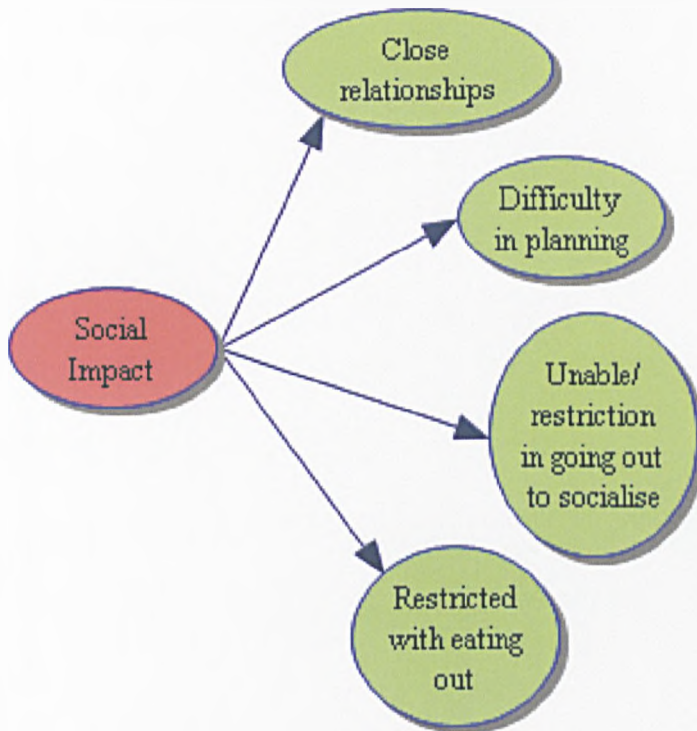
Figure 5.24 Social Impact

The impact of SSc on the individual's social life was expressed by many interviewees and has been alluded to in other themes such as eating and planning (sub-theme in the Family theme). The social impact of SSc has several sub-themes which relate to the specific restriction of eating out, but also include the wider physical restrictions relating to going out, the

difficulties in social planning and the effects of social impact on close relationships.

Int 20

"I can't go out with my friends anymore, well I do go out but feel like I'm burdening them because if you go to a night club it gets too warm and I can't breathe and if it's a smoky place that gets on my chest and everything so that's a bit of a downfall because I feel I feel I'm only young still and I want to go out and enjoy myself but I can't be in a confined place where it gets too warm or too smoky because that's when I need to go outside and then that means my friends not enjoying themselves but they're good about that, they understand that I'm not well... I've lost doing my exercised, I can' even do that any more, even going swimming I can't take the kids swimming because it gets far too cold too fast for me.."

These physical effects on social life are not the only influence. The next interviewee describes the effect of lack of motivation on social life:

Int 32

"I really have no interest in going out with my friends... and going out for something to eat, I couldn't eat it and I didn't' want it and it was an effort..... I really lost all interest.."

Int 25

"Its just different, it's a more sedentary social life now, you sit in a pub, or you sit in a theatre or you sit in the pictures rather than going out and doing things.

I don't feel as though I can do just what I want to do or go where I want to go or you know, eat what I want to eat or you know that way, its affects.... It's not that I want to go out all the time just that I'd like to be able to go and not have to think of taking spare knickers and pads and you know one thing and another with you which I have to do because you never now when it's gonna happen."

Difficulty planning

Int 34

"Its like, we were invited to a wedding of some good friends of my parents which has been brought forward. It's a £40 a head wedding and I've turned it down because with something like that it puts too much pressure on me, I can't, because I find, I might be wrong, but I find that if I am under pressure and I'm worrying about an event I can be worse health wise. If I'm worrying I've got to be alright for the day so I can go, chances are I won't be and at £40 a head I daren't not turn up. So, it's just easier to say I'm not going but you know its not nice really. I would like to have gone... you feel like you're missing out a lot of the time. You feel a lot of the time as you're missing out on things."

Int 21

"It's difficult (to plan) outings with friends. I have this friend and we just used to go sort of walking, go out for the day for walking around gardens and the houses and things like this which I haven't been able to plan when I've got a flare up like this because I don't' know now I'm going to feel that particular day which is very frustrating."

Close relationships

Int 19

"Relationships with men, its always a fine line deciding when to have the conversation (about the condition), how to have the conversation and what you want from them because immediately a lot of men will want to protect you and you want to say oh, it'll be alright, well not it won't be alright but I can live with it so I want you to and I think certainly from that grounds I mean I have told all my boyfriends and they've dealt with it in different ways and probably not as well as I would like quite a lot of the time."

Int 19

"With friends, its I think I'm slower to trust because I feel once I do trust someone I trust them with a lot and I tend to try and judge people before I do, do I think they can handle it and most people are fine when you say what it is and what the implications are and that it is serious. .."

5.3.3.2 Dependence
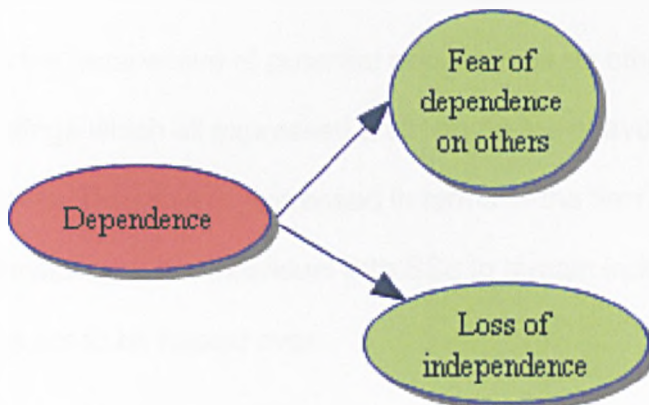
Figure 5.25 Dependence

When considering how to label this theme, it was a choice between the label of Dependence or Independence. The reason for this debate was that people spoke in terms of a loss of independence due to their SSc, or of a fear of becoming dependent upon others in the future.

Int 5

" I haven't driven for years, because my hands. so I lost my independence there, I've lost my independence since the flare up"

Int 12

"I got a bid dodgy on my legs sometimes so I was a bit concerned about going out on my own, shopping. People think if you walk along a road and you're staggering a bit, people think you're a kind of drunkard, people are thinking like that about me, so I tended not to go out unless there was someone with me."

Int 5

"I can't, I don't feel able to do things on my own as I did".

From the perspective of potential dependence on others there were a range of feelings which all expressed a strong theme of avoidance of dependence of others. These were expressed in terms of the firm belief that it was the responsibility of the individual with SSc to remain independent, and the desire not to be fussed over.

Int 18

"I think everyone should carry their own burden and that everyone around me doesn't need to carry this yet simply because I can keep it a secret: I'm not dependent on anyone."

Int 33

"It may sound really bad but I'm getting pampered and its doing my head in, not in a nasty way but I'm just getting, you know, that I can't do for myself and I'm thinking, God, if I get any worse and people have to do for me, I think I'll be the worst patient ever, I think I will. I'll be the worst patient. I don't like not being able to do for myself; I think that's really hard."

5.3.3.3 Information
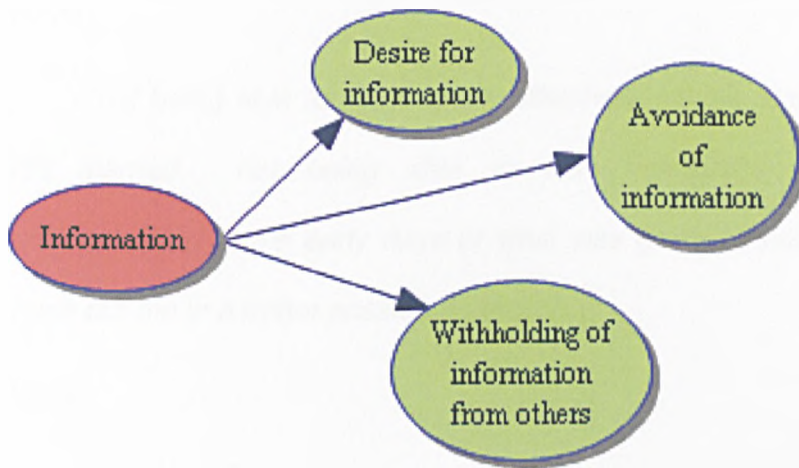
Figure 5.26 Information

Information was a topic that was expressed by many people but in many, often contradictory, ways. Whilst some keenly felt the desire for information and truth, the desire to know the minimum to get by was needed by others. For many, information represented the power to plan their life, for others it represented a vision of how their life may become with which they felt they couldn't cope.

A common comment however was that when they gave information regarding scleroderma to friends and family, no-one had heard of it.

Int 26

" *I do think information is important and I think that's what a lot of people disregard really because I think a lot of people don't like to ask questions because I think a lot of people are frightened of what they're going to hear: well that doesn't bother me. I'd rather know, I'd rather everybody be upfront, everything out in the open and laid on the table and then everybody knows how they're going on and you know what to ask*"

Int 33

"*not being able to plan my life effectively I think. I've got two children, I'm married... not being able to plan financially, I think a better understanding in the early days of what was going to happen to me would have put me in a better position financially..*"

In 19

" *its not a disease you can see and people don't know I've got if unless I tell them, so that for me at this point is the main impact and part of it is about me deciding how much to tell people and deciding the implications*"

5.3.3.4 Finance
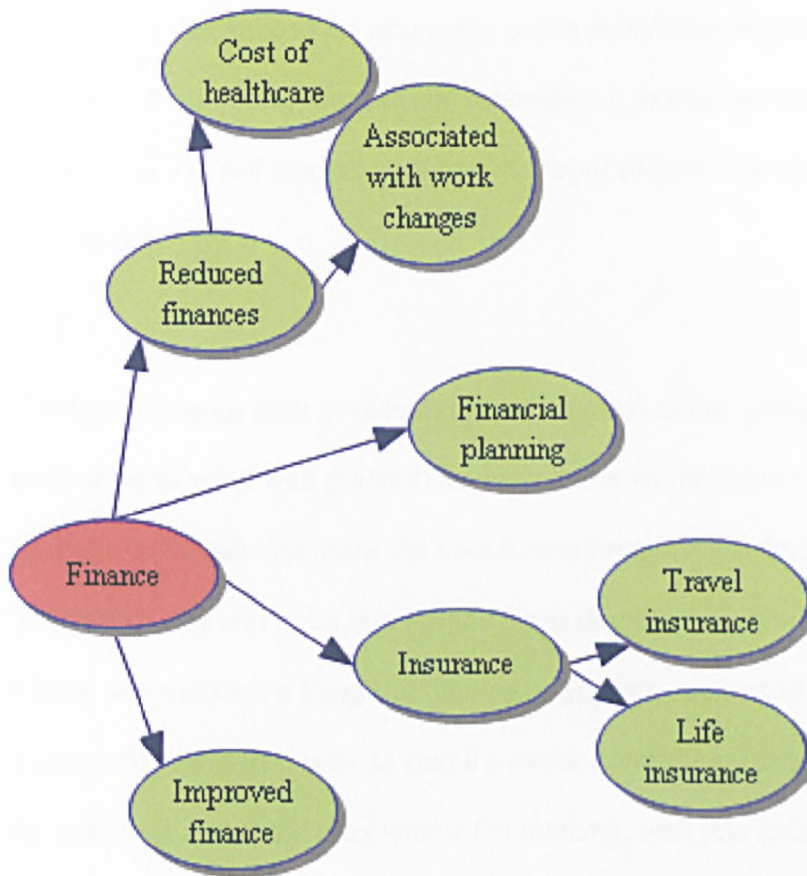
Figure 5.27 Finance

Finance was a complex theme which emerged in the context of several areas of life, such as insurance, financial planning, reduced finance and in the case of one individual, improved financial status due to the effect of SSc. People expressed finance usually when questioned, but had introduced aspects of finance such as insurance and the effect of work loss on finance.

Int 28

"Financially at first when employers didn't know what was wrong with me, I was on sick leave for about four years so they were very good to me

and I was on full pay... I managed to get a deferred pension after about three years, backdated for about two years which has helped quite a lot and I've paid off my mortgage with my redundancy money so really I'm quite alright now, I'm not loaded but I can manager alright. I've no money problems."

Int 33

"I mean not being able to plan financially. I think better understanding in the early days of what was going to happen to me would have put me in a better position financially because the knock on affects for me financially now are everything that you have you should have declared. Do you know what I mean, any insurance thing that you have you are supposed to have declared so as I didn't realise I was so bad it's never something I ever really thought of...and now I'm at the crux where I'm thinking, well you know it may be that I might not get to work the rest of this year because that's now the future holds for me. I may have to stop working, if I'd have known then I would have invoked certain things earlier."

Insurance was mentioned in the context of life insurance and holiday insurance, people commenting on both the difficulty and expense in purchasing these products. This was frustrating, being expressed neatly in the feeling that they were being penalized twice, once with the illness, secondly by then having to pay additional cost for insurance when the disease did allow them to travel.

5.3.3.5 Relationships
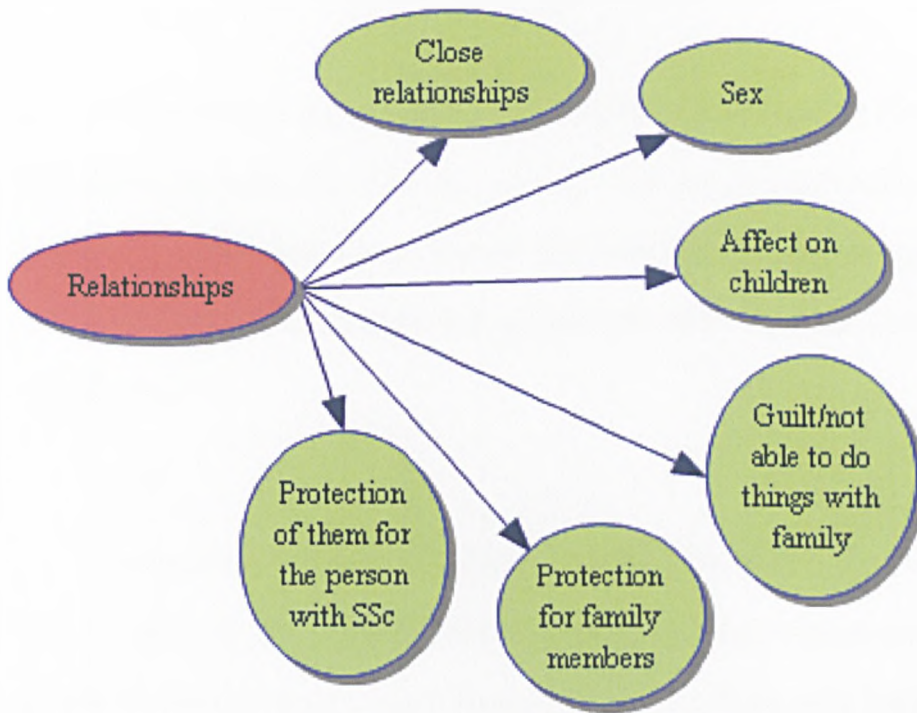
Figure 5.28 Relationships

It is perhaps unsurprising that interviewees frequently described the wider effect of SSc, in particular effect on their relationships and their family and friends.

As Figure 5.28 suggests, this effect was broad, with direct effects on family members, and impacts on other relationships. For example, interviewees talked about their desire to protect their loved ones from the effects of SSc, in the present, and in the future.

Protection for family members

"Int 18

I've become so secretive and evasive, protecting everyone else when probably it should be the other way around. I will not discuss it with anyone so the only person who knows I've got this illness is my husband. I just cannot be bothered to burden other people with what I consider to be a catastrophe."

Int 34

"I've got three children. I don't tell them much because I don't' want them to worry unduly so I'm not one of these people who makes out to them, oh I've this terrible illness, I just make light which is, that's what I want to do anyway,. I don't want it to be anything terrible so I just say well to the youngest one, I just way I'm going to the hospital. I don't' ever go into a lot of detail. I just don't want them to worry, why should they worry about it, I don't want them to so I just make it very light."

Int 33

"It made me feel quite sad that my son should think, I know that the worries about me and I don't think at thirteen you should be worrying about your mother. I think you should be worrying about your play station games are working properly or do you know what I mean. I know he does seriously, seriously worry about me because we are tight, he's my first born son and all that. I don't think any child should lose their parents when they're young but they may have to go through that and I worry about that because I don't think it s fair."

Guilt/Not able to do things with family

Int 10

"(after treatment)... I feel guilty because I can't go with the kids."

Int 20

"I try not to if we try to take the kids like bowling they play and I watch, I can't hold the balls, the balls even a child's ball is far too heavy for me so we still go to these places you know, bowling and stuff because I don't want them to miss out on things but its you know, its limiting.."

Close relationships

Int 4

"My husband is a worrier and he's definitely a worrier and although he doesn't say so to me, he's definitely very wound up about it and I suspect that is at the bottom of his flare up.... He doesn't take it very well (my disease) so he gets all stroppy .. We all wind each other up yes, yeah, .. my condition makes it worse he's worrying about it and he doesn't talk about it "

Int 33

It's really hard for people watching and its really hard for my mum and its mum and dad and my brother and some of my close friends. All they do is get to hear all the bad stuff and they can't do anything about it and I think it's that feeling that they can't do."

Sex

Int 14

"You can get intimate with someone as you would have been before because you're restricted with your joints and I mean when I was in a relationship, I was with him for five and a half years, I know it had a strain on him, me being ill, but just you know obviously we would have sexual intercourse, I would be restricted to what I could do because of the fact that I couldn't bend my legs, or I couldn't, I'd get pains or just general things. So it has really really affected that area and I think that's why I'm probably more scared to meet someone because how to you say, well I can only do certain positions you know. It is really hard to deal with that."

Int 9

"I think we've accepted the effect (lack of sex drive) now"

Affect on children

Int 1

"The children are more jumpy. They're on edge all the time when I come over to hospital, even if its for just a normal outpatient appointment."

Int 2

"She gets so upset (daughter) when I can't do things, and I get upset about it and when I get frustrated I yell at the kids. My son worries about things like tablets. He hates the tablets with a passion, he gets very cross because I have to take them. He gets cross that I struggle taking them some days."

5.3.3.6 Attitudes
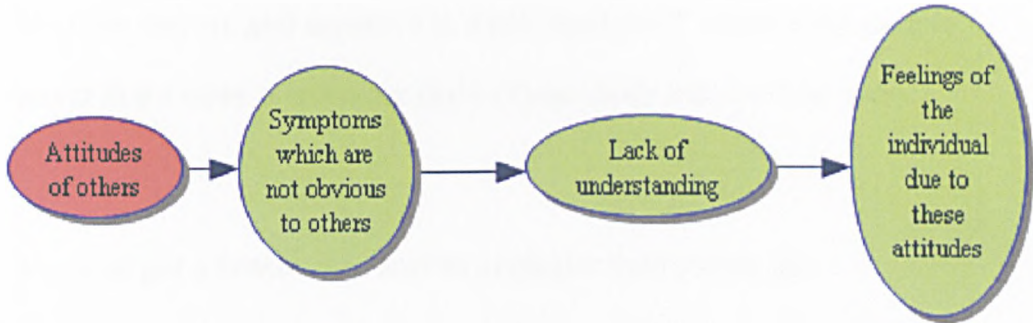
Figure 5.29 Attitudes

Attitudes emerged as a theme which was commonly expressed within the interview transcripts. Attitudes of others towards the individual with SSc were one of the aspects of this theme and commonly linked to the individuals feeling that others were judging them. This could be because they were unable to fulfill the physical activities which they would normally have done. This can be seen in the following transcript example.

Int 20

"You know some people do judge you because even though you're walking, they think you have to be disabled not to walk, they don't realise its other problems so I think that a lot of people might judge, I feel like people judge me because of that, because I'm not walking with a limp so they can't see that I'm like breathing heavily and stuff."

The attitudes of others was continued within this theme, with people feeling that others didn't understand the effect of the disease on them, and that because symptoms of the disease weren't always physically obvious, sympathy and understanding of others was limited:

Int 7

"You can only try and explain it to them, can't you? I don't think people understand that it does affect other parts of your body that can't be seen.."

Int 21

"If you've got a broken limb and its in plaster then you've got everybody's sympathy; when I had the ulcers on my foot I got everybody's sympathy because that toe was all black and gungy and horrible looking and it was great but with this, there's nothing to see, yes my hands are swollen, I mean that's not enough to give everybody sympathy towards you and so there's nothing that they can see so the sympathy is really zilch, so they don't understand."

The effect of the attitude of others is shown by potential effects on the individuals view of themselves, potentially leading to the feeling of a need to justify themselves or their symptoms. Lack of understanding of others was a clear perception on those living with SSc.

Int 34

"You feel that people think that you're silly or a bit useless., like when we were on holiday last year we were in Majorca and it was decided we were all going out one night with some friends we decided we were going out she decided we would walk. I can't walk that far, and talk at the same time but people don't understand unless you tell them everything about it they don't' understand and they think well, she's only young and she's a hypochondriac, you know what I mean. oh, there's a lot of things you tend to withdraw yourself."

The need for a positive attitude of those around the individual is also demonstrated:

Int 26

"I've had friends that have had people that's poorly and its got them down and its affected them and they blame the person that's poorly for making them like they are and I think its not the person that's poorly that's always to blame, you can't always say that its them that's caused it. It think its the attitude of the other person what they've got to come across with, they've either got to take a positive aspect of it, of the person who is till and try their best to help them out, else they don't, the don't bother.. I've been lucky because I've got two great daughters."

5.3.4 Emotions
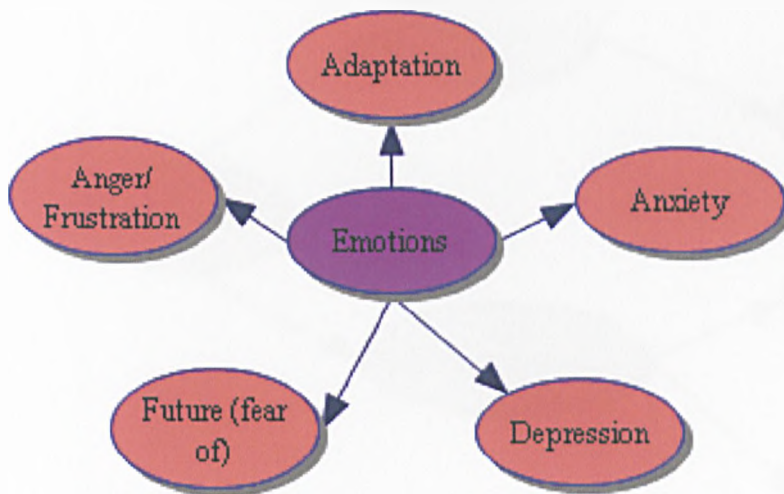
Figure 5.30 Emotions

Emotions were identified as an overarching theme as they represent a group of psychological themes which were expressed widely throughout the qualitative data. For some, these were emotions which were positives such

as a determination not to become depressed, or a feeling that they had adapted to the impacts of SSc on their ability to meet their own needs. For others these were strong negative emotions, in particular a fear of the future and what that could mean to both them and those around them, and feelings of anger and frustration which were predominantly directed against the SSc and how it had effected their lives. Some directed their anger against others such as healthcare professionals, but this was a rare expression of this theme.

The themes which make up 'Emotions' follow, together with examples of statements from the transcripts.

5.3.4.1 Adaptation
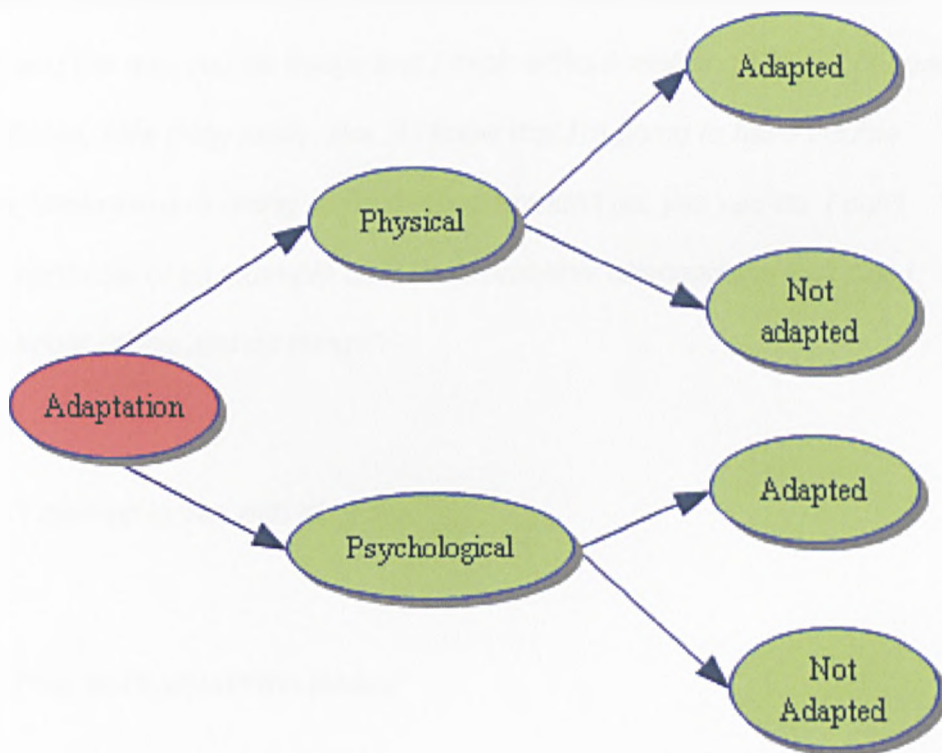
Figure 5.31 Adaptation

Adaptation was an underlying theme in interview transcripts. Interviewees talked about adaptation in terms of acceptance, changing the way they thought about things or altering their expectations. For example:

Int 1

"I accept that there are days when I can be up at a decent time in the morning and I shall go back to bed in the afternoon. You've got to do what you can for as long as you can"

Int 14

"Yes, I think without realising you do that you don't' plan to change, and you don't plan the change the way you think about things, but you do because you know you've got this illness and how it affects parts of your body and the way you do things and I think without realising I have changed. Just things, little thing really, like, if I know that I'm going to have trouble going somewhere or doing some things I wouldn't go, yes you do. I can't think right now of an example but I have probably changed the way that I think about things and do things".

Int 5

"I learned to live with it"

Int 7

"You work around the illness"

Principally adaptation was related to two main areas, Physical adaptation and Psychological adaptation. Within these two sub-themes, interviewees expressed positive statements suggesting that they had adapted, and negative statements which suggested that they had not adapted.

Physical - Adapted

Int 2

"I might stay the same and that's fine, we can live with this."

Int 4

"There are plenty of unpleasant physical symptoms you learn to live with."

Physical - Not adapted

Int 33

"I've always done things I do what you've got to do to get by and whatever and now I can't do that and that's really hard for me to come to terms with and that's really hard to stop yourself doing what you shouldn't be doing because that's going to cause you to be ill so even rushing out to move the car I'm supposed to do that slowly but you just don't function like that , you don't go slow so then you get (gasping sound) and you think oh gosh, should have slowed down but its really hard to change the habits of a life time and it's one of the things that does get to me..."

Psychological - Not adapted

Int 2:

"I wish I didn't' have it. I still haven't come to terms with it".

Int 33

"I've always done things, I do what you've got to do to get by and whatever and now, I can' t do that and that's really hard for me to come to terms with. It's very hard to stop yourself doing what you shouldn't be doing

because that's going to cause you to be ill, so even rushing out to move the care. I'm supposed to do that slowly but you just don't function like that. You don't go slow so then you get (makes gasping sound) and you think, oh gosh, should have slowed down. But its really hard to change the habits of a lifetime and it's one of the things that does get to me."

Int 26

"You've got to come to terms with your way of life, that you've got to, you've got to make a plan of action and you've got to try and stick to it and you've got to do things that you think, you know you're capable of doing and not go beyond the bounds of it, that's going to make you badly."

Psychological Adaptation

Int 12

"You just go on and adapt and er, you give way on this and you won't give way on that and er, I'm feeling so much better mentally, emotionally and physically since I've been on the, as I call the treatment, and as I say I'm very grateful for it but the biggest problem for me personally, I think was not so much the physical because I knew what was happening there, I could see and feel and I could understand what was happening there, but emotionally and mentally I think that was the biggest hurdle I had to overcome. I don't give in easily and I didn't want to think you can't do this, and you can't do that anymore but I had to compromise.. I didn't give in, no way did I give in, but I did compromise and I found life has got far better for me."

Int 3

"I've go to the stage where...ummm I don't feel 100%, I never will do, I

know that I won't but, but that's the thing, I've got things sorted out in my

own mind, yeah which is a good thing. I feel I can control it an um and all

your emotions are um, that helps a lot. Sort yourself out in your mind and

know what's going to happen and also because I've had a lot of help."

Int 4

"But you adapt to anything so I just get used to it and just get on with it."

Int 8

"I've had to adapt."

5.3.4.2 Anger/Frustration
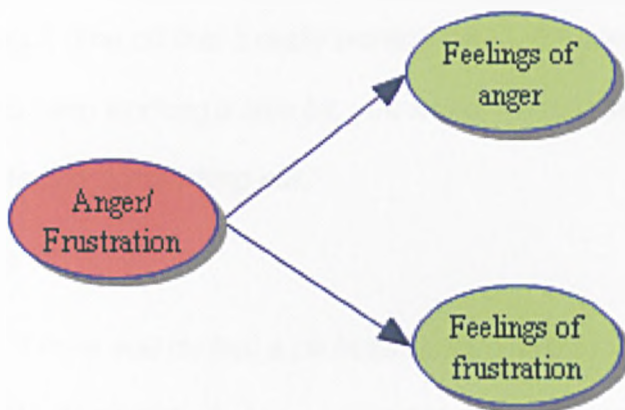
Figure 5.32 Anger / Frustration

Anger and frustration were statements which frequently occurred within the

interview transcripts. They were expressed with varying degrees of intensity,

many of the statements below illustrating the strength of feelings of anger

and frustration experienced. Frustration and anger were often mentioned together, with frustration being particularly related to the limitations imposed by SSc.

Int 26

"What I can do and what I can't do (is controlled by the disease) as I said before, and you get frustrated, mad about it, because you can't do the things you could be doing , do before, and you get frustrated... I can't do jobs for my daughters which I used to do, which I used to enjoy doing and that's where I get frustrated in that way because I can't do things for people that I could do before"

Int 9

"It annoyed me; it really annoyed me because I like working .. it did annoy me because I did like working but I just couldn't do it so..I were having so much time off that it really weren't fair. ...I'm annoyed because I would like to keep working a little bit, you know, I would like to keep working but ah.. its just not working out."

Int 29

"I think you do feel a bit frustrated sometimes yeah, when you've been used to doing just what you wanted to do and then you can't do you do, yeah, but like I say I just think "Well I shouldn't because it, I shouldn't grumble because it could have been something much worse"

Sometimes however, anger and frustration were discussed in the context of anger against the disease itself:

Int 2

"Frustrated, angry and upset, yeah I do feel sometimes that I'm letting them down and I get very angry because I feel sometimes like its bad enough having the disease but the punishments that come with are a hassle"

Int 12

"I was very angry about it... I felt this was so unfair and I was the one who was suffering for it and I hadn't' done anything to bring this on. It was completely, you know, out of the blue .."

Int 18

"And so within me there is a real burning anger which again is part of me and it has to be accepted. I have a screaming, burning anger against the GP that gave me those drugs and that sounds awful but it will never, never go away you know. And that's another burden that I have to carry because I'm always left with "What if?"

5.3.4.3 Anxiety

Figure 5.33 Anxiety

Anxiety was mentioned by interviewees in the context of their behavior and feelings, rather than anxiety about SSc itself. This did not emerge as a widely expressed theme but was clearly stated as illustrated in the following quotes.

Int 7

"Little things seem to make me anxious, you know I seem to worry about little things which aren't important. But other than that I don't think I'm particularly anxious about the illness because it's just something you've to learn to live with."

Int 28

"I think I do get anxious more than I used to, but I'm trying to not get as anxious or control it, I get worked up more than I used to or worry about things more but I don't' know why so really as far as I know I haven't anything to worry about."

5.3.4.4 Depression
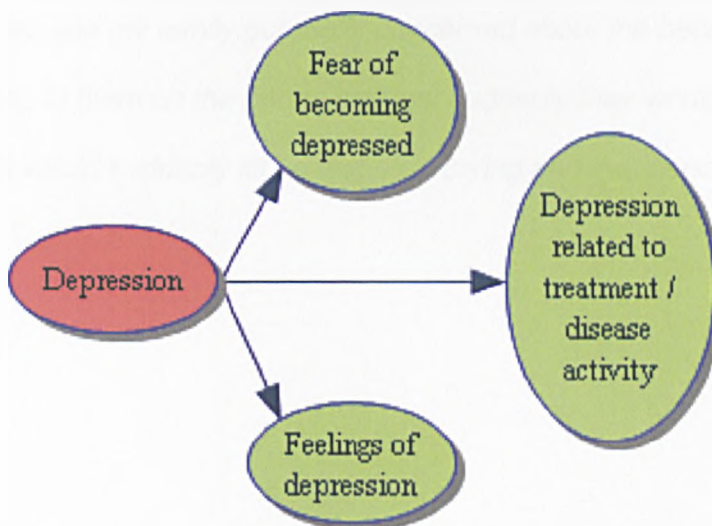
Figure 5.34 Depression

Depression was a subject which was introduced in many interviews, but in varying degrees of severity. For example, people would talk about not letting it get them down, feeling low, or the need to be positive. The actual term 'depression' also arose in many peoples' transcript.

Int 13

"I don't want to think about the bad things and there are days when you sort of, you feel a bit down and think, oh, I hope I'm not going to get really depressed again"

Int 21

"When its in a flare up as it is at the moment life is very depressing, its frustrating, I get quite low at times with it simply because it limits me to what I can do... I can get quite depressed and I tend then just to say in the house which I've done like the past couple of days."

Int 12

"I used to get really, really depressed, really depressed and that's not like me and my family got really concerned about me because I would be talking to them on the phone and just suddenly they would say something and I would suddenly fill up and start crying and that concerned them"

5.3.4.6.5 Future

Figure 5.35   Future

Interviewees talked about the effects of SSc on the future or their feelings about the future. Many people expressed uncertainty about their future and how SSc would effect them, and in turn, that of those around them such as children.

Int 33

"I can only hope that things will turn out, or I'll last a bit longer to at least let the kids finish school and stuff but I don't know, so that's hard, that's very hard."

Int 20

"I worry a lot about them (children) thinking "am I going to pass it onto them, what are they going to do then?" but its like if I keep fighting you know, I will beat it, but I'm scared that I'm going to die and leave them."

Some interviewees were particularly concerned about how SSc may cause physical deterioration in the future.

Int 32

"I thought I'm going to end up in a wheelchair here because that's how I felt at the time..."

Int 7

"I realise how bad some people can get it and yet I just hope I never get it like that"

Int 26

"It does (make you think about the future) because you don't know what's going to happen, you don't know where you're going to end up being able to do nothing, I mean twelve months since I had no trouble whatsoever with my hands, I could do anything, which now I can't."

For others the loss or alteration of the future which they had originally planned or anticipated was an impact of SSc.

Int 18

"I don't mean I've stopped living, but I'm no-longer the person I was so I can't have the same goals. So, my hope for the future was to work amongst rescued horses – I can't do it, I can't work outside."

5.4 Formation of the Descriptive Framework

Following this thematic analysis, the descriptive framework of QoL in SSc was developed as reported in Chapter 4. The descriptive framework consists of the themes identified in the transcripts of those with SSc who were

expressing how they felt SSc had affected their QoL, and is shown in Figure 5.36.

5.5 Comparison of themes generated by one to one interview and focus group methodologies

Thematic analysis of data from interviews and focus group were carried out simultaneously. A comparison of the themes identified from both data sources revealed that there were no new themes produced from the participants in the focus group setting in comparison to their individual interviews. Therefore, no further focus groups were conducted, as they did not add to the thematic generation. Observation notes of the focus group are shown in appendix 6.

Figure 5.36 Descriptive Framework of QoL in SSc
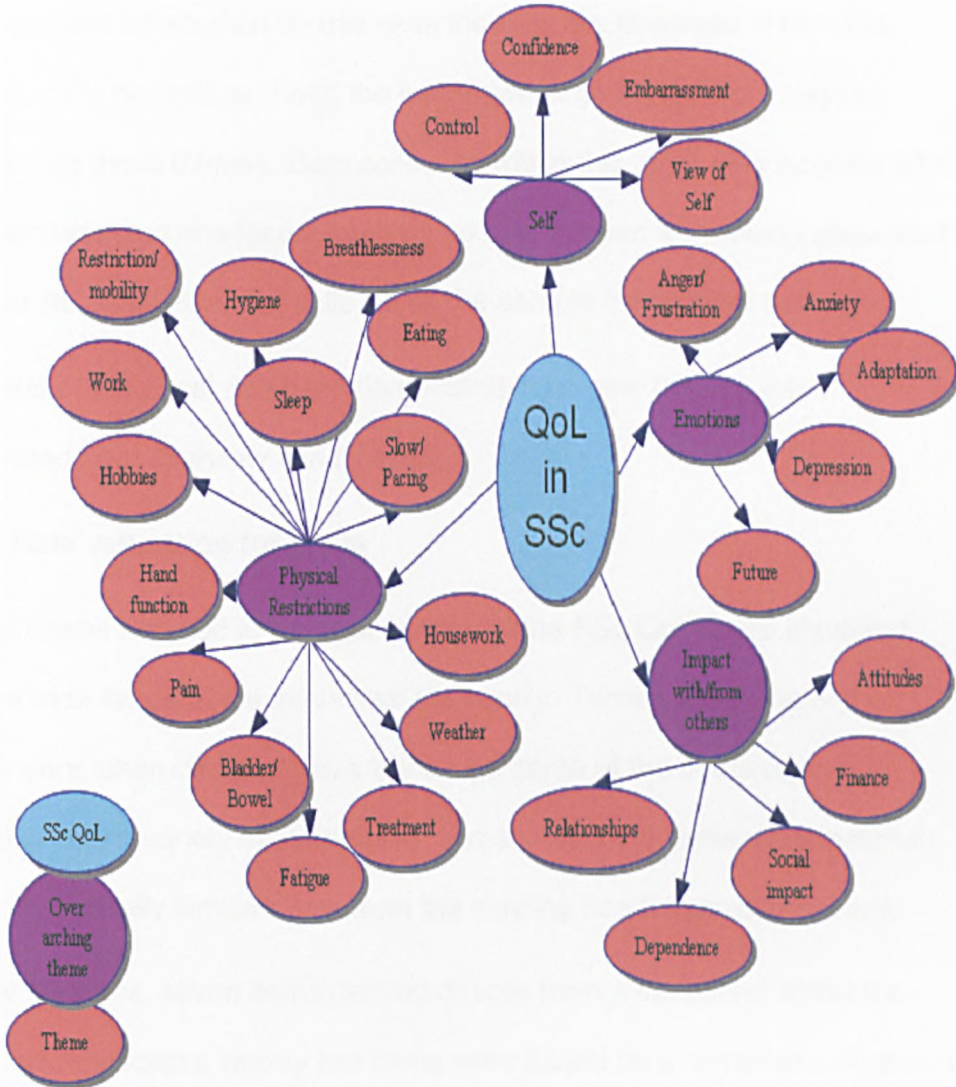
Key - The shapes represent a theme generated by the interviews relating to QoL in SSc, colours representing either SSc QoL, a theme or an over arching theme. The length of the arrow or placement of the theme has no significance

5. 6 Data Saturation

5.6.1 Data saturation of themes

Data saturation is the term used to describe the stage in qualitative research

when no new information (in this case themes) are observed in the data.

This is not to be confused with the interviewees giving different ways of

expressing these themes. Data collection within this study was stopped after

31 interviews and one focus group as no new themes were being generated

and, as far as possible, all cells within the sample frame were recruited.

Analysis of the Excel database demonstrates no new themes were

generated after interview 4 in this study.

5.6.2 Data saturation for items

The 29 items retained in the final version of the SSc QoL, were identified

from a wide range of the interviews (as seen in Table 6.8). Some of the

items were taken directly from a transcript, some of the items were a

composite of a variety of statements, and some of the items were matched

with conceptually similar items from the existing needs based item bank.

Of the 29 items, seven items derived directly from a statement within the

interview transcripts, twenty two items were based on a composite of several

statements which were made into an acceptable format (that is generalisable

to the SSc population without reference to gender, age etc).

5.6.3 Summary of Chapter 5

Chapter five has presented the qualitative results of the study including the

descriptive framework of patient-perceived SSc QoL, and given details of the

themes identified within it. Four overarching themes were identified: Physical restriction, Self, Emotions and Impact with/on others.

Data saturation for themes was identified after four interviews, but items were still being identified from the final interview. An additional focus group did not produce any different themes to those produced by interviews.

6. The SSc QoL - results

This chapter presents the results of the development, validity and reliability testing of the SSc QoL. It begins by looking at the demographics of those who responded to the questionnaires, and then proceeds to describe the results of the item selection and item reduction processes. Finally, results of the psychometric testing of the SSc QoL are presented.

6.1 Responder demographics

The sample groups for the postal questionnaire and test-retest analysis were identified in Chapter 4, table 4.3, and the questionnaires were posted out as described in Chapter 4. The following sections, including Tables 6.1 and 6.2, describe the demographics of the respondents at each stage of development of the SSc QoL.

Table 6.1 Responder demographics – First postal questionnaire

	dcSSc	lcSSc	Male	Female	Age	Gender missing	Total
First postal questionnaire responders	112 Disease duration : 1 missing 20 below 5 years 91 above 5 years	91 Disease duration: 0 missing 5 below 5 years 86 above 5 years	17 dcSSc 7 lcSSc	82 dcSSc 65 lcSSc	58 below 50 yrs 96 above 50 yrs	13 dcSSc 20 lcSSc	203 (return rate of 61% of live sample)

6.1.1 First postal questionnaire

Of the 336 questionnaire booklets sent out (sample described in Chapter 4, Table 4.3), the researcher was notified of seven patients who had deceased. Of the 329 remaining, 203 were returned completed. This gave a return rate of 61%. The demographics of the first questionnaire responders can be found in table 6.1.

There was a similar distribution of males and females across the disease sub-types of the sample frame, with males in a minority in both disease sub-types. In those who responded, there are fewer males in the limited group than the diffuse group; (Table 6.1), which reflects the distribution of the original sample frame. Very little missing data was shown in the responder group, however thirty-three gender responses, and thirty-five age responses were missing. There were more respondents in the over 50-year age group than the under 50 age group (Table 6.1), but there was no significant link demonstrated between age and gender of the respondents (chi sq of 0.62 and a p value of 0.489)

Those with lSSc are significantly older than those with dSSc (Table 6.1) and those with lSSc have a higher proportion of those with disease duration of greater than 5 years.

6.1.2 Test/Retest questionnaire

A total of 369 participants were sent the rest-retest questionnaire (sample as described in Table 4.3, chapter 4). Of the 159 responders, 119 responded to the retest questionnaire within four weeks, giving a response rate of 74.2%.

Table 6.2 Responder demographics – Test/rest questionnaires

	dcSSc	lcSSc	Male	Female	Gender missing	Total
Test questionnaire responders	85 Disease duration: 0 miss 77 above 5 years 8 below 5 years	74 Disease duration: 1 miss 68 above 5 years 5 below 5 years	11dcSSc 9 lcSSc	74 dcSSc 64 lcSSc	1 lcSSc	159
Re-test questionnaire responders	63 Disease duration: I miss 8 below 5 years 54 above 5 years	54 Disease duration: 1 miss 4 below 5 years 49 above 5 years	7dcSSc 7 lcSSc	54 dcSSc 46 lcSSc	2 dcSSc 1lcSSc	117 (response rate of 74.2% of test responders)

The demographics of the test and retest responders are summarized in Table 6.2. No statistical significance was found for age (t test 0.624, p 0.533), gender (Chi sq 0.976, p 0.412), sub-type (Chi sq 0.111, p 0.856) between the retest responders and non-responders.

Further analysis of the responder data

Within the postal questionnaire respondents were asked their disease sub-type as it was recognised within the literature review that disease classification of sub-type is not a standard process within clinical care. Responder's knowledge of their disease sub-type was compared with their sub-type as recorded on the National Scleroderma database. This demonstrated that 91.7% of dcSSc responders, and 84.6% of lcSSc responders gave a sub-type which matched that on the database. Therefore

only 15.4% of those with lcSSc and 8.3% of those with dcSSc did not correctly identify their disease sub-type.

As the items of the SSc QoL were generated from qualitative interviews from a specific sample frame, the demographics of the respondents of the questionnaire were analyzed according to that sample frame. The results are shown in Table 6.3. The results indicate that both age and disease duration varied significantly across disease sub-type.

Table 6.3 – Relationship between Sub-type, Age, Gender and Disease Duration

	DcSSc	LcSSc	Total	'p' value*
Age above 50 years	60.9%	80.2%	69.7%	0.003
Female	82.8%	90.1%	85.9%	0.177
D Duration > 5 years	82.8%	94.5%	87.6%	0.007
A level and above	38.4%	37.4%	37.9%	0.880

*p value from Mann Whitney

A variety of measures were included in the questionnaire for potential use in the SEM process. This allowed analysis of the levels of impairment (fatigue and psychological impairment), health status and QoL within the responder group, results of which are shown in Table 6.4. The levels of impairment (fatigue and psychological impairment as well as general health status and QoL are not significantly different between disease sub-type (Table 6.4). For example, the Fatigue Severity Score (FSS) shows a mean score of 5.78 (4.50 – 6.17) in dcSSc, and 5.89 (4.33 – 6.75) in lcSSc (Mann Whitney p 0.494). However, functioning as shown by both the HAQ and UK Function Index (UKFI), demonstrate significant difference between dSSc and lSSc

subtypes. This analysis is not fundamental to the hypothesis testing but

offers further insight into the responder group.

Table 6.4 − Relationship between measures of Health Status and disease subtype, Overall health and VAS QoL across subtype and total responders.

	DcSSc	LcSSc	Total	p value *
FSS	5.78 (4.50 − 6.17)	5.89 − (4.33 − 6.75)	5.78 (4.50 − 6.56)	0 .494
Anxiety	7 (4 − 10)	7 (5 − 10)	7 (4-10)	0.440
Depression	5 (3-9)	6 (2.75 − 9.25)	6 (3 − 9)	0.933
RSE	19 (14 − 24)	20 (16 − 24)	20 (15 − 24)	0.252
GPSE	30 (28 − 36.75)	30 (26 − 35)	30 (27 − 35)	0.096
HAQ	1.25 (0.53 − 2.13)	0.75 (13 − 1.75)	1.13 (0.25 − 2.0)	0.007
UKFI	13 (6 − 19)	9 (2 − 19)	11 (4 − 19)	0.040
EQ5D	0.59 (0.52-0.76)	0.66 (0.52 − 0.80)	0.59 (0.52-0.80)	0.210
LHS	72.70 (61.37 - 80.80)	72 (62.40 − 87.60)	72.50 (62.40 − 83.90)	0.429
Overall Health (VAS)	55 (37 − 71)	53 (29 − 75)	54 (35 − 73)	0.659
QoL (vas)	59 (40 − 79)	57 (34 − 80)	58.50 (37.25 − 80.00)	0.975

*P value from Mann Whitney test

Scoring format for the comparator measures: FSS - higher score (maximum of 7), higher fatigue level; HAD - each item scored 0 − 3, 7 items for each, anxiety and depression. Higher scores indicate higher levels; RSE − 10 − 40, higher score, higher self-esteem; GPSE − Score 10 − 40, higher score more self-efficacy ; HAQ − Maximum score of 3 for worst function; EQ 5D − Weighed score, calculated by syntax; LHS − 0 − 100 range. 0 = maximum handicap, 100 = no handicap; VAS − 100 mm range, the higher score the better QoL/Health; UKFI − 0 − 3 each item with an overall score 0 − 33

6.2 Development of the questionnaire

Results of development of the SSc QoL are divided into section 6.2.1

describing results of the item selection process used to produce the items to

go into the draft SSc QoL, and section 6.2.2 which describes results of item reduction which occurred during psychometric testing of the measure following its postal administration.

6.2.1 Item selection to develop the draft SSc QoL

The process of selection of items for the draft SSc QoL has been outlined in section 4.2.1, and this process resulted in identification of 90 items for use in the SSc QoL. Details of the outcome at each item selection process are described below.

Stage one – The researcher identified 1790 statements from the 31 interview transcripts; these represented key statements with no criteria applied.

Stage two - Interview transcripts were analysed by independent assessors who applied the needs based model to the statements and identified items. At this stage 710 items remained.

Stage three - Items were removed at this stage chiefly for the reasons of duplication, they were not applicable to all potential responders or were ambiguous. Three items were exchanged from the item bank into the draft questionnaire as their meaning was agreed to be the same as that identified in the item selection of the SSc QoL, but that the wording of the item bank item better fitted the item selection criteria. These items were:

- I worry that I let people down

- I cannot rely on how I will be tomorrow

- I worry about the effects on others

At the end of stage three, ninety items were identified to go forward into the draft SSc QoL measures, the SSc QoL 90.

6.2.2 Item reduction during the psychometric testing of the SSc QoL

An iterative process of Rasch analysis was undertaken during development of the SSc QoL (shown in detail in section 6.3), which resulted in item reduction at each stage of analysis. A summary of item reduction of the SSc QoL during the stages of its development is seen in Table 6.5.

Item reduction during the first stage of Rasch analysis (the first postal questionnaire) resulted in item reduction from a 90-item SSc QoL to a 39-item SSc QoL.

Test/retest reliability of the 39-item SSc QoL (as described in section 4.2.6) generated data for the second element of Rasch analysis. Item reduction the during test/retest stages of SSc QoL development can be seen in Table 6.5 from stage 23 onwards. Item reduction in this stage of Rasch analysis (shown in detail in section 6.3), resulted in the final 29 item SSc QoL measure seen at stage 30 in Table 6.5.

Table 6.5. Item reduction (together with rationale for removal) during the first postal questionnaire of the SSc QoL questionnaire development.

Stage of questionnaire development	Item number removed	Rationale for removal	Items remaining in the SSc QoL
1	78,81,a34	DIF	87
2	22,26,31,32,74,7017,50,73	DIF	78
3	4,9,38,87	DIF(age)	74
4	24,57,76,36,48,54,4419,20,33,37,7	DIF	
5	13,15,8	Item chi sq	62
6	14	Item chi sq	59
7	18	Fit residual	58
8	12	Chi sq	57
9	79	Chi sq	56
10	61, 68	High chi sq	54
11	71	Low chi sq	53
12	41	F stat	52
13	89	F stat	51
14	10, 90	Positive pca	49
15	64,58	Positive pca	47
16	65	DIF	46
17	40	F stat	45
18	86, 62	Positive pca	43
19	47	Low chi sq	42
20	53	Low chi sq	41
21	30	Low F stat	40
22	89	F stat	39
Second Rasch Analysis (following administration of the SSc QoL 39)			
23	18	Fit res and Chi sq	38
24	24, 29	Chi sq	36
25	5	Chi sq and item fit	35
26	15	Redundancy and Chi sq	34
27	16	Chi sq	33
28	22, 33	Low Chi sq	31
29	17	DIF and Chi sq	30
30	30	DIF	29

Key: DIF – Differential Item Functioning; Fit res – Fit residual; – For further explanation see section 4.2

Response rate to the items of the SSc QoL 90

Following postal administration of the SSc QoL 90, the items were found to have a highly variable affirmation rate. Table 6.6 highlights the five most and least affirmed items in the first postal questionnaire. The most affirmed item is the item 'I just don't know what I'm going to be like in the future with 88.1% of responders stating this item to be true.

Table 6.6 – Five most and 5 least affirmed items from the SSc QoL 90

Item	Percentage affirmed
J25 I don't know what I'm going to be like in the future	88.1%
J28 No-one around me has heard of this disease	83.7%
J5 I have had to slow down	83.7%
A4 I can't do what I used to	83.7%
J1 I need to rest more often	82.3%
J33 I do not like being touched	25.2%
J16 I can't cope in the house on my own	19.3%
J19 I can't go out on my own anymore	18.8%
J 22 Talking about my Scleroderma upsets me	17.8%
J15 I can't cope at all	3.3%

Origins of items of the SSc QoL

The items that entered into questionnaire development were all derived from patient views. In order to explore if the items within the SSc QoL were representative of this patient data, Table 6.7 links the items of the final version of the SSc QoL back to the themes of the descriptive framework and the interviews from which they originated.

Table 6.7 Items of the SSc QoL related back to the interview from which they were identified

Item of the SSc QoL	Interview source of the item	Theme represented by the item
I can't do anything without really thinking it through	composite	Future - Emotions
Its always on my mind	Int 31 composite	Anxiety -Emotions
I worry that I let people down	Int 1 composite	Family/Relationships – Impact with/on others
My condition makes me angry	Int 2, 12 composite	Anger/frustration - Emotions
I get upset when I can't do things	Int 14 composite	Anger/frustration - Emotions
I often get frustrated	Int 1,2 composite	Anger/frustration - Emotions
I cannot rely on how I will be tomorrow	Int 21 composite	Future – Emotions
I feel like I'm fighting all the time	Int 2	Anger/frustration - Emotions
My condition means I have disturbed sleep	Int 1,5 composite	Sleep – Physical restrictions
It has affected me a lot socially	Int 5 composite	Social impact - Impact with/from others
It has affected the health of people around me	Int 4	Family/Relationships – Impact with/from others
My hands don't work as well as they did	In1 composite	Hand function – Physical restrictions
It puts a strain on my personal relationships	Int 1,2 composite	Family – Impact with/on others
I need to rest more often	Int 16, 27 composite	Slow pacing – Physical restrictions
Any sort of activity is difficult	composite	Restriction/mobility – Physical restrictions
I avoid certain social situations because I am embarrassed	Int 12, 16 composite	Social impact – Impact with/from others
I take to heart things which wouldn't have worried me before	Int 9	Anxiety - Emotions
Life is just not what it was	Int 10	View of self – Self
I can't cope at all	Int 3,10	View of self – Self
Sleeping badly has affected me a lot	Int 4 composite	Sleep – Physical restrictions
I feel very isolated	Int 9,10	Family/Relationships – Impact with/on others
Household tasks can be a problem	Int 2 composite	Housework – Physical restrictions
I have had to stop some of my hobbies	Int 2	Hobbies – Physical restrictions
I feel guilty at being ill	Int 17	Family/Relationships – Impact with/on others
I struggle to wash myself as I would like	Int14,15, 17 composite	Hygiene – Physical restrictions
Pain limits what I can do	Int1,14,15,21 composite	Pain – Physical restrictions
I feel helpless	Int 34 (I feel disempowered)	Control - Self
Pain tires me out	Int 19	Pain –Physical restrictions
I miss being able to sort things out	Int 28	Control – Self

Table 6.7 shows that the items of the SSc QoL originated from a wide range of interviews. When described as 'composite', this refers to items is coming from a variety of interviews. Also, it is clear from Table 6.8 that the items of the SSc QoL represent all four of the over-arching themes of the descriptive framework, with eight from 'Emotions', seven from the 'Impact with/from others' over-arching theme, ten from the 'Physical restrictions' over-arching theme and the remaining four items came from the 'Self' over-arching theme.

6.3 Psychometric properties of the questionnaire – construct validity and test/retest reliability

The psychometric properties of the SSc QoL were tested throughout its stages of development. Rasch analysis of the data from the first postal questionnaire gave an item reduction from the original 90-item questionnaire, to a 39-item questionnaire. This analysis is summarised in Table 6.9. Initially there was considerable misfit to Rasch model expectation (discussed in section 6.3,Table 6.8, analysis 1). Eventually, a 39-item solution was obtained which satisfied model expectation (Table 6.8, analysis 15).

The test for uni-dimensionality of the SSc QoL at this stage of analysis was 0.041, lower than 0.05 threshold and so showing acceptable unidimensionality.

The discarded items (discard pile), were examined using Rasch analysis for the presence of an alternative scale, however no solution could be achieved.

This left a 39-item scale, SSc QoL 39, to go forward to the test-retest stage

Table 6.8 - Summary of Rasch analysis of the SSc QoL 90

	Item Residual Fit		Person Residual Fit		Chi-Square Interaction		PSI
Analysis SSc QoL 90	Mean	SD	Mean	SD	Value (df)	p	
1	-0.354	2.099	-0.169	1.041	835.192	0.0000	0.96091
2	-0.339	2.100	-0.161	0.952	875.307	0.0000	0.96142
3	-0.277	1.733	-0.166	0.881	541.730	0.0000	0.96551
4	-0.308	1.764	-0.144	0.846	451.017	0.0000	0.95939
5	-0.317	1.696	-0.149	0.818	414.537	0.0000	0.95758
6	-0.269	1.336	-0.176	0.755	225.320	0.0000	0.95170
7	-0.296	1.297	-0.181	0.732	198.534	0.000005	0.95006
8	-0.307	1.235	-0.186	0.728	196.795	0.000004	0.95170
9	-0.293	1.204	-0.189	0.725	182.835	0.00047	0.95060
10	-0.294	1.175	-0.190	0.719	168.267	0.000472	0.95176
11	-0.297	1.157	-0.190	0.704	159.516	0.001445	0.95132
12	-0.313	1.108	-0.187	0.653	156.844	0.000991	0.94990
13	-0.279	1.134	-0.190	0.642	145.036	0.004903	0.95083
14	-0.292	1.124	-0.189	0.641	131.091	0.27705	0.94934
15 39 item scale	-0.238	1.102	-0.187	0.583	81.788	0.362451	0.93592

Second stage of Rasch analysis

The data from the 39 items of the SSc QoL were then subjected to further Rasch analysis. Items displaying DIF and misfit were deleted, resulting in a shortened 29-item scale (Table analysis 6.9, analysis 10).

Table 6.9 Analysis Monitor for the SSc QoL 29 from Rasch analysis of the group 2 data

	Item Fit Residual		Person Fit Residual		Chi-Square Interaction			Uni dimensionality
	Mean	SD	Mean	SD	Value (df)	p	PSI	Independent T-Tests (CI)
1	-0.328	1.523	-0.199	0.759	260.369	0	0.953	
2	-0.38	1.523	-0.199	0.759	260.369	0	0.953	11.92%
3	-0.352	1.372	-0.212	0.762	232.683	0	0.9528	10.81%
4	-0.375	1.283	-0.223	0.734	190.923	0.000002	0.9509	13.13%
5	-0.397	1.206	-0.229	0.715	166.027	0.00014	0.9517	11.28%
6	-0.376	1.165	-0.21	0.666	161.04	0.000179	0.9494	8.27%(0.06-0.11)
7	-0.0399	1.159	-0.214	0.659	147.164	0.001226	0.9474	7.78% (0.05-0.1)
8	-0.386	1.154	-0.217	0.64	121.573	0.025004	0.9436	9.73% (.07-0.12)
9	-0.403	1.117	-0.225	0.641	126.332	0.006985	0.9498	6.61% (0.05 – 0.9)
10	-0.378	1.088	-0.222	0.622	107.359 df =87	0.068459	0.9389	5.84% (0.032-0.085)

A Lower 95% CI-Proportion lower than or equal to 0.05 shows acceptable unidimensionality.

6.3.1 Non-parametric testing of the SSc QoL across time points

Non-parametric analysis of the test-retest correlation of the SSc QoL measure is presented in Table 6.10.

Table 6.10 Test retest correlation (Spearman) of the SSc QoL 29 items

	SSc QoL 29 (Second)	SSc QoL 29	Current Overall health (VAS)	Quality of Life (VAS)
SSc QoL 29 (Second)	1.000			
SSc QoL 29	.764	1.00		
Current overall health (VAS)	-.480	-.515	1.000	
Quality of Life (VAS)	-.587	-.612	.781	1.000
Quality of Life VAS (Second)	-.633	-.524	.591	.705
Current overall health VAS (Second)	-.453	-.394	.681	.597

The test-retest correlation of the two time points of the SSc QoL 29 was 0.764, Table 6.10. To put this in context, the test-retest correlation for the summary Health and QoL Visual analogue scales was 0.681 and 0.705 respectively. Correlation between the SSc QoL 29 with other summary scales, such as overall health and quality of life, were of an expected magnitude. For example, the correlation between the SSc QoL 29 and the HAQ was 0.592 (Spearmans).

6.3.2 Non-parametric testing of the study hypothesis (differences in the SSc QoL by disease subtype)

The SSc QoL (29 items) when summed into a simple ordinal scale showed no statistical significance for disease sub-type (p - 0.836) in the first postal dataset.

6.3.3 Summary of Chapter 6

The needs-based SSc QoL, (29 items), fits modern psychometric requirements of Rasch analysis and is more reliable across two time points than a VAS of Overall health or QoL as estimated by patients. The SSc QoL (29 items) when summed into a simple ordinal scale showed no statistical significance for disease sub-type (p - 0.836) in the first postal dataset.

7. Testing the hypothesis – Modelling of QoL in SSc

Non-parametric testing of the study hypothesis has been presented in section 6.3.2. Chapter presents the results of multivariate testing of the study hypothesis using structural equation modelling.

7.1 Structural Equation Modelling – Testing the hypothesis

The study hypothesis is that there will be differences in the level of QoL between people with different subtypes of SSc.

This has been tested in two ways; a simple non-parametric test of the difference between two groups, and the multivariate approach of SEM which acknowledges that patient perceived QoL may be determined by the associations within the broader biopsychosocial model.

7.1.2 SEM testing of the hypothesis

Preparation of data for use in SEM was carried out using the Rasch transformed score for each comparator measures, as well as the SSc QoL items. The individual person fit estimate for each measure was exported for use in the SEM model.

7.1.3 Presentation of SEM models

AMOS 7 software was used for this analysis. SEM models have conventions as to their appearance (Schumacker and Lomax 2004) . Shapes are used to represent key aspects of the model, the measured variable, error and the latent variable as shown in figure 7.1

Figure 7.1 Key to shapes in the SEM model

Shapes:
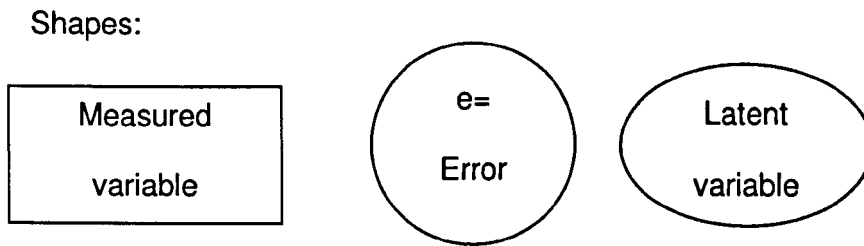
Explanation of the model developed to test the study hypothesis (Figure 7.2).

Figure 7.2 is a diagrammatic representation of the model of SSc QoL which was the result of the SEM process for this study. This model can be described as 'parsimonious', that is it is a simple model which meets the statistical levels of fit required for an SEM model (levels of fit described in section 4.3.1).

The shapes in the diagram have been explained above, and within each shape is the title or abbreviation of a measure that was distributed within the development of the SSc QoL. The measures used in this model were prioritized for inclusion in the model due to their emphasis within the SSc literature. More measures were available for use but were not included within the model, as parsimonious fit had already been achieved.

Assessment of the hypothesis through this model, is made by tracing the impact of each measure following the arrows coming from the measured variable (rectangle), through the latent variable (oval) to the focus of the study, SSc QoL. Figures attached to the lines are regression weightings imported with the Rasch transformed score. The figure '1' is attached to each grouping as a standard within the SEM model

Figure 7.2 Diagram of the Specification model for the SSc QoL Structural

Equation Modelling
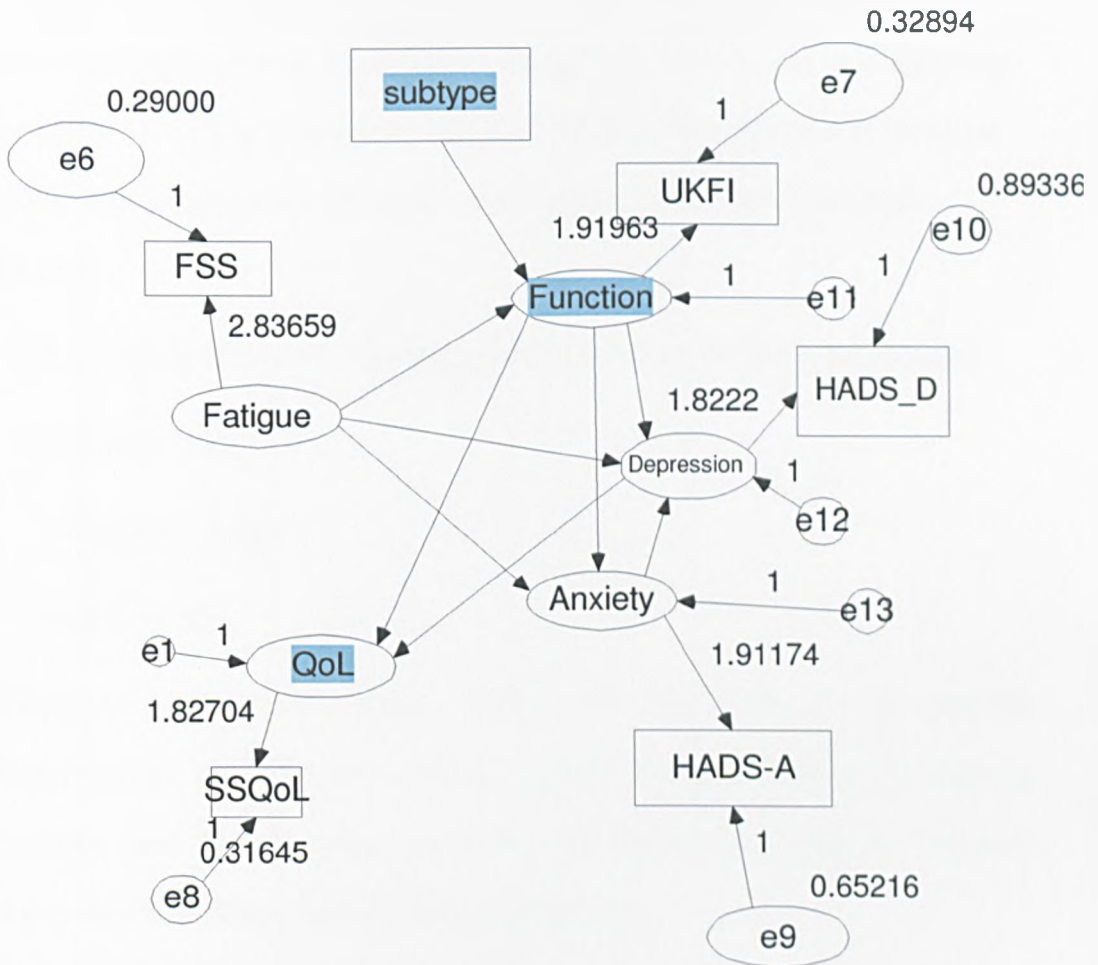
Key:

HAD-A – Hospital Anxiety and Depression measure – Anxiety

HAD-D – Hospital Anxiety and Depression measure – Depression

UKFI- UK Functional Index

FSS – Fatigue Severity Scale

SSc QoL – 29 item Systemic Sclerosis Quality of Life measure

Subtype – disease subtype, that is DcSSc or LcSSc

Figures attached to the lines are regression weightings. The figure '1' is attached to each grouping as a standard within the SEM model

The shapes labeled with blue (in Figure 7.2) indicate disease sub-type (dcSSc and lcSSc), function and SSc QoL. There is no arrow leading directly from sub-type to SSc QoL. However, there is an indirect link made by arrows leading from sub-type to function and then to SSc QoL. This indirect link would not been seen in univariate non-parametric testing, nor in a regression analysis. Therefore, this model supports the study hypothesis that sub-type does have an effect on SSc QoL, this being an indirect effect through function.

The summary fit statistics (as described in 4.3.2) of the SEM model were:

- Chi Sq – 5.074

- RMSEA – 0.000

- GFI – 0.991

Therefore, this parsimonious model fits the summary fit statistic requirements of SEM. The direct, indirect and total effects of disease subtype and health status measures are shown in Table 7.1 in their numerical form (standardised beta co-efficients).

Table 7.1 Standardised Direct, Indirect and Total Effects of Disease Sub-type and health status variables upon QoL

	Direct effect	Indirect effect	Total
Depression	0.785	0	0.785
Fatigue	0	0.693	0.693
Function	0.204	0.302	0.506
Anxiety	0	0.380	0.380
Sub-type	0	-0.112	-0.112

This shows that depression has the greatest impact upon QoL followed by fatigue and function. The former, together with anxiety and disease sub-type have significant but indirect upon QoL, and this contrasts with the univariate analysis which shows no significant association between QoL and disease sub-type

7.1.4 Summary of findings from the SEM model

The SEM specification model (Figure 7.2), and standardized direct and indirect effects (Table 7.1), have been summarised to present the following findings:

- Disease sub-type effects QoL indirectly through its effect on function

- Fatigue effects QoL through anxiety, function and depression

- Depression has a direct effect on QoL

- Anxiety has an indirect effect on QoL by effecting Depression

- Function has a direct effect on QoL, but also and indirectly through its effect on Depression and Anxiety.

To summarise, the finding of this SEM process show that a parsimonious model of SSc QoL reveals an indirect link between SSc QoL and disease sub-type mediated by disability. This would support the hypothesis that disease sub-type is reflected in QoL for those with SSc.

8. Discussion

8.1 Overview

This study has developed a needs-based QoL measure for people with SSc. During the course of this development, the experience of living with SSc has been explored and a descriptive framework of QoL in SSc has been developed.

The principle findings of this research are:

- The descriptive framework of SSc QoL consists of overarching themes of Physical restriction, Emotion, Self, and Impact on/with others. These were made up of thirty themes representing the physical, social and psychological aspects of patient-perceived SSc QoL.

- The needs based SSc QoL fits modern psychometric requirements of Rasch analysis

- The SSc QoL has good test-retest reliability.

- Non-parametric testing shows no significant difference in levels of patient perceived QoL between disease sub-types (as measured by the SSc QoL)

- SEM testing of the research hypothesis demonstrates that disease sub-type has an indirect effect through impact on QoL, working through function.

- There is a significant link between disease sub-type and function: higher impact on function being seen in those with dcSSc than those with lcSSc.

8.2 The impact of living with SSc

People with SSc vividly expressed the many ways in which SSc had affected their lives and their ability to meet their individual needs. The richness of the collective transcript data brings alive the wide-ranging effect SSc can have on the life both of the individual and those around them. This is reflected in the descriptive framework of SSc QoL which has been developed in this study. The overarching themes identified in the study were Physical restrictions, Emotion, Self, and Impact with/from others.

What is first apparent from the overarching themes is that only one of them is a chiefly physical theme, the other three primarily relating to the psychological and social impacts of SSc on both the individual and those around them. The overarching themes therefore present a biopsychosocial picture of patient perceived SSc QoL.

Two previous qualitative research studies have looked at the impact of SSc, (Joachim and Acorn 2003; Suarez-Almazor et al. 2007); each with differing methodologies. One study was very restricted in its focus, this focus being the effects of scleroderma as a disease with visible symptoms (Joachim and Acorn 2003). The second study reviewed the literature relating to the known impact of SSc arriving at a script of questions related to the effects of disease on QoL: perceptions of disease progression; overall symptom burden; and specific organ symptoms (Suarez-Almazor et al. 2007). What is

interesting is that despite this, patients still identified themes beyond the interview questions, including themes of being normal, and facing the future (Joachim and Acorn 2003) and social relationships (Suarez-Almazor et al. 2007).

This study differs from these previous publications by acknowledging the patient as the expert informant. Whilst having a conceptual basis for the interviews and focus group, this study utilized prompting techniques (topic list) only, as opposed to exclusive use of a formal interview question schedule.

Whilst it is difficult to compare the outcomes of the Joachim study due to the narrowness of their questioning, many of the themes identified in this research study are echoed in the themes identified by Suarez and colleagues (Suarez-Almazor et al. 2007). These common themes include: self-efficacy (control); coping; adaptation; positive and negative views of the future; physical symptoms such as gastrointestinal, skin and fatigue; emotional distress; appearance; lifestyle; marital/sexual problems and social issues (including social relationships).

Another aspect common to both this study and that of Suarez and colleagues (Suarez-Almazor et al. 2007), is that participants did not simply identify and rate symptoms, they operationalised them into the context of their lives, and how the symptoms affected their ability to do what they needed to do as individuals. This is echoed in the transcripts of this study of SSc QoL.

When interviewees spoke of the impact of SSc, they described these impacts in a way which can be related back to the components of the ICF,

impairment, activity limitation and participation (section 2.5). For example, when people described the physical impairment of gastrointestinal SSc they did not simply explain that they had gastrointestinal dysmotility, which would have been describing the impairment. Instead, they talked about difficulty in swallowing and related this to how their social life was affected, as they were often embarrassed to go out to eat. This reflects activity limitation (difficulty swallowing), and participation in their withdrawal from eating out socially. Activity limitation and participation is seen throughout the qualitative data, impairment (that is describing the impact of the disease on body structure and function), was used much less with only a few interviewees describing the purely medical aspect of their disease.

The descriptive framework of QoL in SSc did not venture to explore more detailed levels of analysis. For example the link between themes such as cause and effect, and interactions across the whole framework. This is a reflection upon the analytical approach used, thematic analysis. Whilst thematic analysis provided an appropriate and pragmatic tool to describe the qualitative data, it does not provide a means of making those more in-depth analytical links between themes. An alternative approach, such as phenomenological analysis, may have offered a more in-depth understanding of QoL in SSc, and may be a useful tool for future analysis and insight.

A further reflection on the qualitative data analysis is that it was not used to explore the qualitative experience of QoL in SSc from a perspective of disease sub-type. This approach may have provided complementary information for discussion of the study hypothesis that disease sub-type is

reflected in their QoL. This would be an interesting approach for further research into the impact of disease sub-type in SSc.

8.3 Physical and psychological influences of patient-perceived SSc QoL

The primary purpose of this study was to test the hypothesis that the sub-type of SSc will be reflected in the level of patient-perceived QoL. SEM suggests strongly that disease sub-type is an indirect influence on patient-perceived QoL in SSc, working through function (Figure 7.2). This study also found that those with dcSSc reported a higher impact on their physical function than those with lcSSc (Table 6.4). This correlates well with previous findings that the physical impact of SSc is greater in those with dcSSc than lcSSc (Georges et al. 2006), and an earlier study,(Benrud-Larson et al. 2002), which also report patients with dcSSc have a higher level of impact on their function that those with lcSSc.

Therefore, clinically we can expect that patients with dcSSc will have higher levels of functional impairment than those with lcSSc. The needs-based model of SSc QoL tested in this study, presents new knowledge in this area. SEM analysis illustrates that sub-type has an indirect effect upon QoL through function.

The effect of function on patient-perceived QoL has been clearly demonstrated in both the qualitative results of this study, with physical restrictions forming one of the four overarching themes. Therefore, impact on physical function is both a quantitative and qualitative finding of this study.

The parsimonious SEM model used in this study also shows the importance of other factors such of depression, and their relationship with patient-perceived QoL. Depression was found to have a direct effect on SSc QoL, and anxiety showed an indirect effect upon SSc QoL, again through depression (Figure 7.2). In previous studies the link between the physical and psychological aspects of SSc has been shown to vary (2.11.5). The strength of the SEM technique, has allowed this study to show the complex patterns of associations between physical and psychological dimensions of SSc QoL (7.1.4), particularly those between depression, anxiety fatigue and function.

The ability of SEM to reveal both direct and indirect effects, as shown in this study, is a beginning. Further explorations of potential indirect relationships in disease models may help clarify many enigmas, for example, the disability paradox (section 3.4.1) and its role in chronic disease.

The disability paradox represents those non-physical elements which influence people with severe physical disability to rate their QoL as good. Other concepts related to this finding may be adaptation (see section 3.4). It has been noted that one of the difficulties of studying patient-perceived QoL, is that it can mean different things to the same person over a disease trajectory (Schwartz and Sprangers 2000). Adaptation to chronic disease is a complex concept, which cannot be explored in the confines of this discussion, however it is a concept that requires acknowledgement.

Attempts to incorporate any effects of adaptation in the design of this study were principally the inclusion of disease duration into the sample frame requirements of the qualitative participants. These participants provided the

qualitative data both for the theoretical framework of SSc QoL, and the potential items of the SSc QoL measure. Results of this study show a mixture of statements relating to the theme of adaptation (5.3.4.1), illustrating both the physical and psychological, adapted and not-adapted aspects interviewed. This provides some evidence of the range of adaptation present in the qualitative sample.

Another profound effect of SSc on patient-perceived QoL was that of impacts with and on those around the person with SSc (5.3.3). This included relationships within a family, with friends, loss of social contact through job loss, or the inability to meet role needs such as that of being a parent or a partner. Social relationships were clearly identified in an earlier study of people with SSc, who told researchers of how they relied on friends, supports groups and networks. Some people reported that others misunderstood and mistook their illness because they did not appear physically ill (Suarez-Almazor et al. 2007), and indeed some examples recounted in the Suarez publication are echoed in the interviewees in this study. And an example common to both studies, is that people expressed concern that those around them did not understand the disease and did not acknowledge its effect because their disabilities were not always visible.

8.4 Implications for Clinical Practice

The descriptive framework of patient-perceived SSc QoL developed in this study, demonstrates the physical, psychological and social impacts of living with SSc. Currently, clinical provision is focused around health care, often working in isolation. Care frequently focuses on physical symptoms of SSc, (section 2.12), and may be unlikely to meet the needs of individuals as

illustrated in this descriptive framework of SSc QoL. This suggests a need for a wider model of care, which can address psychological and social issues, asset within a biopsychosocial model of care.

8.4.1 Addressing the impacts of SSc on patient-perceived QoL though a pragmatic care pathway

A guideline for the care of patients with a range of connective tissue diseases is currently available (ARMA 2007), however whilst it does aim for a user-centred approach, it has a health focus based on a medical model and is not specific to SSc. Many of the aspects of patient-perceived QoL identified in this study are not represented.

This study adds significantly to our current body of knowledge of the effect of SSc on patient-perceived QoL. In order to turn this knowledge into a pragmatic tool for clinical practice, a care pathway has been developed drawing on both the qualitative and quantitative findings of this study (Figure 8.1

Also, as the SSc QoL has been found to fit modern psychometric requirements and to be reliable over two time points, it provides a tool ready for use in a UK population) and is therefore included for use within the care pathway proposed.
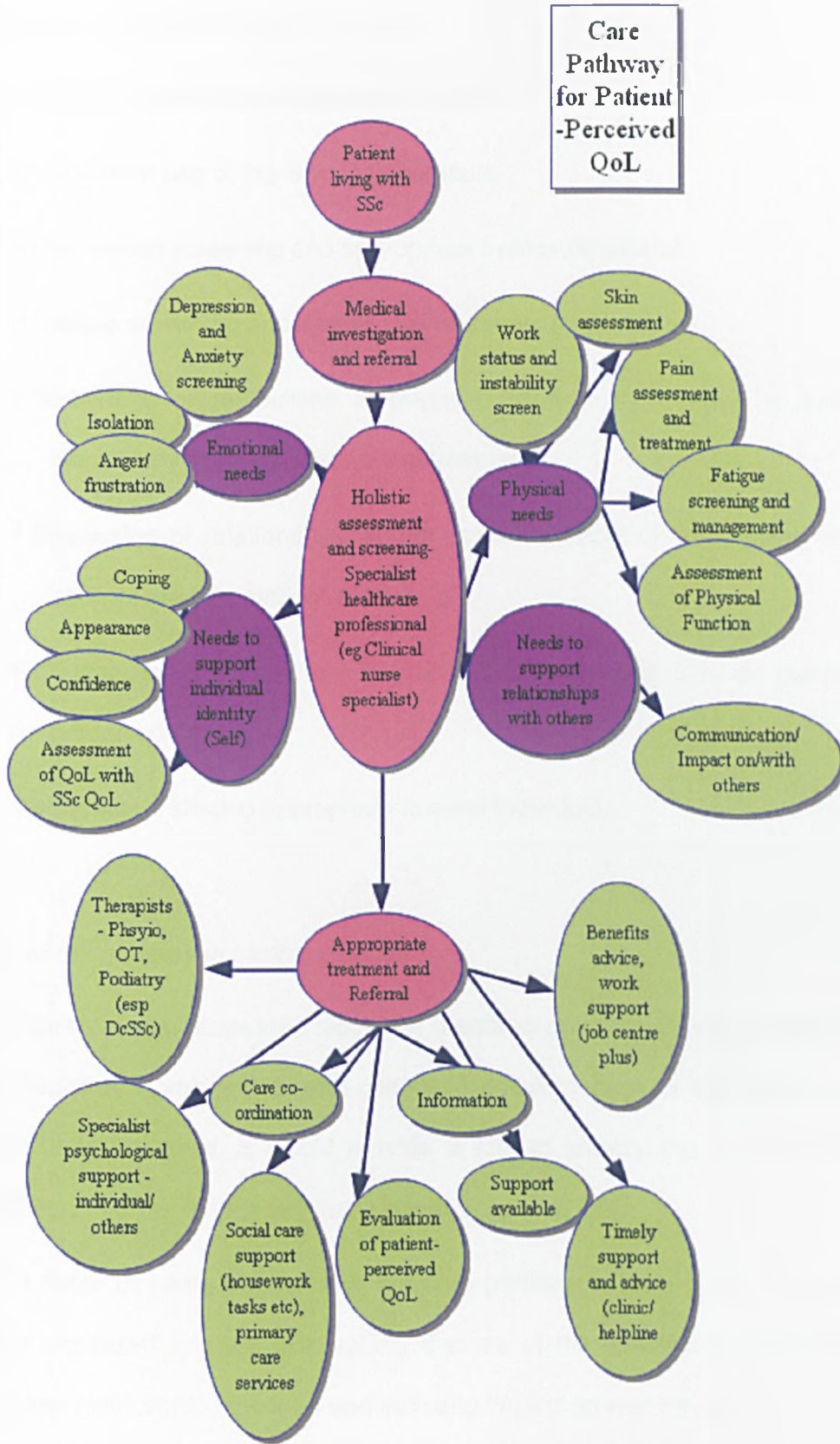
Figure 8.1 Care Pathway - Patient-perceived QoL

Key elements of this care pathway are:

- Use of a biopsychosocial model of care

- Consistent use of the SSc QoL measure

- Depression screening and appropriate treatment/referral

- Fatigue screening and appropriate treatments/referral

- Screening for restrictions in physical function and referral to multi-disciplinary team for appropriate treatment

- Discussion of relationships and/or sexual impacts of SSc, linked with appropriate information/referral

- Counseling to support the psychological impacts of SSc on patient-perceived QoL

- Information sharing appropriate to each individual.

Use of the pathway in clinical practice

The care pathway illustrated would be a shared document and prompt both the healthcare professional and patient to consider each of the issues that have been identified. It would provide a tool to identify the needs of the individual in order to improve their patient-perceived QoL.

More detail of some elements of the care pathway is now given. This has been organised into the overarching themes of the theoretical framework: physical restrictions; emotions and self; and impact on/with others.

8.4.2 Physical restrictions

Physical support and rehabilitation

The effects of SSc on physical function have been clearly demonstrated. The care pathway seeks to address these impacts by appropriate therapies to promote physical function in those with SSc; in particular, those with DcSSc. Therefore, therapies should be part of the treatment pathway for people with SSc, namely routine referral to physiotherapy, occupational therapy and podiatry services who can provide specialist knowledge of the management of function in those with SSc.

These services should work in tandem with other treatments such as drug therapy, or skin treatments such as PUVA and paraffin hand baths (Vincent and Wilson 2006) for other physical symptoms. Research into appropriate and effective physical therapies in SSc is limited, with a small exercise study indicating some benefits (Reay et al. 2002). This is clearly a gap in our knowledge of the treatment of functional impacts of SSc, and is a potential area for future research to inform clinical provision.

Work

Work emerged as a complex theme in the qualitative data. It was explained in two key impacts, the difficulties in maintaining work, and the implications of work loss through the effects of SSc. The potential for work loss, work instability, is an issue in other chronic diseases and there are assessments available to identify those at risk of job loss (Gilworth et al. 2003; Gilworth et al. 2006; Gilworth et al. 2007). Whilst no specific assessment exists for SSc, there are more generic assessments available (Allaire 2003; Gilworth et al.

2008). Clinically, this information translates into the need for those working with people with SSc to establish the work status of patients on diagnosis of SSc. Information on the type of employment (self-employed, employed, unemployed), can then be documented and built up to establish the potential support available to maintain employment. These services include occupational health, job centre plus work-place assessment, and ideally the involvement of a supportive employer. It is important to ensure patients have information for all these services and access to advocacy when required.

These measures may prevent or delay job loss, but for many people job loss or taking early retirement had already occurred (5.3.1.14). These people had mixed emotions, some feeling this to be good in that there was no longer pressure to spend energy at work, for others this was a profound loss affecting their self-esteem. If all adaptation has been exhausted within the workplace, the possibility of job loss may need to be considered, and prepared for. The most appropriate path for the patient must be foremost. For example, patients may feel too ill to deal with extensive paperwork and simply leave work. They may not appreciate the long-term financial benefits of acknowledging the role of SSc in their inability to continue in work by leaving work through ill health. These are issues that require both accurate information and support through these decision-making processes. The qualitative data of this study suggest that people may not be open with their employer regarding their disease, and therefore there needs to be a clear understanding of the information patients are happy to share.

This may be a new undertaking for some healthcare professionals, although for some, such as occupational therapists, this is a more acknowledged

aspect of their role. There are currently insufficient resources to lead on this aspect of care in many healthcare teams. However, healthcare professionals can and should identify those at risk of work instability or suffering from the effects of work loss and direct them to appropriate services who can lead on this element of the individuals care.

Fatigue management

SEM modeling has clearly demonstrated the direct effect of fatigue on patient-perceived SSc QoL (Table 7.2). Qualitative data of the interview transcripts have also given insight into the experience of living with fatigue associated with SSc, and the Fatigue Severity Scale (FSS) was scored highly as a comparator measure in this study (Chapter 6, table 6.4). To put this into context, available figures for the FSS in a 'normal' population give a mean of 2.3 (st+/- 0.7) (Krupp et al. 1989), showing fatigue scores in SSc to be over twice that of the available 'normal' (Reay 2007).

For those living with chronic disease who often rely on the support and strength of relationships with those around them, we begin to see how fatigue can extend beyond the purely physical. People are often unable to participate in any of their desired activities or relationships in any regular or reliable way, as they cannot predict the level or frequency of their fatigue.

The combination of evidence generated from this study underlines the significance of fatigue for those living with SSc. It is alarming to note that there is no standard care for the management of fatigue in SSc. The need for this provision was identified in presentation of emerging results from this study (Reay 2007). The clinical implication of this knowledge is the need to formally recognise fatigue as a significant co-morbidity in SSc and to screen

patients for their fatigue levels. Once identified, fatigue management strategies can be jointly developed between healthcare professional and patient (and those around them if possible).

Examples of management strategies for fatigue in other chronic diseases are available (White 1998; Harrison 2007), and offer a tool to research effective management of fatigue in those living with SSc. This research could be conducted alongside the development of service provision to manage this debilitating symptom.

8.4.3 Emotions and Self

The two overarching themes of Emotions and Self have been brought together in this discussion of clinical implications as, whilst they are conceptually different, service provision to address their impact is likely to overlap.

Patient-Perceived QoL

A primary implication of this study is the use of the SSc QoL measure in clinical practice. This provides a measure of patient-perceived QoL, which conforms to psychometric expectations, is reliable over time, and is a sum score, which can be easily calculated in the clinical setting. It consists of two sides of A4 paper with 29 questions and therefore offers both a pragmatic and psychometrically proven measure of patient-perceived SSc QoL.

Psychological support

This study has identified existing evidence of the psychological associations with SSc (Chapter 2), and added to this body of knowledge with the

demonstration of how depression and anxiety influences QoL as described by the SEM model in Chapter 7.

Current NHS services for people with SSc frequently focus on the health of the patient with SSc and are likely to have few service provisions to address the psychological impacts of SSc. This study has demonstrated both the modeled and lived evidence of the effect of depression, (and anxiety), across both dcSSc and lcSSc (Chapter 6, Table 6.4, Chapter 7, Figure 7.2). It therefore lends evidence to support the existing call for screening of SSc patients for depression (Thombs et al. 2007).

Wider psychological support services for those with SSc are therefore a clinical implication of this and previous research. In order to provide this, skills in identification of psychological association of SSc are required. It is possible for existing staff involved in the care of these patients to acquire a level of competencies to screen, deliver basic counseling, and refer appropriately to higher level services when required. There may however be resource implications of such a screening programme, which may increase referrals into clinical psychology and counseling services.

8.4.4 Impact on/with others

Information

Information was an issue that emerged through many interviews. In some contexts this was the request for appropriate information at appropriate timing in relation to SSc, its treatment or its potential effects. For others information was mentioned in the context of withholding information, often from friends and family members either to protect them, or to protect the patient from having to deal with the reactions of others. For clinical practice,

this translates into a need to discuss information with the patient, including a private conversation, in order to agree a strategy for the exchange of information between professionals and the patient, and the level of information to be discussed with those around the patient. There is little existing evidence regarding the sharing of information in SSc, with only two studies found (Samuelson and Ahlemen 2000; Ndosi et al. 2008). The earlier study presents a SSc patient education programme, evaluated in only six female patients, showing variable results and highlighting the need for further study in this area. The later study, (Ndosi et al. 2008), provides evidence to support the use of the Educational Needs Assessment Tool (ENAT), in patients with SSc.

The rigour of patient information held on databases will be explored in section 8.6.5. However, it a clinical implication, that all patients should be offered the opportunity to have their data entered on the National Scleroderma Database, as this will increase their access to research studies such as this one.

Finance

Finance was highlighted as a concern for some people with SSc, and particularly those who had given up their work role. Whilst it may not be within the resources of rheumatology healthcare teams to offer detailed advice, it is important that they signpost patients towards the possibility of financial support such as disability allowances, blue parking badge and incapacity benefits to ensure that patients have information of what is available, and can then seek out specialist advice from more appropriate services.

Relationships

Whilst relationship counseling may extend beyond the skills of many healthcare workers, holistic assessment will help to identify these relationship difficulties and may trigger the need for listening, counseling or, in some cases, specific relationship counseling to meet the individuals needs for social relationships.

8.5 Testing the hypothesis

The hypothesis of the study was that there will be differences in the level of QoL between people with different subtypes. This was tested in two ways, by simple univariate non-parametric testing of the difference in QoL between subtype, and by multivariate SEM. The results of this testing are presented in chapters six and seven. The non-parametric test showed no association between disease sub-type and QoL as measured by the SSc QoL. However, SEM revealed that disease subtype had a significant indirect effect upon QoL, mediated by disability. Thus a significant effect of disease subtype was observed, but revealed only by the more sophisticated analytical approach of SEM.

8.6 Contribution to Methodological Developments

This study has investigated several aspects of research methodology, the results of which may inform future research practice.

8.6.1 Data saturation

As a novel addition to the development of the SSc QoL, the amount of interviews required to reach data saturation was analysed. Data saturation,

that is the point at which no new themes were generated, was reached after four interviews. This compares with twelve interviews presented in previous research (Guest 2006). The interviews were continued past this point in order to ensure that, as far as possible, the demographics within the sample frame were represented.

Whilst it can be concluded from this study that four interviews were sufficient to generate all the themes of SSc QoL, it must be considered that this may have been dependent upon the four interviewees themselves. Interviewee's experiences and the data they give vary; therefore a conclusion that any four interviews will provide data saturation is not supported by this study. In order to prove the number of interviews required to consistently provide data saturation, a further study would be required with randomly selected groups of interviews/interviewees.

8.6.2 Item mapping

An interesting contrast is seen in this study between data saturation for themes, and data saturation for items. Whilst the themes were all present within the first four interviews, the items of the SSc QoL, (Table 6.7), were still being generated up to and including the final interview.

As demonstrated in chapter six, the items of the SSc QoL came from a variety of interview sources, many items being a composite of several statements to form an item which conformed to the requirements of items (McKenna et al. 2004).

A possible rationale for this difference in the amount of interviews required for thematic data saturation and those required for item generation lies in the use of this data. Themes are broad and do not have statistical requirements

of validity applied to them. Items however, have strict requirements on their conceptual background (that is they need to apply to the needs-based model of QoL), they have to conform to wording criteria in order to be applicable across the SSc population, and they need to conform to the statistical requirements of Rasch analysis, providing a range of items across the scale. Therefore, it is reasonable to anticipate that it will require more data in which to locate items which meet these requirements, rather than themes which are emergent from the data itself and do not have to meet such strict requirements.

8.6.3 Use of a focus group

The addition of a focus group to the established method of qualitative data collection for a needs-based QoL measure, allowed comparison of themes generated between the two data collection methods. The focus group produced no new themes, in comparison to the interviews and therefore was not pursued within this study. However, there are alternative types of analysis that may further inform this comparison. For example, the focus group transcript was not analysed for the items generated, which has been demonstrated by the results of this study to be unrelated to the data saturation required for generation of themes.

Also, the observational notes (see Appendix 6) suggest the potential to alter the format of the focus group if repeated. For example, it may be that more data is generated from an all male or all female gender group where perhaps more personal topics could be discussed freely. The focus group within this study consisted of four women and one man.

8.7 Limitations of the research

The process of qualitative data gathering generated several reflections upon the methodology used within this study and the lessons to be learnt for future research. These reflections are now discussed in order to contribute to a body of experience of qualitative research interviews.

8.7.1 Male participants

Despite the additional interviews, several cells of the sample frame were not recruited, namely males with dcSSc age 49 and below, males with lcSSc with disease duration below five years and age 50 and above. The scarcity of male participants had been anticipated due to the fact that SSc is a rare disease and predominantly effects females. All males within the recruiting centre were approached, one of whom refused, the others all participated in the study. It was at this point that the qualitative interviews were stopped, as it was clear that no further cells of the sample frame could be recruited.

An expected paucity of male participants with SSc was also reflected in the postal returns of the questionnaire booklets, and is likely to remain a limitation for future research into this disease population.

8.7.2 Response rates

When reviewing response rates in market research average response rates of 36% are suggested (Byrom and Bennison 2000). Within healthcare research it has been suggested that judgment of response rates should use norms in similar studies as their comparison (Parahoo 1997). Therefore, whilst improvements in response rates are desirable, the response rates of this study equate well with published norms.

8.7.3 SEM

The SEM model constructed in chapter 7 utilized comparator measures selected for their representation of the ICF and their prominence as associations with SSc identified in the literature review. These were included in the model specification together with the measure of patient-perceived QoL, the SSc QoL. Whilst this presents a parsimonious model, which conforms to the requirements of SEM, it does not incorporate all the comparator measures. Further research may explore the possible models created by use of a varying selection of comparator measures to see if other models are possible.

8.7.4 Discarded items and use of the item bank

During the process of item selection many items are discarded. This may give rise to concerns regarding the importance of the items discarded, and therefore the implications of using an item selection tool such as the Galen tool (Galen 2006) used in this study.

There are several systems in place within the SSc QoL development protocol to address this concern. Firstly as demonstrated by the fact that all themes identified in this study were present in the first four interviews, analysis of the additional twenty-seven interviews generated large amounts of repetition in the themes and content of the potential items identified. Therefore the majority of the items were discarded for reasons such as duplication.

For example, in transcript 26 there were four items on tiredness, in transcript 28 there were three, and in transcript 31 there were four items on sleep. Therefore conceptually each item was repeated many times. The

researchers tried to preserve items on the same theme. This is reflected in Table 5.2 where the source of some items is described as 'composite', meaning that the single item represented duplicates.

Item selection criteria (described in section 4.2.1) were applied to those items remaining after deletion due to duplication. Clearly, all items generated by interviewees have importance to that individual, however it is essential if the QoL measure is to be applicable for use with all people with SSc. This is essential so that respondents are not excluded from any questions. Items were removed if they were not applicable to all potential respondents. However, prior to removal, the item was reviewed by the study researcher and an independent researcher to see if altering the wording of the item and provide a statement which was universally applicable. An example of this would be:

"I can't wear high heels anymore"

Could be altered to:

"I can't wear the shoes of my choice anymore"

This example was used in the first postal of the SSc QoL (item j7 in the first postal questionnaire 90 item SSc QoL).

Therefore, whilst it may appear that these items are lost, they can in fact be minimally adapted to create a universal meaning that applies to all respondents whilst maintaining the interviewees words as far as possible. The example above represents the more extreme of the alteration of an items wording: the item selection group felt strongly that items such as this were key to include as they linked to other key concepts of the theoretical framework, this case, appearance.

The item selection guidance tool (Galen 2006), has been used in the development of other needs-based QoL measures (Keenan 2008), but its use does apply strict criteria to the item selection process. However, it is rigid in order to ensure the measure is both applicable to a wide population, uses simple language and establishes a tool which fits criteria for future use in different languages.

Another technique utilized to ensure that conceptually significant items are not disregarded, is that of analysis of the items discarded from during the initial Rasch analysis process. Of the items selected from the discard pile of items rejected during Rasch analysis of the first postal questionnaire, a small number were felt by the researcher to have conceptual validity for those living with SSc (based on the qualitative analysis). Therefore, these were incorporated into the test/retest booklet stage of the SSc QoL development (as a separate item scale). Rasch analysis of these items revealed that they did not represent a sub-scale of items in that they did not fit the Rasch model requirements.

Use of the item bank

Another potential methodological issue is the use of items from the item bank (4.2.1.1). It may be a concern that after such efforts to acknowledge the SSc patient as the expert informant, and to gather specific data from people with SSc, items from measures used in other diseases would form the SSc QoL. However, only three items within the SSc QoL have been drawn from the item bank. This substitution showed only a small number of items were interchangeable with the item bank, suggesting that generic

items do not widely represent patient-perceived QoL in SSc. This also supports the argument for this disease-specific SSc QoL.

8.7.5 Use of databases for research

This study identified significant issues around the use of a database for patient recruitment. To summarise, these issues included:

- One third of the database entries did not have a disease sub-type entered

- There was no direct link to the hospital patient administration system (PAS) to check patient status

- There was no funding for staff to maintain the database information hence current patient status was not always accurate.

- 11.67% of patients identified by the database were deceased.

This has significance beyond this study. The ethics of this research was beneficence, that is to do no harm. To send out questionnaire booklets to all those people on the database who were actually deceased may have caused significant distress to their relatives. Indeed, even with these rigorous procedures in place, questionnaires were sent to nine people who had died. The impact of this was demonstrated in a letter from the husband of a lady who had died the day the questionnaire booklet had arrived.

Obviously this was unavoidable but what was perhaps most striking was that of all the responses saying that the patient had died, there was a clear message that the patient would have welcomed the opportunity to be involved into research into SSc. The learning from this experience was shared through publication: these issues of accessing databases have been

published as a consequence of the experiences of this study (Firth and Reay 2008).

As England now has detailed guidance regarding data protection of patient records (DoH 2006), there are direct implications for the handling of patient information in research. Data created by an NHS employee has to be handled in line with this 2006 guidance, which means that it has to be anonymised if sent electronically and cannot be carried on a standard data stick unless anonymised. As a consequence, the researcher had to physically access data from the database, anonymise it and then send it electronically. The data had to be coded in order to match it up with the address information required for the printing of address labels for the postal questionnaire aspect of this study. The time implications of this were substantial and should be a key methodological consideration in future studies.

There were consequences of the guidance for data analysis also, with several aspects of data not available for use in this study, particularly those of the non-responder group. In future studies, the researcher would plan a data strategy which would aim to accommodate the governmental guidance, but would allow full demographic data to be gathered on the sample population, so as to identify potential research bias. The issues generated from the effect of the Records Management Guidance 2006 (DoH 2006) on research have been published in response to the experiences gained in this study (Reay and Firth 2008).

8.7.6 Difficulties in measurement of QoL in healthcare

Conceptual agreement on QoL

The variety of conceptual backgrounds to QoL assessment has been outlined in this study, illustrating the lack of consensus, not only on models of QoL, but even on definition of QoL within healthcare. Contention around QoL measurement in healthcare has been highlighted in a negative review of QoL measurement (Hunt and Leplege 1997) which highlights both the lack of definition and conceptual consensus in QoL measurement.

Earlier in this study, the many models and dimensions of QoL were described. It is clear that QoL is a term used in publications to describe a range of conceptual approaches, from that of subjective well being as seen in the needs-based QoL model, to that of HRQoL, and indeed, to publications which do not identify the conceptual basis for their QoL measurement.

In order to explore this potential confusion within SSc QoL, three electronic databases, EMBASE, MEDLINE and CINHAL (Feb 2008), were accessed in order to explore models of QoL used in SSc. As no needs-based SSc QoL measures had been identified in the literature review of this study, it was unsurprising that a needs-based model of SSc QoL was not found. However, further exploration revealed that the SSc QoL articles found, were either based either upon a HRQoL model, did not propose any conceptual base for their QoL assessment, or proposed their use of one model and used another.

This does not directly reflect as a limitation of this study, because a clear conceptual model of QoL was identified prior to data collection, together with the rationale for its choice. However, it is a limitation of QoL studies in SSc where conceptual frameworks of QoL may be absent or misleading.

8.8 Directions for Future Research

The findings of this study have highlighted several implications for clinical practice, and also identified gaps in the knowledge of care management in SSc.

Directions for future research indicated by this study are:

- Research into promotion of physical function in those with SSc. Currently there is little evidence regarding models of therapy or treatments which effectively promote physical function in those with SSc. As research findings suggest those with dcSSc have higher levels of functional impact than those with lcSSc, future research should ensure that models of care are effective for both disease sub-types.

- Further understanding of the impact of disease sub-type in SSc on QoL may be gained through analysis of qualitative data gathered from people living with each sub-type to explore commonalities and differences between dcSSc and lcSSc. This could be supported by a different analytical approach, such as phenomenological approach to analysis, to allow the development of a theoretical framework of QoL in SSc.

- Evaluation of the Care pathway resulting from this study (8.4.1). The care pathway of patients with SSc in the UK is currently unclear. Whilst there has been some research conducted in Canada (Johnson et al. 2006), the patients journey through service provision remains largely unmapped. In order to assess the impact of the proposed

Care Pathway, initial research into current patient pathways would be required in order to provide baseline data. Following this, a re-evaluation of implementation of the pathway could be carried out together with evaluation of patient outcomes and subjective patient views of their experience. Therefore, the Care pathway could be evaluated in terms of its implementation, outcomes, and patient experience.

• This study identified fatigue as a key issue for patients, and highlighted levels of fatigue in SSc patients to be twice that of a 'normal' population (Reay 2007). It is likely that many patients with SSc do not receive specific fatigue management services, however there is no empirical knowledge of current levels of fatigue management provision in SSc services. Initial mapping of current provision is required, followed by design of fatigue management strategies which can then be implemented and evaluated in a multi-centre research programme.

• Links between the psychological, social and physical associations of SSc are unclear and require further study, using valid and reliable Patient Reported Outcome Measures in a population including patients with dcSSc and lcSSc. SEM modeling of the data would build upon the findings of this study, and provide a broader insight into the direct and indirect relationships between physical impacts, psychological impacts and disease sub-type in SSc.

• Methodological evidence from this study suggested data saturation for qualitative themes to be four interviews. Further study is required to

test this finding in randomly selected transcripts. The hypothesis to be tested would be that data saturation in the development of needs-based QoL measures is achieved with four one to one interviews. A nested study would also test the number of interviews required to achieve item saturation in the development of needs-based QoL measures.

• Research into information requirements of people with SSc and the best mode of delivery (group/individual, timing and content of information), is sparse. A further study into these aspects of information sharing with SSc patients is indicated. Possible methods for this study could involve use of the ENAT tool to design education around the needs of the individual (Ndosi et al. 2008).

8.9 Summary

The principle findings of this research are:

• A descriptive framework of patient-perceived SSc QoL has been developed, consisting of overarching themes of Physical restriction, Emotion, Self, and Impact on/with others. These are made up of thirty themes representing the physical, social and psychological aspects of patient-perceived SSc QoL.

• The needs-based SSc QoL has been developed and fits modern psychometric requirements of Rasch analysis. The SSc QoL has been found to demonstrate good test-retest reliability.

• Non-parametric testing shows no significant difference in levels of patient perceived QoL between disease sub-types (as measured by

the SSc QoL). SEM testing of the research hypothesis demonstrates that disease sub-type has an indirect effect through impact on QoL, working through function. Therefore, multivariate analysis has identified an indirect link between disease sub-type and patient-perceived SSc QoL.

• There is a significant link between disease sub-type and function, with higher impacts on function being seen in those with dcSSc than those with lcSSc.

References

Abraham, D. and Distler, O (2007). "How does endothelial cell injury start? The role of endothelin in systemic sclerosis." Arthritis Research and Therapy 9(Supple): S2.

Albrecht, G. and Devlieger, P. (1999). "The disability paradox: high quality of life against all odds." Social Science and Medicine 48: 977-988.

Allaire, S. (2003). "Measures of Adult Work Disability." Arthritis and Rheumatism 49(5S): S85-89.

Andrich, D. (1978). "Rating formulation for ordered response categories." Psychometricka 43: 561073.

Andrich, D. Lyne, A. Sheridan, B. Luo, G. (2003). RUMM 2020. Perth, RUMM Laboratory. Angelopoulos, N. Drosos, A. Moutsopoulos, HM. (2001) "Psychiatric Symptoms Associated with Scleroderma." Psychotherapy and Psychosomatics 70: 145-150.

Arlett, C. Welsh, K. Black, CM. Jimenez, SA.(1997). "Fetal-maternal HLA compatibility confers susceptibility to systemic sclerosis." Immunogenetics 47(1): 17-22.

ARMA (2007). Standards of Care for People with Connective Tissue Diseases. ARMA Alliance, ARMA.

Assassi, S. and Mayes, M. (2003). "The Genetics of Scleroderma: What Every Rheumatologist Should Know." Scleroderma Care and Research 1(2): 3-11.

Badley, E. (2006). Patient centred outcomes: Mapping the ICF. Care IV. Weetwood hall, Leeds, UK, Care IV.

Balbir-Gurman, A. Denton, C Nichols, B. Knight, C. Nahir, AM. Martin, G. Black, C (2002). "Non-invasive measurement of biomechanical skin properties in systemic sclerosis." Annals of the Rheumatic Diseases 61: 237-241.

Bandura, A. (1994). Self-Efficacy. Encyclopedia of Human Behaviour. V. Rhamachaudran. New York, Academic Press. 4: 71-81.

Barst, R. and Seibold, J. (2003). "Pulmonary Arterial Hypertension Related to Systemic Sclerosis: A Primer for the Rheumatologist." Scleroderma Care and Research 1(1): 12-20.

Belch, J. (1991). "Raynaud's phenomenon: its relevance to scleroderma." Annals of the Rheumatic Diseases 50: 839-845.

Benrud-Larson, L, Haythornthwaite, J. Heinbery, LJ. Boling, C. Reed, J. White, B. Wigley, FM. (2002). "The impact of pain and symptoms of depression in scleroderma." Pain 95(3): 267-275.

Benrud-Larson, L. M., Heinberg, L.J. ,Boling, C. Reed, J. White, B. Haythornthwaite, J.A. Wigley, F. - (2003). "Body Image Dissatisfaction Among Women with Scleroderma: Extent and Relationship to Psychosocial Function." Health Psychology 22(2): 130-139.

Bhakta, B., Tennant, A. Horton, M. Lawton, G. Andrich, D. (2005). "Using item response theory to explore the psychometric properties of extended matching questions examination in undergraduate medical education." BMC Medical Education 5(9).

Black, C. (1995). "The aetiopathogenisis of systemic sclerosis: Thick skin-thin hypothesis." Journal of the Royal College of Physicians 29: 119-128. Black, C. (1995). "Measurement of skin involvement in scleroderma." Journal of Rheumatology 22: 1217-1219.

Black, C. (2005). "Pulmonary arterial hypertension: are we doing enough to identify systemic sclerosis patients at high risk of this rare condition?" Rheumatology 44: 141-142.

Bland, J. and Altman D (1995). "Multiple significance tests: the Bonferroni method." British Medical Journal 310: 179.

Bloor, M., Frankland, J. Thomas, M. Robson, K. (2002). Focus Groups in Social Research. London, Sage publications.

Bond, T. and Fox, C (2001). Applying The Rash Model. Fundamental Measurement in the Human Sciences. Mawah, Lawrence Erlbaum Associates inc.

Bowling, A. (2001). Measuring Disease. Buckingham and Philadelphia, Open University Press.

Boyle, C., Browne J. Hickey, A. McGee HM. Joyce, CRB. (1993). The Schedule for the Evaluation of Individual Quality of Life (SEIQoL): a Direct Weighting procedure for Quality of Life Domains (SEIQoL-DW), Department of Psychology, Royal College of Surgeons in Ireland.

Bramwell, B. (1914). "Diffuse scleroderma: its frequency, it's occurrence in stonemasons: it's treatment by fibroylsin-elevations of temperature due to fibrolysin injection." Edinburgh Medical Journal 12: 387-401.

Brickman, P. and Campbell, D (1971). Hedonic relativism and planning the good society. Adaptation-level theory: A symposium. M. Apley. New York, Academic Press: 287-302.

Brickman, P, Campbell, D. Janoff-Bulman, R. (1978). "Lottery winners and accident victims: Is happiness relative?" Journal of Personality and Social Psychology 36: 917-927.

Briggs, D. and Welsh, K. (1991). "Major histocompatability complex class 11 genes and systemic sclerosis." Annals of the Rheumatic Diseases 50(862-865).

Britten, N. (1995) "Qualitative Research: Qualitative interviews in medical research." British Medical Journal Volume, DOI: http://www.bmj.com/cgi/content/full/311/6999/251

Bryan, D., Knight, C. Black, CM. Silman, A. (1999). "Prediction of Five-Year Survival Following Presentation With Systemic Sclerosis." Arthritis and Rheumatism 42(12): 2660-2665.

Byrom, J. and Bennison, D. (2000). "The effect of personalisation on mailed questionnaire response rates." International Journal of Market Research 42(3): 357-363.

Cardol, M., DeJong, B. Ward, C.D. (2002). "On autonomy and participation in rehabilitation." Disability and Rehabilitation. 24(18): 970-974.

Carr, A., Gibson, B. Robinson, P.G. (2001). "Is quality of life determined by expectations or experience?" British Medical Journal 322: 1240-3.
Carreira, P. E. (2006). "'Quality of pain' in systemic sclerosis." Rheumatology 45: 1185-1186.

Casciola-Rosen, L., Wigly, F. Rosen, A. (1997). "Scleroderma autoantigens are uniquely fragmented by metal-catalyzed oxidation reactions: implications for pathogenesis." Journal Experimental Medicine 185: 71-9.

Clements, P., Lachenbruch, P. Seibold, J. Zee B. Steen, VD. Brennan, P. (1993). "Skin thickness score in systemic sclerosis: An assessment of interobserver variability in 3 independent studies." Journal of Rheumatology 20: 1892-1896.

Costa, P. and McCrae, R (1988). "Personality in adulthood: A six year longitudinal study of self-reports and spouse ratings on the NEO Personality Inventory." Journal of Personality and Social Psychology 54: 853-863.

Cummins, R. (1996). "The domains of life satisfaction: an attempt to order chaos." Social Indicators Research 38: 303-28.

Cummins, R. (1997). The Comprehensive Quality of Life Scale - Intellectual Disability. Toorak, Deakin University School of Psychology.

Danieli, E., Airo, P. Bettoni, L.Cinquini, M.Antonioli, AM.Cavazzana, I.Franceschinni, F.Cattaneo, R. (2005). "Health-related quality of life measured by the Short Form 36 (SF36) in systemic sclerosis: correlations

with indexes of disease activity and severity, disability, and depressive symptoms." Clinical Rheumatology 24: 48-54.

Darzi, A. (2007). Our NHS, Our Future: Next Stage Review. DoH.

De Croon, E.,Cluiter, E. Nijssen, TF. Dijkmans, BAC. Lankhorst, GL. Frings-Dresen, MH. (2004). "Predictive Factors of Work Disability in Rheumatoid Arthritis: a systematic literature review." Annals of the Rheumatic Diseases 63: 1362-1367.

De Jong, Z., De Hiejde, D. McKenna, SP. Whalley, D. (1997). "The Reliability and Construct Validity of the RAQoL; A Rheumatoid-Arthritis Specific Quality of Life Instrument." British Journal of Rheumatology 36: 878-883.

Deiner, E. and Biswas-Diener, R (2000). "New directions in subjective well-being research: The cutting edge." Indian Journal of Clinical Psychology 27: 21-33.

Deiner, E. D. (1984). "Subjective Well-Being." Psychological Bulletin 95(3): 542-575.

Denton, C. (2007). "Therapuetic targets in systemic sclerosis." Arthritis Research and Therapy 9(Supplement 2): S6.

Denton, C. and Black, C (1999). "Systemic sclerosis: an overview of pathogenisis and treatment" CPD Rheumatology 1(1): 33-39.

Denton, C. Black, C. (2004) - "Scleroderma - clinical and pathological advances" Best Practice and Research Clinical Rheumatology 18 (3): 271-290

Denton, C. and Black C. (2005). "Targeted therapy comes of age in scleroderma" Trends in Immunology 26 (11): 596-602

Denton, C. Black, C. Abraham, DJ. (2006). "Mechanisms and consequences of fibrosis in systemic sclerosis" Nature Clinical Practice Rheumatology 2: 134 - 144

Derk, C (2007). " Associations of breast cancer development in patients with systemic sclerosis: an exploratory study" Clinical Rheumatology 26 (10): 1615 - 1619

DiMarinao, A., G. Carlson, Myers, A. (1973). "Duodenal myoelectric activity in scleroderma; abnormal responses to mechanical and hormonal stimuli." NEJM 289: 1220-23.

DoH (2006). Records Management: NHS Code of Practice, Parts 1 and 2. Health, HMSO.

DoH (2007a). 18 Weeks - Commissioning Pathways. Department of Health

DoH. (2007b). World Class Commissioning - the vision, HMSO.

DoH. (2008) "National Service Frameworks." **Volume,** DOI: http://www.dh.gov.uk/en/Healthcare/NationalServiceFrameworks/index.htm

Dorian, L. and Garfinkel, P (1987). "Stress, immunity and illness - a review." Psychological medicine **17**: 393-407.

Doward, L., McKenna, S. Meads, D. (2004). "Effectiveness of Needs-Based Quality of Life Instruments." Value in Health **7**(Supplement 1): S35-S38.

Doward, L., McKenna, S. Meads, DM. Twiss, J. Revicki, D. Wong RL. Luo, MP. (2007) "Translation and validation of non-English versions of the Ankylosing Spondylitis Quality of Life (ASQOL) questionnaire." Health and Quality of Life Outcomes **Volume,** 1-10 DOI

Doward, L., Meads, D. Thorsen, H. (2004). "Requirement for Quality of Life Instruments in Clinical Research." Value in Health **7**(Supplement 1): S13-S16.

Doward, L., Spoorenberg, A. Cook, SA. Whalley, D. Helliwell, PS. Kay, LJ.McKenna, SP. Tennant, A. van der Heijde, D. Chamberlain, MA. (2003).

"Development of the ASQoL: a quality of life instrument specific to ankylosing spondylitis." Annals of the Rheumatic Diseases **62**: 20-26.

Dustoor, M., McInerney, M. Mazanec, DJ. Cathcart, MK. (1987). "Abnormal lymphocyte function in scleroderma: a study on identical twins." Clinical Immunology and Immunopathology **44**(1): 20-30.

Eklund, M. and Sandqvist, G (2006). "Psychometric properties of the Satisfaction with Daily Occupations (SDO) instrument and the Manchester Short Assessment of Quality of Life (MANSA) in women with scleroderma and without known illness." Scandanavian Journal of Occupational Therapy **13**: 23-30.

Faber, H. and Loscalzo, J (2004). "Mechanisms of Disease: Pulmonary Hypertension." The New England Journal of Medicine **352**(16): 1655-1666.

Fagundus, D. and Le Roy, E (1995). Systemic Sclerosis (Scleroderma) Connective Tissue Diseases. London, Chapman and Hall.

Farquhar, M. (1995). "Definitions of quality of life: a taxonomy." Journal of Advanced Nursing **22**: 502-508.

Fayers, P. and Machin, D (2000). Quality of Life: Assessment, Analysis and Interpretation. Chichester, Wiley and Sons.

FDA, U. F. a. D. A. (2007). The Importance of Patient-Reported Outcomes... It's All About the Patients, US Food and Drugs Administration (FDA).

Feghali-Bostwick, C., Medsger, TJ. Wrogtj. TM. (2003). "Analysis of Systemic Sclerosis in Twins Reveals Low Concordance for Disease and High Concordance for the Presence of Antinuclear Antibodies." Arthritis and Rheumatism 48(7): 1956-1963.

Firth, J. and Reay, N (2008). "Clinical and research databases in healthcare research." Nurse Researcher 15(4): 27-34.

Fisher, W. J. (1992). "Reliability Statistics." Rasch Measurement Transactions 6(3): 238.

Foundation, K. (2006). Living with kidney disease. 4th Edition.

Fries, J., Spitz, P. Kraines, RG. Holman, HR. (1980). "Measurement of patient outcome in arthritis." Arthritis & Rheumatism. 23(137-45).

Galen, R. (2006). Item Selection Guide, Galen Research: 1.

Gardner, H., Shearstone, J. Bandaru, R. Crowell, T. Lynes, M. Trojanowska, M. Panu, M. Smith, E. Jablonska, S. Blaszczyk, M et al. (2006). "Gene profiling of scleroderma skin reveals robust signature of disease that are imperfectly reflected in the transcript profiles of explanted fibroblasts." Arthritis and Rheumatism 54: 1961 - 1973.

Georges, C., Chassany, O. Toledano, C. Mouthon, K. Tiev, K .Meyer, O. Illie, D. Rambeloarisoa, J. Marjanovic Z. Cabane, J.Sereni, D.Pouchot, H. Farge, D. (2006). "Impact of pain in health related quality of life of patients with systemic sclerosis." Rheumatology 45: 1298-1302.

Gilworth, G., Bhakta, B. Eyres, S. Carey, A. Chamberlain, M.A. Tennant, A. (2007). "Keeping nurses working: development and psychometric testing of the Nurse-Work Instability Scale (Nurse-WIS)." Journal of Advanced Nursing: 543-551.

Gilworth, G., Carey, A. Eyres, S. Sloan, J. Rainford, B .Boddenham, D, Nuemann, V. Tennant, A. (2006). "Screening for job loss: Development of a work instability measure for traumatic brain injury." Brain Injury 20(8): 835-843.

Gilworth, G., Chamberlain, M. Bhakta, B. Haskard, D. Silman, A. Tennant, A. (2004). "Development of the BD QoL: A Quality of Life measure Specific to Betchets disease." The Journal of Rheumatology 31: 931-7.

Gilworth, G., Chamberlain, M. Harvey, A. Woodhouse, A. Smith, J. Smyth, MG. Tennant, A (2003). "Development of a work inability scale for rheumatoid arthritis." Arthritis Care and Research 49(3): 349-354.

Gilworth, G., Smyth, G. Smith, J. Tennant, A. (2008). "The development and the validation of The Office Work Screen." Occupational Medicine 58(4): 289-294.

Glaser, B. and Strauss, A (1967). The Discovery of Grounded Theory. New York, Aldine.

Grand round, R. F. (1996). "Systemic Sclerosis: current pathogenetic concepts and future prospects for targeted therapy." The Lancet 347: 14531458.

Group, E. (1990). "EuroQoL - a new facility for the measurement of health related quality of life" Health Policy 16 (1990): 199-208.

Guest, G. (2006). "How Many Interviews Are Enough?" Field Methods 18(1): 59-82.

Guseva, N., Folomeeva, O. Oskilko, TG. (1981). "Familial systemic scleroderma: a follow-up study of concordant monzygotic twins." Ter Arkj 53: 43-7.

Hachulla, E. and Coghlan, J (2004). "A new era in the management of pulmonary arterial hypertension related to scleroderma: endothelin receptor antagonism." Annals of the Rheumatic Diseases 63(9): 1009-1014.
Harrison, S. (2007). Fatigue Management for People with Multiple Sclerosis. Guidance, College of Occupational Therapists, London.

Haustein, U. (2002). "Systemic Sclerosis - scleroderma." Dermatology Online Journal 8(1)(3): 1-86.

Haustein, U. and Zeigler, V (1985). "Environmentally induced systemic sclerosis-like disorders." International Journal of Dermatology 24: 146-51.
Hawking, S. (2008). "Hawking - A brief history of mine." Retrieved October 2008.

Hennes, S. and Wigley, F (2007). "Current drug therapy for scleroderma and secondary Raynauds phenomenon: evidence-based review." Current Opinion in Rheumatology 19: 611-618.

Herrick, A. (2005). "Pathogenesis of Raynaud's phenomenon." Rheumatology 44: 587-596.

Herrick, A. llingworth, K. Hollis, S. Gomez-Zumaquero, JM. Tinahnes, FJ. (2001). "Antibodies against oxidized low-density lipoproteins in systemic sclerosis." Rheumatology 40: 401-405.

Hewlett, S., Hehir, M. Kirwan, JR. (2007). "Measuring Fatigue in Rheumatoid Arthritis: A Systematic Review of Scales in Use." Arthritis and Rheumatism 57(3): 429-439.

Heyt, G., Oh, M. Aemzadeh, N. Rivera, S. Jimenez, SA. Cohen, S. DiMarinao, AJ. (2004). "Impaired rectoanal inhibitory response in scleroderma (systemic sclerosis): an association with fecal incontinence." Digestive Diseases and Sciences 49(June): 1040-5.

Holloway, I. and Wheeler, S (2002). Qualitative Research in Nursing. Oxford, Blackwell publishing.

Hoyle, R. and Smith, G (1994). "Formulating Clinical Research Hypotheses as Structural Equation Models: A Conceptual Overview." Journal of Consulting and Clinical Psychology 62(3): 429-440.

Hunt, S. and Leplege, A (1997). "The Problem of Quality of Life in Medicine." Journal of the American Medical Association 278(1): 47-50.

Hunt, S. and McKenna, SP (1992). "The QLDS: A scale for the measurement of quality of life in depression." Health Policy 22: 307-319.

Hyphantis, T., Tsifetaki, N. Siafaks, V. Voulgari, PV. Pappa, C. Bai, M. Palieraki, K. Venetsanopoulou, A. Mavreas, V. Drosos, A. (2007). "The Impact of Psychological Functioning upon Systemic Sclerosis Patients' Quality of Life." Seminars in Arthrits and Rheumatism 37: 81-92.

Jaffe, B. and Claman, H (1983). "Chronic Graft-versus-Host Disease (GVHD) as a Model for Scleroderma." Cellular Immunology 77: 1-12.

Joachim, G. and Acorn, S (2003). "Life with a rare chronic disease: the scleroderma experience." Journal of Advanced Nursing 42(6): 598-606.

Johnson, S., Carette, S. Dunne, J. (2006). "Scleroderma: Health Services Utilization from Patients' Perspective." Journal of Rheumatology 33: 1123-7.

Johnson, SR., Gladman, DD. Schentag, C.T. Lee, P. (2006). "Quality of Life and Functional Status in Systemic Sclerosis Compared to Other Rheumatic Diseases." Disability and Health.

Johnston, M. and Pollard, B (1996). Measuring Emotional, Disability, Handicap and Quality of Life Outcomes of Chronic Disease, Department of Health: http://www.dh.gov.uk.en.Researchanddevelopment/A-Z/Physicalandcomplexdisabiliti.

Joreskog, K. (1973). A general method for estimating a linear structural equation system. Structural equation models in the social sciences. A. Goldberger and O. Duncan. New York, Seminar: 85-112.

Kahan, A. and Allanore , Y (2006). "Primary myocardial involvement in systemic sclerosis." Rheumatology 45: iv14-iv17

Kawut, S., Taichman, D. Archer-Chicko, CL. Palevsky, HI. Kimmel, SE. (2003). "Hemodynamics and survival in patients with pulmonary arterial hypertension related to systemic sclerosis." Chest 123: 344-350.

Keenan, A. (2008). The development of a quality of life instrument for Osteoarthritis. School of Medicine. Leeds, University of Leeds. PhD: 200.
Keesling, J. (1972). Maximum likelihood approaches to causal flow analysis. Chicago, University of Chicago.

Khanna, D. (2008). "A standardized core set for systemic sclerosis clinical trials. First step in development of combined response index." Rheumatology 47(Supplement 5): v31-v32.

Khanna, D., Furst, D. Clements, PJ. Park, GS. Hays, RD. Yoon, J. Korn, J. Merkel, P. Rothfield, N. Wigley, FM. Moreland, L. Silver, RM. Steen, V. Weisman, M. Mayes, M. Collier, D. Medsger, TA. Seibold, J. (2005). "Responsiveness of the SF-36 and the Health Assessment Questionnaire Disability Index in a Systemic Sclerosis Clinical Trial." Journal of Rheumatology 32(5): 832-840.

Khanna, D. and Merkel, P (2007). "Outcome Measures in Systemic Sclerosis: An Update on Instruments and Current Research." Current Rheumatology Reports 9(2): 151- 157.

Khanna, D., Yan, X. Tashkin, DP. Furst, DE. Elashoff, R. (2007). "Impact of Oral Cyclophosphamide on Health-Related Quality of Life in Patients with Active Scleroderma Lung Disease." Arthritis and Rheumatism 56(5): 1676-1684.

Kilbourne, E., De La Plaz, P. Borda, A. (2002). Epidemiologic Studies in Toxic Oil syndrome. Current knowledge and future perspectives. Regional Publications. European Series., World Health Organisation: 5-26.

Korn, J., Mayes, M. Mattucci-Cerinic, M. Rainisio, M. Pope, J. Hachulla, E .Rich, E. Carpentier, P. Molitor, J. Seibold, JR. Hsu,V.Guillevin, L.Chatterjee, S. Peter, HH. Coppock, J. Herrick, AL. Merkel, PA. Simms, R. Denton, CP. Furst, DE.Nguyer, N.Gaitonde, M. Black, CM. (2004). "Digital Ulcers in Systemic Sclerosis." Arthritis and Rheumatism 50(12): 3985-3993.

Krupp, L., La Rocca, N. Muir-Naxh, J. Steingery, AD. (1989). "The Fatigue Severity Scale. Application to Patients with Multiple Sclerosis and Systemic Lupus Erythematosus." Archives of Neurology 46.

Kumagai, Y., Shiokawa, Y. Medsger, TA. Rodnan, GP. (1984). "Clinical spectrum of connective tissue disease after cosmetic surgery." Arthritis and Rheumatism 27: 1-12.

La Montagna, G., Baruffo, A. Tirri, R. Buono, G. Valentini, G. (2002). "Foot involvement in systemic sclerosis: a longitudinal study of 100 patients." Seminars in Arthritis and Rheumatism 4(Feb 31): 248-55.

Lai, J., Cella, D et al. (2003). "Item banking to improve, shorten and computerize self-reported fatigue: an illustration of steps to create a core item bank from the FACIT-Fatigue Scale." Quality of Life Research 12: 485-501.

Laing, T., Gillespie, B. Toth, MB. Mayes, MD.Gallavan, RH jr.Cooper, BC. Keroack, BJ. Wasko, MCM. Lacey, JV jr. Schottendeld, D. (1997). "Racial differences in scleroderma among women in Michigan." Arthritis and Rheumatism 40: 734-742.

Le Roy, E. (1992). "A brief overview of the pathogenisis of scleroderma (systemic sclerosis)." Annals of the Rheumatic Diseases 51: 286-288.

Le Roy, E., Black, C. Fleischmaher, R. (1998). "Scleroderma (systemic sclerosis): classification, subsets and pathogenisis." Journal of Rheumatology 15: 202-5.

Lee, P., Alerdice, C. Wilkinson, S. Keystone, EC. Urowitz, MB. (1983). "Malignancy in progressive systemic sclerosis-association with breast carcinoma." Journal of Rheumatology 10: 665-6.

Legendre, C., Allanore, Y. Ferrand, I. Kahan, A. (2005). "Evaluation of depression and anxiety in patients with systemic sclerosis." Joint Bone and Spine 72: 408-411.

Leidy, N. and Hasse, J (1999). "Functional status form the patient's perspective: the challenge of preserving personal integrity." Research in Nursing and Health 22: 67-77.

Lewis, C. (2001). Grappling With the Quality of Life: Patients, FDA and Drug Companies Struggle to Link Therapies with Well-Being - US. Food and Drug Administration (FDA).

Linacre, J. (2007). WINSTEPS Rasch measurement computer program: version 3.64.1. Chicago, Winsteps.com.

LoBiondo-Wood, G. and Haber, J (1994). Nursing Research. Methods, Critical Appraisal, and Utilisation. London, Mosby.

Maddison, P. (2002). "Prevention of vascular damage in scleroderma with angiotensin-converting enzyme (ACE) inhibition." Rheumatology (41): 965-971.

Magliano, M., Isenberg, D, Hilson, J. (2002). "Pulmonary Hypertension in Autoimmune Rheumatic Diseases. Where are we now?" Arthritis and Rheumatism 46(8): 1997-2009.

Malcarne, V. and Greenbergs, H. (1996). "Psychological Adjustment to Systemic Sclerosis." Arthritis Care and Research. 9(1): 51-59.

Malcarne, V., Hansdottir, I. Greenbergs, HL. Clements, PJ. Weisman, M.H. (1999). "Appearance self-esteem in systemic sclerosis." Cognitive Therapy and Research 23: 197-208.

Malcarne, V., Hansdottir, I. McKinney, A. Upchurch, R. Greenbergs, HL. Henstorf, GH. Furst, DE.Clements, PJ Weisman, M. (2006). "Medical Signs

and Symptoms Associated with Disability, Pain and Psychosocial Adjustment in Systemic Sclerosis." Journal of Rheumatology 34(2): 34-2.

Marijke, W. and Vrakrijker, DKD (2003). "The long way from the International Classification of Impairments, Disabilities and Handicaps (ICIDH) to the International Classification of Functioning, Disability and Health (ICF)." Disability and Rehabilitation 25(11-12): 561-564.

Marq, H., Weinrich, M. Keil, JE. Le Roy, CE. (1986). "Prevalence of Raynaud's phenomenon in the general population" Journal of Chronic Disease.

Masi, A., Rodnan, G. Medsger, TA. Altmanm RD. D'Angelo, WA. Fries, F. LeRoy, C. Kirsner, AB. MacKenzie, AH. McShane, DJ. Myers, AR. Sharp, GC. (1980). "Preliminary Criteria for the Classification of Systemic Sclerosis (Scleroderma)." Arthritis and Rheumatism 23(5): 581-590.

Maslow, A. (1970). A theory of motivation. Motivation and Personality. New York, Harper and Row.

Masters, G. (1982). "A Rasch model for partial credit scoring." Psychometricka 47: 149-74.

Matsuura, E., Ohta, A. Kanegae, F. Haruda, Y. Ushiyama, O. Koarada, S. Togashi, R. Tada Y. Suzuki, N. Nagasawa, K. (2003). "Frequency and Analysis of Factors Closely Associated with the Development of Depressive symptoms in Patients with Scleroderma." Journal of Rheumatology 30(8): 1782-1787.

Mattucci-Cerinic, M. and Seferovic, P (2006). "Heart involvement in autoimmune rheumatic disease: the "phantom of the opera"." Rheumatology 45: iv1-iv3.

Mattucci-Cerinic, M., Steen, V. Furst, DE. Seibold, JR. (2007). "Clinical trials in systemic sclerosis: lessons leaned and outcomes." Arthritis Research and Therapy 9 (Supplement 2): s 7.

Mayes, M. (1997). "Epidemiology of systemic sclerosis and related diseases." Current Opinions in Rheumatology 9(6): 557-61.

Mayes, M. (1999). The Scleroderma Book. London, Oxford University Press. Mayes, M., Lacey, JJ. Beebe-Dimmer J. Gillespie, BW. Cooper, B. Laing, TJ. (2003). "Prevalence, incidence, survival and disease characteristics of systemic sclerosis in a large US population." Arthritis and Rheumatism 48(8): 2246-55.

Mayes, M. and Trojanowska, M (2007). "Genetic factors in systemic sclerosis." Arthritis Research and Therapy 9(Supplement 2): S5.

McGee, H., O' Boyle, C. Hickey AM. O'Malley K. Joyce CRB. (1991). "Assessing the quality of life of the individual: the SEIQoL with a healthy and a gastroenterology unit population. 1." Psychological Medicine 21: 749-759.

McHorney, C. (2003). "Ten Recommendations for Advancing Patient-Centred Outcomes Measurement for Older Persons." Annals of Internal Medicine 139(5 (1)): 403-409.

McKenna, S. (2004). "The Needs-Based Approach to Quality of Life Assessment." Value in Health 7(Supplement 1): S1-S3.

McKenna, S., Doward, L. Niero, M. Erdman, R. (2004). "Development of Needs-Based Quality of Life Instruments." Value in Health 7(Supplement 1): S17-S21.

McKenna, S. P., Doward, L. Meads, D. Patrick, D. Tennant, A. (2004). "Summary of Needs-Based Quality of Life Instruments." Value in Health 7(supplement 1): S39-S40.

McKinley, P. Ouellette, S. Winkel, GH. (2005). "The contributions of disease activity, sleep patterns, and depression to fatigue in systemic lupus erythmatosus." Arthritis and Rheumatism 38(6): 826-834.

Medical Outcomes Trust, S. A. C. (2002). "Assessing health status and quality-of-life instruments: Attributes and review criteria." Quality of Life Research 11: 193-205.

Medsger, T. and Masi, A (1971). "Epidemiology of systemic sclerosis (Scleroderma)." Annals of Internal Medicine 74: 714-21.

Merkel, P., Clements, P et al. (2003). "Current status of outcome measure development for clinical trials in Systemic sclerosis. Report from Omeract 6." Journal of Rheumatology 30(7): 1630-1647.

Miles, M. and Huberman, A (1994). Qualitative Data Analysis. London, Sage.

Milio, G., Corrado, E et al. (2006). "Iloprost treatment in patients with Raynaud's phenomenon secondary to systemic sclerosis and the quality of life: a new therapeutic protocol." Rheumatology 45: 999-1004.

Molta, C., Khan, M. Aponte, CJ. Reynolds, TL. Macintyre, SS. (1989). "Familial occurrence of systemic sclerosis, rheumatoid arthritis and other immunological disorders: report of two kindreds with study of HLA antigens and review of the literature." Clinical and Experimental Rheumatology 7(3): 229-236.

Morison, M. and Moir, J (1998). "The role of computer software in the analysis of qualitative data: efficient clerk, research assistant or Trojan horse?" Journal of Advanced Nursing 28(1): 106-116.

Morse, J. and Field, P (1998). Nursing Research. The application of qualitative approaches. Cheltenham, Stanley Thornes - Nelson Thornes.

Moser, D., Clements, P. Brecht, M. Weiner, SR. (1993). "Predictors of Psychosocial Adjustment in Systemic Sclerosis." Arthritis and Rheumatism 36(10): 1398-1405.

Mukerjee, D., St George, D. Coleiro, B. Knight, C. Denton, CP. Davar, J. Black, CM. Coghlan, J (2003). "Prevalence and outcome in systemic sclerosis associated pulmonary arterial hypertension: application of a registry approach." Annals of the Rheumatic Diseases 62: 1088-1093.

Muldoon, M., Barger, S. Flory, JD. Manuck, SB. (1998). "What are quality of life measures measuring?" British Medical Journal 316: 542-545.

Naparstek, Y. and Plotz, P (1993). "The role of autoantibodies in autoimmune diseases." Annual Review of Immunology 11: 79-104.

Ndosi, M., Hill, J. Tennant, A. Hale, C Hardware, B. Adebajo, A et al. (2008). Validation of the Educational Needs Assessment Tool in Four Rheumatic Diseases. EULAR. Paris.

Nietert, P. J., Mitchell, H.C. Bolster, M.B. Curran, M.Y. Tilley, B.C. Silver, R.M. (2005). "Correlates of Depression, Including Overall and Gastrointestinal Functional Status, Among patients with Systemic Sclerosis." Journal of Rheumatology 32(1): 51-57.

Nijsten, T., Unaeze, J. Stern, R.S. (2006). "Refinement and reduction of the Impact of Psoriasis Questionnaire: Classical Test Theory vs. Rasch analysis." British Journal of Dermatology 154: 692-700.

Noll, H. (1996). Social Indicators Research: Societal Monitoring and Social Reporting. Trends and Perspectives in Empirical Social Research P. P. M. Ingwer Borg. Berlin, New York, De Gruyter: S. 1-16.

Noll, H. (2000). Social Indicators and Social Reporting: The International Experience.

Nord, E. (1992a). "Methods for quality adjustment of life years." Social Science and Medicine. 34: 559-69.

Nordenfelt, L. (2003). "Action theory, disability and ICF." Disability and Rehabilitation 25: 1075-1079.

Oishi, S., Deiner, E. Suh, EM. Lucas, RE. (1999). "Value as a moderator in subjective well-being." Journal of Personality 67: 157-184.

Olsen, N. and Neilson, S (1978). "Prevalence of primary Raynauds phenomena in young females." Scandanavian Journal of Clinical and Laboratory Investigation 37: 761-4.

Pallant, J. (2005). <u>SPSS survival manual</u>. Maidenhead, Oxford University Press.

Pallant, J. and Tennant, A (2007). "An introduction to the Rasch measurement model: An example using the Hospital Anxiety and Depression Scale (HADS)." <u>British Journal of Clinical Psychology</u> **46**: 1-18.

Parahoo, K. (1997). <u>Nursing Research. Principles, Process and Issues</u>. London, Macmillan.

Pearson, J. (1991). "The endothelium: its role in scleroderma." <u>Annals of the Rheumatic Diseases</u> **50**: 866-871.

Peters-Goldern, M., Wise, R. Hochberg, M. Stevens, MB. Wigley, FM. (1985). "Incidence of lung cancer in systemic sclerosis." <u>Journal of Rheumatology</u> **12**: 1136-9.

Phillips, C. and Thompson, G (1998). <u>What is a QALY?</u> London, Hayward. Pope, C., Zeiberland, W. Mayes, M. (2000). "Qualitative research in health care: Analysing qualitative data." <u>British Medical Journal</u> **320**: 114-116.

Pudifin, D., Dinnematin, H. Duursma, J. (1991). "Anti-nuclear antibodies in systemic sclerosis." <u>SAMJ</u> **80**: 438-440.

Rapley, M. (2003). <u>Quality of Life Research. A critical introduction.</u> London, Sage.

Rasch, G. (1960). <u>Probalistic Models for Some Intelligence and Attainment Tests</u>. Copenhagen, Denmarks paedgogiske Institut.

Reay, N. (2007). Levels of Fatigue in Diffuse and Limited Systemic Sclerosis – Validation of the Fatigue Severity Scale. <u>British Society of Rheumatology</u>. Birmingham, UK.

Reay, N. and Firth, J (2008). "Records management guidance and its implications for research." <u>Nurse Researcher</u> **15**(3): 26-31.

Reay, N., Stevens, R. Morenno, P. (2002). "Evaluation of a Hand and Face Exercise Programme Use in Patients With Scleroderma." <u>Rheumatology</u> (ACR Supple).

Richards, H., Herrick, A. Griffin, K. Gwilliam, PDH. Loukes, J. Fortune, DG. (2003). "Systemic Sclerosis: Patients' Perceptions of Their Condition." <u>Arthritis and Rheumatism</u> **49**(5): 689-696.

Riemekasten, G. and Sunderkotter, C (2006). "Vasoactive therapies in systemic sclerosis." <u>Rheumatology</u> **45**: iii49-iii51.

Roca, R., Wigley, F. White, B. (1996). "Depressive symptoms associated with scleroderma." <u>Arthritis and Rheumatism.</u> **39**(6): 1035-1040.

Roumm, A. and Medsger, T (1985). "Cancer and systemic sclerosis: An epemiological study." Journal of Rheumatology **12**: 1336-40.

Rubin, L., Black, C. Denton, CP. Seibold, J. (2007). "Systemic sclerosis and related connective tissue diseases; present and future." Arthritis Research and Therapy **9**(supp 2): Preface.

Ruof, J., Michel, B.A. Brulmann, P. Stucki, G. (1999). "Development and validation of a self-administered systemic sclerosis questionnaire (SYSQ)." Rheumatology **38**: 535-542.

Salonen, J., Yla-Herttuala, S. Yomamoto, R. Butler, S. Korpela, H. Salonen, K. et al. (1992). "Auto antibody against oxidised LDL and progression of carotid atherosclerosis." Lancet **339**: 883-7.

Samuelson, U. and Ahlemen, E (2000). "Development and Evaluation of a Patient Education Program for Persons with Systemic Sclerosis (Scleroderma)." Arthritis Care and Research **13**(3): 141-148.

Scheumringer, M. Stucki, G. Omega Huber, E. Brach, M. Schwawrzkopg, SR. Kostanjsek, N. Stoll, T. (2005). "ICF Core Set for patients with musculoskeletal conditions in early post-acute rehabilitation facilities." Disability and Rehabilitation **27**(7/8): 405-410.

Schumacker, R. and Linacre, J (1996). "Factor Analysis and Rasch." Rasch Measurement Transactions **9**(4): 470 - 471.

Schumacker, R. and Lomax, R (2004). A Beginners Guide to Structural Equation Modeling. London, Lawrence Erlbaum Associates.

Schwartz, C. E. and Sprangers, M.A.G (2000). Adaptation to Changing Health. Response Shift in Quality of Life Research. Washington DC, American Psychological Association.

Seibold, J. (1993). Connective Tissue Diseases Characterized by Fibrosis. Textbook of Rheumatology. H. Kelly, Ruddy Sledge. Philadelphia, WB Saunders.

Senecal, J., Henault, J. Reynond, Y. (2005). "The Pathogenic Role of Autoantibodies to Nuclear Autoantigens in Systemic Sclerosis (Scleroderma)." Journal of Rheumatology **32**(9): 1643-1649.

Sibley, A., Kersten, P. Ward, CD. White, B. Mejta. R. George,S. (2006). "Measuring autonomy in disabled people: validation of a new scale in a UK population." Clinical Rehabilitation. **20**: 793-803.

Silman, A. (1997). "Scleroderma: demographics and survival." Journal of Rheumatology **48**(58-61).

Silman, A., Harrison, M. Brennan, P. (1995). "Is it possible to reduce observe variability in skin score assessment of scleroderma?" Journal of Rheumatology 22: 1277-1281.

Silman, A., Howard, Y. Hicklin, AJ. Black, CM. (1990). "Geographical clustering of scleroderma in South and West London." British Journal of Rheumatology 29: 92-6.

Silman, A. J. (1991). "Epidemiology of Scleroderma." Annals of the Rheumatic Diseases 50: 846-853.

Silman, A. J. and Hochberg, M.C (1996). "Occupational and Environmental Influences on Scleroderma." Rheumatic Disease Clinics of North America 22(4): 737-749.

Silver, R. (1991). "Unraveling the eosinophilia-myalgia syndrome." Arthritis and Rheumatism 35(9): 1097-105.

Silver, R. and Clements, P (2003). "Interstitial Lung Disease in Systemic Sclerosis: Optimising Evaluation and Management. ." Scleroderma Care and Research 1(1): 3-11.

Silverman, D. (2003). Interpreting Qualitative Data. Methods for Analysing Talk, Text and Interaction. London, Sage.

Simeon, C., Armadans, L. Fonollosa, V. Solans, R. Selva, A. Villar, M. Lima, J. Vaque, J. Vilardell, M. (2003). "Mortality and prognostic factors in Spanish patients with systemic sclerosis." Rheumatology 42: 71-75.

Sireling, L., Paykel, E. Freeling, P. Rao, BM. Patel, SP. (1985). "Depression in general practice: Case thresholds and diagnosis." British Journal of Psychiatry 17: 61-65.

Smith, E. (2002). "Detecting and Evaluating the Impact of Multidimensionality using Item Fit Statistics and Principal Component Analysis of Residuals." Journal of Applied Measurement 3(2): 205-231.

Spilker, B. and Revicki, D.A. (1996). "Quality of Life and Pharmacoeconomics in Clinical Trials": 25-31.Philadelphia. Lippincott-Raven

Stamm, R., Cieza, A. Coenen, M. Machold, KP. Nell, VP. Smole, JS.Stucki,G. (2005). "Validating the International Classification of Functioning, Disability and Health Comprehensive Core Set for Rheumatoid Arthritis From the Patient Perspective: A Qualitative Study." Arthritis and Rheumatism 53(3): 431-439.

Stastny, P., Stembridge, V. Ziff, M. (1963). "Homologous Disease in the Adult Rat, A Model for Autoimmune Disease: General Features And Cutaneous Lesions." Journal of Experimental Medicine 118: 635.

Steen, V. and Medsger, T (1997). "The Value of the Health Assessment Questionnaire and special patient-generated scales to demonstrate change in systemic sclerosis patients over time." Arthritis and Rheumatism. 40(11): 1984-1991.

Steen, V. and Medsger, T (1998). "Case-Control study of corticosteroids and other drugs that either precipitate or protect from the development of Scleroderma renal crisis." Arthritis and Rheumatism 41: 1613-9.

Steen, V. and Medsger, T (2000). "Severe Organ Involvement in Systemic Sclerosis with Diffuse Scleroderma." Arthritis and Rheumatism 43(11): 2437-2444.

Straszecka, J., Kucharz, E. Jonderko, G. Kotulska, A. Bendharczyk-Kaluzny. Brzezinska-Wcislo, L. Rubisz-Brzezinska, J. (1996). "Depression and Anxiety in Patients with Systemic Sclerosis." Clinical Rheumatology 15(6): 621.

Streiner, D. and Norman, G (1995). Health Measurement Scales. Oxford, Oxford University Press.

Suarez-Almazor, M., Kallen, M. Roundtree, AK. Mayes, M. (2007). "Disease and Symptom Burden in Systemic Sclerosis: A Patient Perspective." Journal of Rheumatology 34(8): 17181726.

Subar, A., Zeigler, R. Thompson, FE. Johnson, CC. Weissfeld, JL Reding, D. Kavounis, KH. Hayes, RB. (2001). "Is Shorter Always Better? Relative Importance of Questionnaire Length and Cognitive Ease on Response Rates and Data Quality for Two Dietary Questionnaires." American Journal of Epidemiology 153(4): 404-410.

Tennant, A. (2006). Advances in assessing Quality of Life. Care IV. Weetwood hall, Leeds, Care.

Tennant, A. and Conaghan, P (2008). "The Rasch Measurement Model in Rheumatology: What Is It and Why Use It? When Should It BE Applied, and What Should One Look for in a Rasch Paper?" Arthritis and Rheumatism 57(8): 1358-1362.

Tennant, A. and Horton, M (2006). Rasch Analysis Training Introductory Course Booklet. Leeds, University of Leeds.

Tennant, A., McKenna, S.P. (2004). "Application of Rasch Analysis in the Development and Application of Quality of Life Instruments." Value in Health 7(s1): S22-S26.

Tennant, A., Penta, M. Tesio, L. Grimby, G.Thonnard, J. L. Slade, A. Lawton, G. Simone, A. Carter, J. Lundgre-Nilsson, A. Tripolski, M. Ring, H. Biering-Sorensen, F. Marincek, CRT. Burger, H. Phillips, S. (2004). "Assessing and Adjusting for Cross-Cultural Validity of Impairment and Activity Limitation Scales Through Differential Item Functioning within the

Framework of the Rasch Model. The PRO-ESOR Project." <u>Medical Care</u> **42**(1): 37-48.

Thombs, B., Taillefer, S. Hudson, M. Baron, M. (2007). "Depression in Patients with Systemic Sclerosis: A Systematic Review of the Evidence." <u>Arthritis and Rheumatism</u> **57**(6): 1089-1097.

US National Cancer, I. (2006) "Item Response Theory Modelling." <u>National Cancer Website - Applied Research</u> **Volume**, DOI: <u>http://appliedresearch.cancer.gov/areas/cognitive/item.html</u>

Valentini, G. and Mattucci-Cerinic, M (2007). "Disease-specific quality indicators, guidelines and outcome measures in scleroderma." <u>Clinical and Experimental Rheumatology</u> **25**(Supplement 47): S159-S162.

van Lankveld, W., Vonk, M. Teunissen, H.van den Hoogen, FHJ. (2007). "Appearance self-esteem in systemic sclerosis - subjective experience of skin deformity and its relationship with physician-assessed skin involvement, disease status and psychological variables." <u>Rheumatology</u> **46**: 872- 876.
Veale, D. and Belch, J (1993). "A physicians approach to vasospasm." <u>Scottish Medical Journal</u> **38**(5): 133-136.

Vincent, R. and Wilson, H (2006). "Scleroderma in practice: the role of the nurse." <u>Nursing in Practice</u> **26**(Jan/Feb): 58 - 63.

Wan, M., Moore, T et al. (2001). "Ankle brachial pressure index in systemic sclerosis: influence of disease subtype and anticentromere antibody." <u>Rheumatology</u> **40**: 1102-1105.

Wang, P., Badley, E. Gignac, M. (2006). "Exploring the role of the contextual factors in disability models." <u>Disability and Rehabilitation.</u> **28**(2): 135-140.
White, C. (1998). Fatigue and sleep. <u>Rheumatology Nursing. A Creative Approach</u>. J. Hill. London, Churchill Livingstone: 155-169.

WHO (2001). <u>International Classification of Functioning, Disability and Health</u>. Geneva, World Health Organisation.
WHO website, WHO. (2001. Accessed online Nov 2006). "ICF - Introduction." <u>available from</u> <u>http://www3.who.int/icf/icftemplate.cfm?myurl=introduction.html%20&mytitle =Introduction</u>: 1-25.

WHO website, WHO. (2002). "Towards a Common Language for Functioning, Disability and Health. ICF." <u>http://www3.who.int/icf/beginners/bg.pdf:</u> 1-22.

WHO. (2001). <u>International Classification of Functioning, Disability and Health</u>. Geneva, World Health Organisation.

WHOQOL, G. (1998). "The World Health Organisation Quality of Life Assessment (WHOQOL): development and general psychometric properties." <u>Social Science and Medicine.</u> **46**(12): 1569-85.

Wigley, F., Korn, J. Csuka, ME. Medsger, TA jr. et al. (1998). "Oral lloprost treatment in patients with Raynauds Phenomenon secondary to systemic sclerosis: a multicentre, placebo controlled, double blind study." Arthritis and Rheumatism 41(4): 670-7.

Williams, M.H, Das, C. Handler, CE. Akram, MR. Davar, J. Denton, CP. Smith, CJ. Black CM. Coghlan, JG. (2005). "Systemic Sclerosis associated pulmonary hypertension: improved survival in the current era." Heart (online) **doi:10.11.36.hrt.2005.069484.**

Wilson, H. and Vincent, R (2006). "Autoimmune connective tissue disease: scleroderma." British Journal of Nursing 15(15): 805-809.

Wilson, I. B. and Cleary, P.D. (1995). "Linking Clinical Variables With Health Related Quality of Life. A Conceptual Model of Patient Outcomes." Journal of the American Medical Association 273(1).

Wilson, M. (2005). Constructing Measures. An Item Response Modeling Approach. Mahwah, Lawrence Erlbaum Associates, Inc.
Winter, G. (2000). "A Comparative Discussion of the Notion of 'Validity' in Qualitative and Quantitative Research." The Qualitative Report 4(3&4).

Witztum, J. and Steinberg, D (1991). "Role of oxidized low density lipoprotein in atherogenisis" Journal of Clinical Investigation 88: 1785-92.
Wollheim, F. (2005). "Classification of systemic sclerosis. Visions and reality." Rheumatology 44: 1212-1216.

Wong, O. (1996). "A crucial assessment of the relationship between silicone breast implants and connective tissue diseases." Regulatory Toxicology and Pharmacology 1(1): 74-85.

Wright, B. and Panchapakesan, N (1969). "A procedure for sample-free item analysis." Education and Psychological Measurement 29: 23-48.
Wu, M., Adams, R. Wilson, M.R. (1998). ACER ConQuest. Melbourne, Acer Press.

Appendix 1   Evidence for microchimerism

Table Appendix 1 – Evidence for microchimerism

Evidence	Reference
Female preponderance in SSc Idiopathic SSc is much commoner in women, suggesting that the constellation of events leading to it's development occurs more in females	Englert et al 1992
Timing with respect to child-bearing Onset of the disease or deterioration is often observed 1-5 years after child-bearing	Silman and Black 1988
HLA considerations Similarly, between maternal and child HLA haplotype is greater for mothers who develop SSc. This would potentially predispose to persistence of foetal cells.	Arlett et al 1998
Foetal DNA in SSc patients blood Increased levels (and perhaps frequency) of foetal DNA in SSc mothers.	Nelson et al 1998
Foetal DNA in lesional tissues in SSc Demonstration of foetal DNA in lesional tissue of SSc patients. Also demonstrated increased frequency of foetal DNA in SSc patients' blood compared with controls.	Arlett et al 1998
Animal model – chronic GVHD Minor mismatch bone marrow allograft can produce an animal disease with feature similar to human SSc. Also human GVHD skin disease has some features of diffuse SSc	(Casciola-Rosen et al. 1997) Charley et al 1982

Appendix 2   Oxidative stress

Table Appendix 2 – Oxidative Stress

Adapted from Denton and Black 1999. Potential Involvement of oxidant stress n SSc Pathogenesis (Herrick et al. 2001).

Evidence	Reference
Elevated isoprostanes in urine. Increased urinary levels of oxidative metabolites of prostaglandin's in patients with SSc suggests in vivo oxidative stress.	(Witztum and Steinberg 1991)
Reduced micronutrient antioxidants in SSc. Levels of vitamin C, vitamin E and other dietary antioxidants lower in SSc patients – suggests increased susceptibility to reactive oxygen species.	(Salonen et al. 1992)
Reduced in vitro LDL oxidation lag-time in SSc Oxidation lag time in vitro is reduced for LDL isolated from SSc patients serum. Suggests greater susceptibility to oxidation in vivo. Oxidised LDL are potentially injurious to endothelial cells.	(Herrick et al. 2001)
Oxidant stress effects on fibroblasts. Increased fibroblast proliferation and matrix synthesis induced by oxidative stress in vitro.	(Pearson 1991)
Fragmentation of SSc-associated auto-antigens. Oxidative fragmentation of SSc-associated auto-antigens in the presence of heavy metal ions.	(Maddison 2002)
Beneficial effects of antioxidant administration. Many patients report subjective benefit from diet rich in antioxidant nutrients. The synthetic antioxidant produbol has apparent benefit in treatment of Raynauds phenomenon.	(Denton and Black 2005)
Antibodies against oxidized low-density lipoproteins in systemic sclerosis. Binding to oxidized LDL antibodies increased in patients with DSSc and LSSc. Circulating anti-oxidized LDLD increased in DSSc patients compared with controls. Lends weight to argument that oxidation of LDLD contributes to vascular pathology in SSc.	(WHO website 2001. Accessed online Nov 2006)

Appendix 3 Micro and Macro-Vascular Disease

Micro and macro-vascular disease in SSc

Theories of the pathogenesis of micro vascular involvement in SSc are being explored. Included in this is the role of antibodies against oxidized low-density lipoproteins (LDL) in SSc. Oxidation of LDL has been presented as a key factor in atherogenisis ((Kilbourne et al. 2002), and antibodies to this may predict the progression of atherosclerosis in the carotid vessel (Stastny et al. 1963). Exploration of this principle as applied to SSc showed binding to oxidised LDL to be increased in patients with both LSSc and DSSc in comparison with controls. Also, elevated circulating levels of oxidised LDL were seen in patients with DSSc. This strengthens the argument that oxidated LDL has a role in vascular damage, particularly in DSSc, but it is suggested that further longitudinal studies would be required in order to investigate associations between this and vascular damage in SSc (Jaffe and Claman 1983).

The endothelium in SSc

Included in the micro vascular aspect of SSc, is the endothelium. The endothelium is thought to regulate aspects vascular homeostasis, as well as its traditional role as a selective barrier between the blood and tissues. It responds to molecular signals which may be generated locally or from other areas of the body, hence its role in the control of cellular and metabolic events. (Silver 1991).

Endothelial cell dysfunction is thought to have a key role in the vascular injury seen in SSc, including:

- Up-regulated expression and increased circulating levels of endothelial adhesion molecules.

- Altered levels of endothelial cell products

- Functional abnormalities such as an imbalance in the vasodilator/vasoconstrictor mechanisms

- Increased capillary permeability

- Impaired fibrinolysis

- Increased platelet aggregation

Appendix 4 Scleroderma – like diseases

Toxic Oil Syndrome

Toxic Oil syndrome (TOS) first appeared in 1981. It affected 20,000 people in Spain who had used rapeseed oil with a contaminate, aniline, thought to be the cause. Its label as a Scleroderma like syndrome has arisen from the similar symptoms such as skin tightening. With over 800 deaths, long term symptoms such as skin tightening, peripheral neuropathy and pulmonary hypertension persist and associated deaths continue .

Graft versus host disease (GVHD)

Graft versus host disease is a condition seen in some patients who have bone marrow transplant and its presentation shares many symptoms similar to SSc, notably skin thickening. Links in the literature were made over 40 years ago by Stastny, Stembridge et al who highlighted the resemblance between GVHD and SSc. The potential for use of GVHD as a model for SSc has been explored who induced GVHD in mice and followed the progression of skin involvement. Whilst a preliminary, laboratory based study, the authors findings were particularly interesting as they noted in one of their mice groups that the skin pathologies were not present by Day 78 of the study. The conclusions of the study are somewhat vague however, and no further work seems to be published directly on GVHD and SSc.

Eosinophilia-myalgia syndrome (EMS)

Another recent condition is EMS, first described in 1989. EMS is thought to be associated with contaminated batches of the drug L tryptophan which was used to treat insomnia and depression . The symptoms are thickening

of the skin; erythmatosus macules on the skin arthralgia, myalgia and dyspnoea alongside other haematological and pathological findings. Appropriate treatment for this condition is unclear although some reduction of symptoms is noted with the use of glucocorticoid medication. However even with this treatment patients are left with symptoms including skin lesions, myalgia and neurocognitive dysfunction.

Appendix 5   The International Classification of Functioning Disability and Health.

Table Appendix 5 - Presenting the Structure of the ICF

	Part 1: Functioning and Disability		Part 2: Contextual Factors	
Components	Body Functions and Structures	Activities and Participation	Environmental Factors	Personal Factors
Domains	Body functions Body structures	Life areas (tasks, actions)	External influences on functioning and disability	Internal influences on functioning and disability
Constructs	Change in body functions (physiological) Change in body structures (anatomical)	Capacity Executing tasks in a standard environment Performance Executing tasks in the current environment	Facilitating or hindering impact of features of the physical, social and attitudinal world	Impact of attributes of the person
Positive aspect	Functional and structural integrity Functioning	Activities, participation. Functioning	Facilitators	Not applicable
Negative aspect	Impairment Disability	Activity limitation. Participation restriction. Disability	Barriers/ hindrances	Not applicable

Appendix 6   Focus group Observers notes

5 participants (Numbers 1,2,3 and 5 were female and Number 4 was male)

<u>Overall impressions</u>

1, 3 and 5 were the more vocal and tended to be more attentive to the other group members.

2 tended to focus on Naomi and smiled a lot (? to hide any discomfort).

4 tended to look down and seemed at times separate from the group but did answer direct questions, from both Naomi and other group members, particularly later.

There was more obvious interaction when the main tape was turned off and Naomi left the group. When Naomi returned, she appeared to be made much more part of the group by the participants rather than being seen as 'the interviewer'. The participants used her as a source of information (and perhaps reassurance)

Note – 'Um' – assumes 'agreement'

Themes Discussed	Interactions	Notes
Naomi explains the purpose of the FG		
	Participant 3 joins the group	
How does scleroderma affect life?		
Work?	3 talks about pain restricting ability to perform tasks at work	1 attentive to 3 2 smiles looking between 3 and N 4 looking down
Period of sickness before left work?	3 talks about frustration and attitudes of others	1 and 2 nod /um 4 looking down
	1 talks about effects on enjoyment of letter–writing	1 looking at N – answering N rather than engaging with group 2 looking at N
Response of other people	N directly asks 4 about his experience	All attend to 4 3 nodding as 4 describes the pain experienced
Need to adapt and pace life	3 ...cannot do aerobics ...'could be worse'	1 looks very serious 2 smiles and looks to N
	1... 'only when think about it'	4 more engaged with 1 - interrupts to agree and then looks down when interaction complete
How adapted ?	3 talks about expert patient programme 1 asks how became involved	1 very attentive to 3 2 smiles a lot - appears to becoming less comfortable 4 continues to look down
Relationships with other people? Changed /narrowed?	1 talks about difficulties in standing .... Friends – vanish into the wood work ... find out	3 - small nod

	who your real friends are	
	N directly asks 4 about his experience	4 becomes more obviously involved when asked direct question – others attend to him
	Participant 5 joins the group	
N introduces 5 to theme	5 talks about giving up work … made redundant but would have had to leave	1 and 2 – 'um' and look to 5. 2 nods
Struggling?	No …just diagnosed	All looking at 5. They appear more relaxed together - as if the interruption of 5 joining has provided a 'breathing space' (Methodological Note I wonder if the group becoming larger has made a difference)
Effect around the house and family ?		5 answers N directly
What about others (in group)?	N goes around the group 2 answers directly …manage most things 4 …manage most things	3 nods 4 looking at N
Any more?	4 talks about being self-employed…. otherwise would have been sacked ….do get very tired	2 and 3 attending 4 and nodding
Need to prioritise tasks?	2 … live alone ..please myself 3 …same … live alone	Looks directly at N and then at 1 and 2 (seeking reassurance?) 3 looks at 4 who is looking down (Cannot see 5)
N – direct question to 1 – You live with your husband	1 talks about what is unable to do … what husband and daughter do	1 looking at N

	... effects of Raynauds	
	5 to 1 .... you seem to have more problems	1 and 5 engage with each other.
		? whether others seem 'outside' this conversation
N to 1 .. as a family ...?	1 ...have had to do more	3 watching 1 very closely
	.nothing wrong with that .. men don't...	group laugh - seem to relax again
Memory?	3 ..... age rather than scleroderma?	(Cannot see 5 well)
	concentration rather than memory	all nod and some 'ums'
	5 ...if anything happens you automatically think it is (scleroderma)	more 'ums' (cannot tell who)
Change in ability to cope with stress?	2 ... no .. very stressful	No response from others – looking at N or down
Emotions?	3 ... feel down, isolated ...	3's eyes fill with tears
	Talks about living alone and fears	3 looks to 2 (?seeking agreement as both live alone)
	1 ...always helps to do something physical	1 looks to N
Sleeping?	1 ... a vicious circle	N looks to 2 – 2 nodding
	3 ... is it part of getting older?	
Anyone else?	4 .. not waking up .. pain effects getting to sleep	4 looks directly at N and then looks down again
	2 ...sometimes cannot get to sleep... getting older?	All seem to be addressing N rather than talking with each other – seem awkward
	5 ...if not physically tired	
	3 ...usually busy	
Financially?	3 ...not for me	3 shrugs
		4 shakes head - no
		2 shakes head - no

Bringing up Children? Things cannot do? Stamina?	1 talks about nephews - adaptations to cope with cold ..... you get round it 2 ....looked after grandchildren ....no problems	1 is looking down (previously has appeared more engaged within group) 2 shakes head as speaks
Affect individually?	5 ...positive for me	4 continues to look down but occasionally looks up towards 5
		Others all attending to 5
	5 addresses 4 directly ....being a man...?	5 looks between N and 1 and 2 (Is she seeking reassurance that alright to ask 4 a direct question?)
	4 ....changed life	Group look to 4
	...frustrating.... go to do things automatically	3 nodding
	...brain still works	2 and 3 - low laugh and both nodding
	2 ...has affected to some extent...	5 nodding
	...cannot walk far...	
	...joints not too good...just get on with it.	
	3 could be worse ... returned from holiday in China ... cannot do steps... gets frustrating ... ... grateful	All appear to take more interest at mention of China – look towards 3 Seem more animated.
	4...could get me down.... frustrating...	All attend to 4 5 nods
Future? Faith? Religion?	5 ... like 3 says – will do more holidays	3 smiling and nodding
	1 ...same ... spending inheritance	4 nods
	2...No don't think much .....not particularly religious ... some sort of faith...lost husband 12	2 looking at N 3 nods

	years ago...	
Personal Hygiene?	3 No .but difficulty getting in and out of bath.. 2 ...Yes 4 ...getting out is problem 3 ... walk-in shower and top and tail 2 ... empty water and then stand cannot pull on ... 4 ... slippy as well 1 ...went to parents.. couldn't get in (bath)...	General 'ums' and nods from others 2 indicates rails(?) All lean forward into the group and towards each other – ums Ums from 5 and 3
	1 Does it affect anyone's sex life? 2 and 3 ... have wondered 5 ... don't think so 1 ... does..... explains how and what does to adapt ... no-one ever asks about it	2 and 3 laugh 4 looks up and then down again
Emotional as well as physical?	1 ....humour	1 and 5 looking at each other 2 looking between 1 and N 4 looking down
Has it affected the relationship?	1... it did ... getting older	No obvious response from group
How does it make you feel?	1 ..frustrated ... big aspect ..comfort... being found attractive..	4 looks up and smiles
Anyone else?	1.. dry vagina	
Anyone else?		
	Tape turned off N leaves group for while I had forgotten that there were two tapes and so concentrated more on trying to capture the conversation rather than non-verbal interaction – women generally more engaged with each other.	

	4 did not seem so engaged – still looking down but obviously listening as interjected re. treatment	
	5 ... toe nails dropped off	Others - shaking heads
		Much more verbal interaction – appear to be talking about more issues now the tape is turned off
Anyone else had calcium problems?	2 .. warts? 5...calcium can poke out1... can squeeze out	5 gets up and has a look 3,1,2 very engaged
		The group becomes more a discussion group - begin to ask N questions
	Talk about difficulty with diagnosis	Women attending to each other when sharing experiences 4 not so obviously engaged but does keep looking up.
	Talk about difficulties in dressing 1 involves 4 ... What about you 4 – do you have trouble with bra's 4 ... yes .... with socks	All laugh including 4
Anything specific to being a man?		When N turns the direct questioning to 4 all are engaged and attend to him.
		In final stage of the discussion appear more engaged with each other – more nods and looking at each other rather than N.

Reflections

I wonder whether or not I should have revealed so much about living in

Holmfirth and whether or not this may have influenced any of the 'local'

participants. The group seemed to work well – perhaps because the

participants knew Naomi. She was able to say that 'other people with

scleroderma experience...' either as a leading question or as a reassurance

if a participant asked a direct question regarding whether their experience

was unusual (therapeutic aspect of focus group?). I wonder what the

dynamics of the group would be if single sex? I do not know the ratio of men:

women affected. If group of men would they reveal more to a male facilitator

or would they actually be happy with a familiar female such as Naomi?

Notes re. process of observation

Positioning of participants – sometimes it was difficult to see No 5 when she

leant forward and N leant forward and perhaps I should have noted this fact

more in the observational notes – perhaps increased attentiveness when

leant forward. There were times when I got the number of the participant

wrong. It may be easier for the sake of my own notes use real names/initials.

I found at times that I was so fascinated by what was being said that I found

my concentration being drawn to listening rather than observing the

interactions as closely as I should.

Using lined rather than plain paper may be better – and pre-number pages.

Need to note when Naomi turns one tape off – rather anxious that could not

capture all the conversation but had not remembered that there were two

tapes! I found it hard to keep track of non-verbal interaction. The strategy

was very effective in getting the group to talk more freely and to expand on

previous themes or begin to talk about aspects which had previously not

seemed to be problems/issues for them.

Appendix 7   The SSc QoL

Please tick the relevant box for each question	True	Not True
I can't do anything without really thinking it through	☐	☐
It's always on my mind	☐	☐
I worry that I let people down	☐	☐
My condition makes me angry	☐	☐
I get upset when I can't do things	☐	☐
I often get frustrated	☐	☐
I cannot rely on how I will be tomorrow	☐	☐
I feel like I'm fighting all the time	☐	☐
My condition means I have disturbed sleep	☐	☐
It has affected me a lot socially	☐	☐
It has affected the health of people around me	☐	☐
My hands don't work as well as they did	☐	☐
It puts a strain on my personal relationships[s	☐	☐
I need to rest more often	☐	☐
Any sort of activity is difficult	☐	☐
I avoid certain social situations because I am embarrassed	☐	☐
I take to heart things which wouldn't have worried me before	☐	☐

Please tick the relevant box for each question   True   Not True

Life is just not what it was   □   □

I can't cope at all   □   □

Sleeping badly has affected me a lot   □   □

I feel very isolated   □   □

Household tasks can be a problem   □   □

I have had to stop some of my hobbies   □   □

I feel guilty at being ill   □   □

I struggle to wash myself as I would like   □   □

Pain limits what I can do   □   □

I feel helpless   □   □

Pain tires me out   □   □

I miss being able to sort things out   □   □

Many thanks for filling in this questionnaire

For staff completion: Date........................   Total score ....

Appendix 8   Potential Comparator Measures

Table Appendix 8 – Potential Comparator Measures

Aspect of conceptual framework	Potential measures	Measure of choice	Rationale for choice
Depression	Hospital Anxiety and Depression (HADs) Scale Montgomery-Asberg depression rating scale Hamilton depression scale Beck's depression inventory	Hospital Anxiety and Depression (HADs) Scale	Clear division into anxiety and depression items.
Anxiety		As above	As above
Finance	London Handicap Scale. Euroqol 5D. Stand alone question. Benefits questionnaire?	London Handicap Scale. Euroqol 5D	Question appeared to fit with conceptual framework and other aspects of the LHS pertinent for other aspects of the cf.
Looking after others	Health-related Hardiness Scale. Emotion and loneliness scale. Sense of coherence scale.		
Fatigue	Fatigue Severity Scale	Fatigue Severity Scale (FSS)	Conceptual match to the things said at interview. Quick to complete.
Travel/holidays	London Handicap Scale	London Handicap Scale (LHS)	
Work	London Handicap Scale	London Handicap Scale. Recent work demographic detail	
Hobbies	London Handicap Scale. Fatigue severity scale.	London Handicap Scale. Fatigue severity scale.	Appear to match conceptually with what was raised at interview
Pain	MaGill Pain questionnaire. Visual analogue scale.	Visual analogue scale	Precedent for use in previous SSc studies
Talking to others about	Sense of coherence scale. Generalized Self	Generalized Self-Efficacy scale	Concise to complete.

others about disease/ venting emotion	scale. Generalized Self-efficacy scale. Hostility and direction of hostility questionnaire. Emotional and Social loneliness scale	Efficacy scale	
Confidence	Generalized Self-efficacy Scale Rosenberg's self-esteem scale	As above	As above
Control - over life/disease/ future	Generalized Self-efficacy Scale. Health related hardiness scale	As above	As above
Coping	Ways of coping checklist. Emotional and social loneliness scale. Generalized Self-efficacy scale. Personal resource questionnaire – PRQ 85	As above	As above
Weather – clothing	None found		
Breathing problems	SHAQ Disability Index. SF36. Symptom distress checklist. SSc Functional Index.	SHAQ, SSc FI	
Eating difficulties	Rosenberg self-esteem. Symptom distress checklist. SSc Functional Index.	Rosenberg Self Esteem. SSc Functional Index.	
Reduced hand function	Arthritis hand function scale. Systemic Sclerosis functional index.	Systemic Sclerosis Functional Index	
Difficulty with housework	SHAQ DI. SSc functional index.	SHAQ DI. SSc Functional Index	
Bowel/bladder problems	Symptom distress checklist		
Friends and family	Social Network Index (SNI). Personal Resource Questionnaire PRQ-85. Emotional and social loneliness scale. London Handicap Scale.	LHS	
Social life	Social Network Index(SNI) Emotional		

	Index(SNI). Emotional and social loneliness scale.		
Sex life		Created single item	
Appearance	Rosenberg's Self-esteem.		
Sleep			
Adaptation	Psychological adjustment to illness scale (PAIS).Illness perceptions questionnaire		
Acceptance	Psychological adjustment to illness scale. Ilness perceptions questionnaire.		
Dressing			
Mobility	Systemic Sclerosis Functional Index. SHAQ Disability Index.		
Healthcare	Illness perceptions questionnaire. General perceived self-efficacy Scale		