Uncertainty in Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA): Development and Validation of a New Patient Reported Instrument

Volume 1 of 2

Thesis submitted to University College London for the degree of Doctor of Philosophy (PhD)

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I, Sophie Cleanthous confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Signature Date: 11/02/2014

Dedication

To my mother, Christina, who first suggested I should do a PhD and without whom none of this work would have been possible.

Acknowledgments

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This work would not have been possible without my mother, who first believed that I could and should pursue a PhD and who has since supported me in every way possible. I dedicate this thesis to her.

Abstract

Background: Patient uncertainty is considered to be an inherent part of the illness experience, and particularly relevant in unpredictable conditions; however, it has not been thoroughly investigated in systemic lupus erythematosus (SLE) or rheumatoid arthritis (RA) and no appropriate instrument is available for its quantification. This thesis presents mixed-method studies aiming to address this gap in the literature.

Phase-1: Qualitative interviews with 32 patients and 8 health care professionals were conducted in order to conceptualise patient uncertainty in SLE and RA. These findings were used to develop a new self-report instrument for patient uncertainty. Items of the new instrument were qualitatively tested through cognitive debriefing interviews.

Phase-2: A field test was set up to evaluate and revise the newly developed instrument psychometrically, using the modern technique of Rasch analysis in a sample of 388 patients. The instrument was subsequently evaluated using traditional psychometrics tests.

Phase-3 (part-1): A second field test was set up to evaluate the psychometric properties of the second draft of the new instrument using a combination of modern and traditional psychometric techniques in an independent sample of 279 patients. The final draft of the instrument consisted of five scales; *symptoms and flares, medication, trust in doctor, self-management* and *impact*.

Phase-3 (part-2): The construct validity of the new instrument, as well as the contribution of the five patient uncertainty scales to SLE and RA patient outcomes, including treatment adherence, mood and health related quality of life, were explored. Statistical tests, including correlational analyses and multiple linear regressions, were used for this exploration.

Conclusions: This thesis offers a conceptual framework and a self-report instrument for the assessment of patient uncertainty in SLE and RA. The findings offer implications for the role of patient uncertainty in these conditions and demonstrate the importance of comprehensive methodology in assessing such constructs.

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Glossary of Terms

Conceptual Framework	A framework representing the conceptual definition of a latent variable an instrument intends to quantify. This involves a thorough definition of the variable and the identification of the concepts comprising it.
Cronbach`s alpha	A coefficient assessing the degree of item convergence within a scale – a test of internal consistency.
Fit statistics	Tests that examine the degree to which the observed item responses (data) are consistent with the expected item responses predicted by a mathematical model e.g. the Rasch model.
Health Measurement	An umbrella term for the development and use of self-report instruments that measure variables from the patient` s perspective.
Internal Consistency	A function of the number of items and their covariation within a scale measuring a single construct – a measure of homogeneity.
Item locations	The position of items along a measurement continuum representing the construct (trait) of interest. Items located on higher measurement logits reflect higher *difficulty* in relation to the trait.
Latent variable	An unobservable variable comprising one or more constructs (concepts).
Logit	A logistic transformation of the probability of a response by a person to an item. Logits are the unit of measurement used in Rasch analysis for calibrating items and measuring persons.
Person locations	The position of a person along a measurement continuum representing the construct (trait) of interest. Persons located on higher measurement logits reflect higher *ability* i.e. higher levels of the trait.
Person separation index (PSI)	A numerical indicator ranging from 0 to 1 comparable to Cronbach`s alpha. It is computed as the ration of linear person measurements (not the raw summed scores) relative to the estimated error.
Psychometrics	The methods, processes and techniques used to construct and evaluate rating scales. Psychometric evaluation examines the extent to which any type of measurement instrument quantifies a construct successfully.

Rasch Analysis	A modern psychometric technique for constructing and evaluating rating scales and for analysing rating scale data. It examines the extent to which a scale works as a measurement instrument and if performing as such, enables linear measurement (with standard errors and fit statistics) to be constructed from ordered category responses of items.
Reliability	The extent to which a scale measures the same construct and is free of random error.
Self-report instruments	Questionnaires, measures or any type of associated way of quantifying latent variables from the patient` s perspective. An instrument may comprise one or more rating scales, depending on the number of sub-scales it contains.
Targeting	The extent to which the range of the construct (trait) measured by the scale matches the range of the trait in the study sample.
Thresholds	The point on the measurement continuum at which the probability of a person responding to two adjacent response categories is equal.
Trait	The construct quantified by a scale.
Validity:	The extent to which an instrument measures the variable it intends to measure.
Content validity	The extent to which items within a scale are sufficient and representative of the construct they are intended to measure.
Construct validity	The extent to which the dimensions of a construct are sufficiently specified, whether they display the expected relation with other dimensions both internally and externally.
Convergent validity	The extent to which a scale is associated with other scales or variables of the same or theoretically similar constructs.
Discriminant validity	The extent to which a scale is not associated with other scales or variables which are theoretically unrelated.

Chapter 1: Introduction

1.1 Chapter 1 Overview

The importance of considering the chronic diseases and their treatment beyond clinical morbidity is increasingly being recognised across many disciplines including rheumatology. Specifically, the patients` perspective including physical symptoms such as pain and fatigue as well as health-related quality of life (HRQoL), is not always associated with clinical markers of disease in systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). Similarly, it is increasingly recognised that patient beliefs play a role in treatment adherence and consequently influence clinical outcomes. Self-report instruments are the most common form of tool developed to quantify such latent variables. The scientific rigour of such instruments lies with the methodology used in their development, which consequently determines the extent to which the instrument is fit for purpose. There is currently a surge of activity in this area and “health measurement” spans a wide number of techniques, approaches and methodologies. This thesis combines current best practice methodologies in conjunction with modern test theory to explore and quantify patient uncertainty in SLE and RA.

Patient uncertainty is considered to be a cognitive stressor which is inherent in the illness experience and particularly relevant in unpredictable conditions like systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). Patient uncertainty has been portrayed as a mediator of important patient outcomes with significant implications for patient well-being and management. Nevertheless, very few studies have focused on exploring and capturing this vague concept. Furthermore, to date patient uncertainty has not been extensively investigated in rheumatology; thus, no appropriate self-report instrument is available for its quantification. This is the focus of the thesis, which comprised a mixed methods approach in three phases of data collection to explore the concept of patient uncertainty and ways of measuring it in patients with SLE and RA.

In Phase-1 of the studies presented herein, qualitative methodology was used to conceptualise patient uncertainty in SLE and RA. These findings were used as the basis of the development of a new patient-reported instrument for uncertainty in SLE and RA. Items of the new instrument were qualitatively tested through cognitive debriefing interviews. In Phase-2, a field test study was set up to psychometrically evaluate and revise the initial scales and items of the new instrument. Modern psychometric techniques (Rasch Measurement Theory, RMT) were used to conduct

this evaluation. In Phase-3, a second field test was conducted to complete the psychometric evaluation. In addition, using data from Phase-3, a cross-sectional cohort study was set up to explore the contribution of patient uncertainty in important patient outcomes like HRQoL, adherence and mood.

Chapter 1 provides the background and justification of the thesis. The first part of this chapter presents a literature review conducted across all chronic conditions to identify existing conceptualisations, theories and instruments of patient uncertainty. The second part of Chapter 1 includes a discussion of health measurement providing justification for the importance of psychometrically developed self-report instruments.

1.2 Patient Uncertainty in Chronic Illness: Literature Review

1.2.1 Literature Review Background: Uncertainty within Psychology

Uncertainty as a general concept has been incorporated in broader theories of social and cognitive psychology both of which characterise uncertainty as an inherent fact of the human existence (1-3). Cognitive psychology theories explore the phenomenology of uncertainty, focusing on the variants of uncertainty and the heuristics and biases of uncertain judgement. Social psychology on the other hand, does not explore the nature of the uncertainty construct, but rather focuses on the importance, management and tolerance or uncertainty across different individuals and groups. Nevertheless, both paradigms adopt a wide-ranging approach towards uncertainty, contrary to paradigms like statistics and decision theory that usually treat uncertainty as uni-dimensional probability or degree of belief (2).

Several psychological studies have followed the uni-dimensional approach but incorporated intuitive judgment to the basic logic of objective probability to describe uncertainty (4-6). Building on these theories, Kahneman and Tversky (1982) (2) offer a more comprehensive psychological perspective, describing four distinct variants of uncertainty categorised under two different loci to which uncertainty can be ascribed. “External” locus refers to events people cannot control and properties of external objects i.e. uncertainty related to the external world. ‘Internal” locus on the other hand, refers to ignorance, events people can control and properties related to the experiencing subject rather than the object i.e. uncertainty related to one`s state of knowledge.

Kahneman and Tversky (1982) (2) propose that external uncertainty can be assessed in either distributional mode by assessing relative outcome frequencies either through estimates or knowledge, or in singular mode, by assessing the propensities of the only

available case at hand. Internal uncertainty on the other hand, can be assessed through reason i.e. by attempting to induce an answer from other knowledge or introspection by searching for an answer that sounds familiar.

Within this perspective it is suggested that uncertainty is present at all levels of the biological complexity related to the "significance of different signs or stimuli and the potential consequences of actions" (2). Authors further suggest that the different conceptualisations of uncertainty are not mutually exclusive, but do highlight that although the language used to describe forms of probability can apply and be relevant to intuitive judgement (i.e. uncertainty), the probability laws are not applicable to all forms of uncertainty. In addition, Kahneman and Tversky (1982) acknowledge that not all experiences of uncertainty can be ascribed to the four variants of uncertainty they described, further highlighting the complexity of the uncertainty construct within the human existence.

Social psychology on the other hand, does not attempt to explore the nature of the uncertainty construct, but rather focuses on the dynamic of uncertainty within the social context and people`s behaviour (1). Uncertainty within social psychology is considered to be an aversive state as different authors propose that people need certainty about their world and their place within it; hence any uncertainty related to attitudes, perceptions, beliefs, feelings and behaviours reduces confidence and is therefore aversive (1, 7-9).

On the basis of Feininger's (10) social comparison theory arguing that people have the "motivation to know that their opinions are correct and to know precisely what they are and are not capable of doing", Hogg (2000) (1) argues that individual subjective uncertainty is the product of contextual variables that limit people`s certainty with regards to their perceptions, feelings, cognitions and behaviours and further challenge their confidence. Hogg (2000) describes how uncertainty reduction is an integral part and natural human motive within the search for social identity and comparison, but also highlights the individual differences in tolerating uncertainty (1).

Contrary to the notion that uncertainty is an aversive state, there is evidence to suggest that people can be differentiated between those who "need to know" and those who do not (1). People who are certainty-oriented are believed to seek self-verification and maintenance of existing beliefs and those who are uncertainty-oriented are believed to pursue situations of increased uncertainty that can be resolved to satisfy their self-assessment motives (1, 11, 12).

Despite the differences of exploratory focus, both cognitive and social psychology theories emphasize the inevitable presence of uncertainty in all aspects of life and further suggest the multiple and diverse aspects of uncertainty that differentiate it from an objective probability. In this view, it can be deducted that patient uncertainty is a concept relevant to the exploration of a chronic illness, which constitutes part of one`s biographical life journey, and is therefore expected to be penetrated by uncertainty.

Popular theories of health, illness and health behaviour (13-19) in the field of health psychology do not explicitly refer to uncertainty. Nevertheless, uncertainty is relevant to these theories as they incorporate constructs which are similar to or overlapping with uncertainty itself, as well as constructs within which the presence of uncertainty is implicit (20). For example the health belief model (HBM) proposes that the likelihood of a health behaviour is a result of a combination of seven core beliefs including "susceptibility" which reflects one`s risk perception. Although not explicitly labelled as a form of uncertainty by the HBM authors (16), the belief of susceptibility involves a subjective probability, on the basis of which the level of risk is perceived (2, 4-6), including intuitive judgement in many instances were objective facts are unattainable,

Similarly, Bandura`s social cognition theory (15) argues that health behaviours are the outcome of three forms of expectancies; (i) situation outcome, e.g. "smoking can cause cancer"; (ii) outcome, e.g. "stopping smoking can decrease the chance of cancer"; (iii) self-efficacy, e.g. " I can stop smoking if I want to". All three expectancies are formed in the absence of absolute certainty and involve assessment of risk benefit and future outcomes further showing overlap with uncertainty as defined within cognitive psychology (2, 4-6).

Without exception, all theories of health psychology incorporate the role of patient beliefs and perceptions in the likelihood of behaviour (13-16, 19) and regulation of health and illness (17, 18). The theory of planned behaviour (TPB) (13, 14) similar to, the social cognition theory (15), proposes that behavioural intentions result from a combination of several beliefs including attitudes towards a behaviour and beliefs of perceived behavioural control. As suggested by theories within cognitive psychology, uncertainty reflects the degree of a belief (2, 4-6) and is therefore an implicit element of beliefs within the TPB.

In the same way, within the self-regulatory model of health and illness (17, 18), patients are believed to hold illness cognitions in their attempt to make sense of their condition.

Illness cognitions refer to beliefs regarding the illness identity and experienced symptoms, causal attributions, the timeline and future consequences of the illness as well as the perceived curability and controllability of illness (21). Comparable to the TPB uncertainty is an implicit element of such illness cognitions as it reflects the degree of a belief (2, 4-6), an element also reflected in the measurement of such beliefs which sometimes includes a response scale option related directly to uncertainty (22).

Theories related to coping with life`s threats such as an illness, often utilised within health psychology, also refer to uncertainty (23-25). Within these theories uncertainty is considered to be a subjective state which results from an individual contextual situation and is aversive, as it is associated with psychological distress. Therefore, active coping with and management of uncertainty is regarded as an important adaptive task of the illness experience by theories of coping (23-25).

Considering that uncertainty has been linked to a spectrum of concepts including intuitive probability judgements, attitudes, perceptions, beliefs, feelings and behaviours (1, 2, 7-9), it can be argued that uncertainty constitutes a property of all subjective states and is therefore inherently relevant to all aspects of a patient`s response to a chronic illness.

1.2.2 Literature Review Background: Why SLE and RA?

A chronic illness diagnosis is a disruptive life event, which is associated with an inevitable sense of uncertainty (25-27). This inherent uncertainty relates to the limited knowledge patients have of the progression and impact of their illness as well as self-management. This is believed to be particularly true in unpredictable conditions with no known precise cause or cure, such as systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) (28-35).

Both SLE and RA are chronic autoimmune rheumatic conditions that are currently incurable (36-39). SLE is a complex multi-system condition with a variable and often irregular course, characterised by unpredictable flares and remissions. Patients with SLE frequently develop diverse clinical manifestations affecting almost any body organ, including the skin, kidney, lung, brain, heart, and joints (37). RA is an inflammatory condition primarily affecting the synovial tissue, cartilage and bones of small and medium-sized joints and, in more severe cases, the lungs, blood vessels and the haematopoietic system (38). RA is often, but not always, characterised by a gradually progressive course of increasing morbidity.

Therefore, clinical manifestations, illness course and general morbidity are diverse and, to some extent, unpredictable in both SLE and RA. Reflecting these parameters, an early study descriptively listed multiple dimensions of uncertainty experienced by patients with RA (34). These included: uncertainty about future symptoms; illness manifestation; level of disability; the speed of illness progression; the duration of a flare; and the frequency of illness flares (34). Another qualitative study aiming to map the experience of living with SLE suggest twelve different concepts related to SLE, including the uncertainty related to the unpredictability of SLE (35).

Within the area of chronic illness, patient uncertainty has been described as a subjective cognitive perception that challenges the sense of control and adjustment (23-25, 29). It has been associated with distress and characterised as a state that requires adaptation (23, 24). However, there is currently no consensus about the exact conceptualisation of patient uncertainty, as different descriptions and frameworks are used in the different scientific disciplines and areas of research (40, 41).

Nevertheless, there is a shared acknowledgment in the literature of the significance and potential utility of patient uncertainty in the research and management of chronic illness. In brief, patient uncertainty has been portrayed as an aversive state that negatively contributes to important psychosocial outcomes such as depression and anxiety, coping skills as well as communication with health care professionals (42-44). Subsequently, patient uncertainty constitutes a potential target mediator of interventions aiming to improve such outcomes in chronic illness (45-48).

Research literature suggests that patient uncertainty in SLE and RA (28, 31-33, 35) could be an important issue and further indicates dimensions of patient uncertainty specifically related to these illness trajectories (34, 35). Within the area of SLE and RA there is an increasing appreciation of the need to assess patient outcomes, as these do not often reflect clinical measurement and big marker changes (49, 50). Assessment of patient uncertainty in SLE and RA requires a comprehensive understanding of the concept and the appropriate quantification of it.

1.2.1.1 Literature Review Aims

The aim of this literature review was to provide a comprehensive account of what is known about the concept of patient uncertainty in chronic illness. A prior brief review conducted in preparation of this literature review indicated that the literature concerning patient uncertainty in SLE and RA was limited. Therefore, the review was extended to all chronic conditions and different methodologies to enable the comparison and cross-

evaluation of quantitative and qualitative findings in chronic illness. Specifically, the review had the following objectives:

- Identify and review qualitative studies related to patient uncertainty
- Identify theories of patient uncertainty
- Identify instruments of patient uncertainty
- Review quantitative studies related to patient uncertainty

1.2.3 Methods

Standard procedures of searching, selecting and extracting articles and study findings were used to retrieve the relevant literature (51, 52).

1.2.3.1 Search Strategies

Three strategies were used to identify relevant literature:

i. Searches were performed on five electronic databases (AMED, CINAHL, EMBASE, Medline & PsychINFO) using the text searches described below.
ii. All the reference lists of the selected articles were reviewed for further potentially relevant articles.
iii. The authors of the key articles in the field were contacted to help to request access to unpublished research studies, widen understanding of the topic, and further clarify their views on the concept.

1.2.3.2 Text Searches

A combination of search terms from five relevant domains was used, including: state (i.e. uncertainty), area (i.e. chronic illness), target population (i.e. patients), disease (i.e. SLE, or RA), and elicitation method (i.e. questionnaire, measure or interview). The OR operator was used to expand search to all potential terms and the AND operator to narrow the search (51) to the literature containing a combination of both the "state" i.e. uncertainty and any of the other terms. Specifically, truncated search terms were used where possible as well as a variety of search term combinations [(uncertain*) and (illness) or (patient*) or (lupus) or (arthritis) or (measure) or (interview)]. Full search strategies are presented in Appendix 1.2.

1.2.3.3 Selection Process

Articles were screened on a title, abstract and full text level to complete the selection process. Articles were selected if they assessed patient uncertainty in any chronic condition using any type of research methodology (quantitative or qualitative). Articles were excluded if they met any of the following exclusion criteria:

- not published in the English language

- dealt with clinical or medical uncertainty
- dealt with parental, family or carer uncertainty
- dealt with childhood patient uncertainty
- dealt with patient uncertainty outside the scope of chronic illness, e.g. trauma/injury, mental illness or acute disease
- used the word *uncertainty* as a lay term and were not referring to a distinct construct

1.2.3.4 Data Extraction

Data extraction was completed using two types of extraction sheet developed for quantitative and qualitative studies retrieved (Appendix 1.1). Where necessary, authors were contacted to request relevant information not reported in the articles.

1.2.4 Literature Review Findings

1.2.4.1 Articles retrieved

A total of 115 articles were selected for review, 87 from the electronic databases search and the remaining 28 from the two additional search techniques. The details of the search and selection procedure are reported in Appendix 1.3. There was significant variability and diversity amongst the selected articles on three main levels: (i) the discipline and scientific perspective (including: Nursing, Psychology, Sociology, Anthropology, and Medicine); (ii) the population under investigation (including: cancer, HIV, heart conditions, multiple sclerosis, RA, and SLE); and (iii) the methodology used (including: quantitative, qualitative, case reports, and reviews). Considering the variability of the retrieved studies, a narrative review of the literature is provided by presenting the retrieved literature in relation to the four objectives.

1.2.4.2 Qualitative Studies in Patient Uncertainty

Only five studies were retrieved with the explicit objective of exploring the concept of patient uncertainty using a qualitative methodology (34, 53-56). Table 1.1 outlines the different dimensions of patient uncertainty revealed in these studies.

Three of these studies were conducted in cancer, one in HIV and an early study in RA. Findings highlight the multidimensionality of the patient uncertainty concept as a variety of dimensions were put forward. Even though Brashers et al. (2003) describe their findings as “sources” of uncertainty, in comparison with the rest of the studies that refer to themes or dimensions, their findings are very similar (54). This overlap between the source and the dimension of uncertainty is often seen in this literature.

Patient uncertainty has been proposed in terms of physical and clinical aspects related to illness prognosis and symptom interpretation: health care and treatment; general understanding of the condition and its cause; the personal and social impact of the illness as well as personal management and adaptation (34, 53-56). These findings (Table 1.1) suggest that uncertainty related to a chronic condition has the potential to prevail in all areas of a patient's life. For example, Brasher et al. (2003) described the interpersonal uncertainty resulting from the fact that HIV is a sexually transmittable disease.

Another study described six types of patient uncertainty in RA, including uncertainty about future symptoms, illness manifestation, level of disability, the speed of illness progression, the duration of a flare, and the frequency of illness flares (34). Although these dimensions relate to the illness characteristics and course only, they highlight the disease-specific nature of uncertainty by referring to duration and frequency of flare-ups.

In addition to the above studies, further qualitative studies were retrieved, which explored other issues within a chronic illness, where patient uncertainty emerged as a finding. Dimensions of patient uncertainty emerging from these studies and the corresponding study objectives are summarised in Table 1.2. These findings further demonstrate the presence of patient uncertainty in the illness experience across different conditions.

Overall, the dimensions of patient uncertainty appear to be diverse and related to all aspects of a patient's life, often reflecting the characteristics of the specific condition under research. For example, patient uncertainty dimensions are reported in relation to the illness course of RA (34), the risk and consequences of transmitting viruses like HIV and Hepatitis C (54, 57), as well as the fear of death, relapse and treatment options in cancer (56, 58-60). Simultaneously, some dimensions of patient uncertainty such as symptom interpretation, illness progression, unreliable body, and future impact are identified across different conditions.

Table 1.1 Qualitative Explorations of Uncertainty

Illness population	Study objective	Dimensions of Uncertainty
RA (34)	examine conditions which produce variable uncertainty	• whether there will be any pain, swelling or stiffness • the area of arthritis involvement • the intensity of the disability • whether onset will be gradual or sudden • how long it will last • the frequency of flare-ups
Cancer (breast, kidney, tongue or lung) (55)	survey decision-related uncertainties	• social integration • diagnosis and prognosis • deciphering information • mastering of requirements • causal attribution • own preferred level of involvement • trust in physician • treatment
Prostate cancer (53)	explore the uncertainties of older men with prostate cancer	• lack of symptoms/discomfort • misattribution of symptoms • ambiguity of testing • physician` s inability to predict tumour progression
Breast cancer (56)	describe and interpret uncertainty post-treatment	• vicissitude of emotions • relying on support through relationships • transitions: learning new ways of being in the world • reflection of self in the world • gaining understanding: putting uncertainty into life` s perspective
HIV (54)	examine the sources of uncertainty	Medical • insufficient information about diagnosis • ambiguous pattern of symptoms • complex system of treatment and care • unpredictable prognosis Personal • complex and conflicting roles • unclear financial consequences Social • unpredictable interpersonal reactions • unclear relationship implications

Table 1.2 Dimensions of Uncertainty Emerging from Qualitative Studies

Illness	Study objective	Emerging Dimensions of Uncertainty
RA (32)	identify the caring needs under treatment	• long-term planning • irregular symptom patterns
SLE (31)	describe daily experiences	• symptom recognition • symptom interpretation • unreliable body • unpredictable flares • inability to plan life • unpredictable cognitive functioning
SLE (35)	explore illness perceptions	• unpredictable prognosis
FM (61)	explore the creation of meaning in a medically unexplained disorder	• causal attributions • symptom interpretation • clinical
Breast cancer (59)	explore patient experiences	• understanding diagnosis • interpreting information received • discrepant treatment advice
PMP (62)	explore impact on patients` lives	• diagnostic • prognostic • treatment choices
Cancer (63)	explore patients` views and experiences of collaborating with health care professionals (HCPs)	• interaction with HCPs • interpretation of HCP feedback
Cancer (60)	describe experience of living with diagnosis	• fear of death • future impact of condition
Leukaemia (58)	compare quality of life in acute and chronic leukaemia	acute • treatment effectiveness • relapse potential • therapy side-effects chronic • health status • diagnostic certainty • future need for treatment
Diabetes (64)	understand patient coping strategies	• unfamiliarity with condition • inadequate health care system support
Hepatitis C (57)	explore factors that affect quality of life	• illness progression • virus transmission
Hepatitis C (65)	explore risk management in drug users	• knowledge of condition
HIV (66)	examine impact of HIV medication	• long-term treatment effectiveness
MI (67)	explore information needs	• occupational • family life future capacity
MI (68)	explore illness experiences	• life & death • unreliable body
MI (69)	investigate illness experiences	• symptom interpretation • existential thread
Chronic illness (70)	describe the meaning of living with chronic illness	• illness progression • impact on personal lives • occupational

FM: fibromyalgia; PMP: pseudomyxoma peritonei; MI: myocardial infarction

1.2.4.3 Theories of patient uncertainty

The vast majority of the current literature is dominated by Michel's nursing theories of patient uncertainty (71). The Uncertainty in Illness Theory (UIT) was developed to address uncertainty in pre-diagnostic, diagnostic, treatment, and acute illness and was re-conceptualised (RUIT) to address enduring uncertainty in chronic illness (72-74). The UIT and RUIT theories are descriptive and have been developed through the author's personal experience with her ill father, preliminary data from hospitalised patients, and discussions with colleagues (71).

Mishel (71) describes how cognitive psychology (24, 75-77) influenced her to conceptualise uncertainty as a cognitive and not an emotional state, a stressful event that can be appraised into either a danger or an opportunity. To this end, the UIT (74, 78) defines uncertainty as "the inability to determine the meaning of illness-related events", and focuses on variables causing uncertainty and its resolution. The UIT incorporates three sections describing: (i) the sources of uncertainty, which are labelled as "antecedents" within the UIT, (ii) appraisal and (iii) coping of uncertainty (Figure 1.1).

The UIT proposes three sources (antecedents) of uncertainty, including characteristics of a specific illness, variables that interact with the interpretation of uncertainty, and an individual's cognitive capacities. Illness characteristics, or (as referred to within the UIT) the "stimuli frame", i.e. characteristics of the perceived stimuli, constitute the primary source of uncertainty. More specifically, these characteristics refer to the pattern of symptoms, event familiarity and congruence between the expected and actually experienced illness events.

The secondary source of uncertainty postulated by the UIT is "structure providers", referring to variables that interact with a person during the interpretation of his/her illness experience. These providers include the health care practitioners or the "credible authority" (as labelled by the UIT), loved ones or "social support", and education level that the UIT proposes being related to the patient's ability to assimilate information.

The third source of uncertainty proposed by the UIT is an individual's cognitive capacities, which are thought to influence uncertainty by hindering a patient's ability to process illness-related information. In other words, cognitive capacities are thought to indirectly contribute to uncertainty by influencing the interpretation of illness characteristics. The UIT suggests that cognitive capacities can in turn become impaired by physiological, psychological and situational factors during an illness.

Figure 1.1 Uncertainty in Illness Theory (UIT)

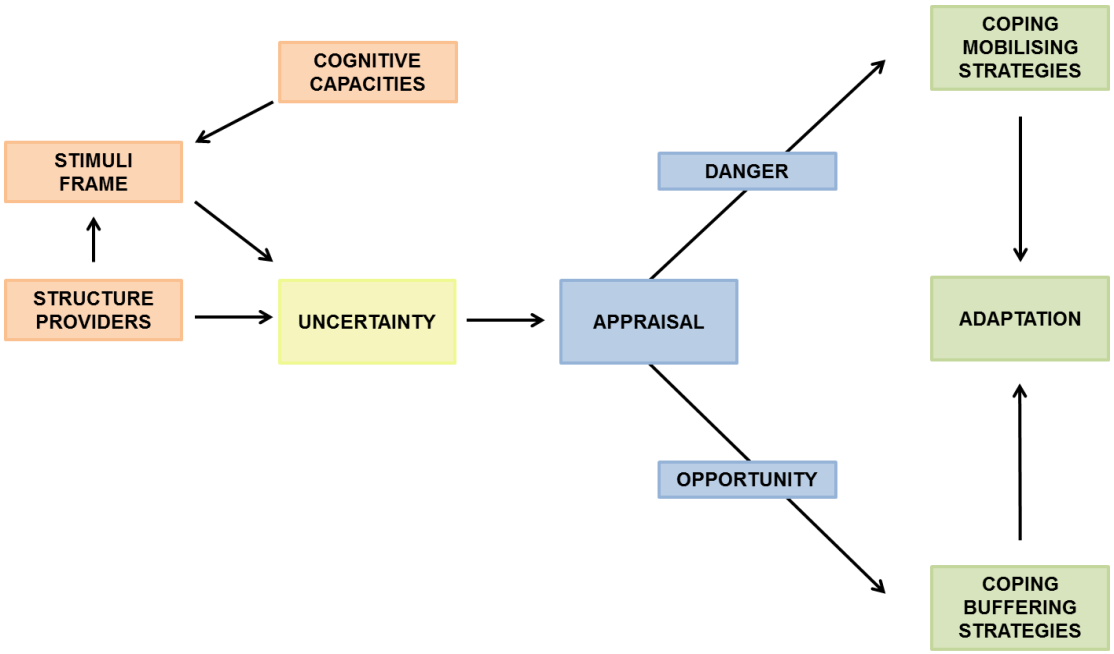


Figure 1.1: *The Uncertainty in Illness Theory (UIT) proposed by Merle Mishel (1988) (74). The UIT incorporates three sections; the uncertainty antecedents (i.e. sources) including stimuli frame (i.e. illness characteristics), structure providers (i.e. health care professionals, loved ones and educational level) and cognitive capacities; the appraisal and the coping.*

The second section of the UIT involves appraisal, which refers to the process of assigning value to the uncertainty event or situation. The UIT proposes that appraisal is based on inference and illusion. Inference refers to personal disposition, knowledge and experiences that affect appraisal. Illusion refers to positive beliefs constructed on the basis of uncertainty. The appraisal process results in the evaluation of uncertainty as either danger or an opportunity.

The third and final section of the UIT involves coping. If the appraisal process values uncertainty as a danger associated with the possibility of a harmful event, coping mobilizing strategies are initiated, aiming to reduce uncertainty and manage the emotions generated by it. On the other hand, if uncertainty is appraised as an opportunity, coping buffering strategies are initiated to maintain the uncertainty as its presence is considered necessary for maintaining a positive view in a situation. If strategies are successful, coping results in a state of adaptation, involving a holistic bio-psychosocial set of behaviours from an individual (71, 73).

Acknowledging that patient uncertainty is not always resolved in chronic illness, authors of the UIT reconceptualised the theory (71, 73) to better reflect enduring patient uncertainty within the spectrum of chronic illness. The Reconceptualised

Uncertainty in Illness Theory (RUIT) retains the same definition and antecedents of uncertainty but introduces two further concepts; self-organisation and probabilistic thinking, to address the enduring uncertainty experienced in chronic illness. Self-organisation refers to reformulation of one's self, following the acceptance of enduring uncertainty. Probabilistic thinking refers to accepting the lack of absolute certainty and predictability.

The RUIT proposes four factors that help a person achieve self-organisation and probabilistic thinking. These include prior life experiences, physiological status, social resources, and health care providers. The RUIT suggests that a person gradually re-evaluates uncertainty from an aversive experience to an opportunity (71, 79). The key difference between the two theories is that adaptation within the UIT is achieved when uncertainty is completely resolved, whereas adaptation within the RUIT refers to growth towards a new value system and acceptance of uncertainty, abandoning the need for certainty.

Both the UIT and RUIT (73, 74) are introduced descriptively and based on primarily deductive approaches. The authors (43, 71) suggest that the theories are supported by both qualitative findings (56, 64) and quantitative (45, 72, 80, 81). However, findings provide less empirical support for the RUIT (43, 44, 71), where enduring uncertainty is expected to be re-evaluated as a positive experience. In addition, several of the retrieved studies were designed on the basis of the UIT, assessing the association of uncertainty with other patient outcomes (see section 1.2.3.6), but were not specifically designed to test the theory.

1.2.4.4 Different Conceptualisations of Uncertainty in Chronic Illness

Currently, the only theories retrieved that specifically describe the concept of uncertainty in both acute and chronic illness are the UIT and RUIT (73, 74). Nevertheless, the concept of uncertainty has been defined and approached in a variety of ways across the literature (40, 82).

In a review of uncertainty across different disciplines, Barbow et al. (1998) presented the perspectives of uncertainty in illness across three major paradigms: individual-psychological models, linguistic and discourse analyses, and sociocultural and historical perspectives[1] (40). The different conceptualisations of uncertainty across these paradigms are synthesised and presented by the authors (40) in a five-dimension framework of the "meanings of uncertainty in illness". These dimensions/forms of

[1] The literature presented in this thesis falls under the individual-psychological models.

uncertainty included complexity, quality of information, probability, structure of information, and lay epistemology.

The UIT/RUIT theories (73, 74) describe uncertainty as a process incorporating antecedents, appraisal and coping phases, as opposed to the static dimensions reported by Barbow et al. (1998). However, an overlap of concepts can be identified as complexity: quality and structure of information are incorporated in the antecedents of uncertainty, whilst lay epistemology is linked with the inference component of appraisal within the UIT and the dimension of probability is introduced descriptively in the RUIT.

Penrod (2001 & 2007) conducted a concept analysis of uncertainty and highlighted the existential perspective of the uncertainty concept neglected by the UIT (41, 83). Existential uncertainty has mainly been addressed in the medical sociology and anthropology literature (33, 84), and refers to the individual experience of having one's mind, body and self in jeopardy. Stockl (2007) demonstrated that existential uncertainty can have negative effects not only for the patients themselves but also for the doctor-patient relationship in SLE. Existential uncertainty is linked with both cognitive and precognitive variables and does not preclude probabilistic modes of uncertainty. However, it is a concept that has not been experimentally tested in the literature.

In all of the above definitions, uncertainty is considered to be a perception that is strongly associated with emotional outcomes. Hilton's work with cancer patients (85, 86) resulted in an overarching definition of uncertainty that includes both perceptual and emotional variables (Table 1.3).

The qualitative studies retrieved in this review, which explore uncertainty empirically (Tables 1.1, 1.2), assess uncertainty in illness from a different standpoint and focus on the different uncertainty aspects experienced by patients with different chronic conditions. These studies (34, 53-56, 87) focused on the issues patients are uncertain about and less so with the sources, nature and appraisal of this uncertainty as a cognitive state or process (73, 74). Focusing on the construct of uncertainty, these studies presented what patients are uncertain about, displaying the multidimensionality and disease-specific nature of patient uncertainty variables. Reflecting this issue, Politi et al. (2007) concluded that there is an overlap of the construct of uncertainty and the risk/sources of uncertainty in the literature.

Table 1.3 Definitions of Uncertainty in Illness

Author	Definition
Mishel, 1988 (74)	"the inability to determine the meaning of illness-related events"
Hilton, 1994 (85)	"…a cognitive perceptual state that ranges from a feeling of just less than surety to vagueness; it changes over time and is accompanied by threatening and/or positive emotions. Uncertainty is not being able to foretell the future; a lack of clarity about the present; being in doubt; being undecided because things are not definite, clear-cut or determined; not being able to rely, count, or depend on someone or something; and having a sense of vagueness about what to do, expect, know and ask."
Penrod 2001 (83)	"…a dynamic state in which there is a perception of being unable to assign probability for outcomes that prompts a discomforting, uneasy sensation that may be affect (reduced or escalated) through cognitive, emotive, or behavioural reactions, or by the passage of time and changes in the perception of circumstances. The experience of uncertainty is pervasive in human existence and is mediated by feelings of confidence and control that may be highly specific (event-focused) or more global (a world view)"

Brashers et al. (1998), bringing together the findings of uncertainty in HIV, suggested the temporal differences of the uncertainty experienced by HIV patients and concluded that there are four phases of HIV uncertainty (87). The "at risk" phase relates to the period prior to diagnosis where uncertainty exists related to the likelihood of an infection, the ambiguity of risk factors, and the accuracy of the HIV test result. The "diagnostic" phase relates to the complexity and ambiguity of the diagnosis and controversy around the aetiology of AIDS. The "latent" phase relates to uncertainty about the HIV status disclosure, the reactions of others, treatment side effects, illness progression, and future impact of HIV on patients' lives.

Finally, the "manifest" phase relates to the ambiguity and unpredictability of symptoms, the optimal treatment strategies, prophylaxis against infections and, finally, uncertainty of the health care providers who are faced with rapid changes in the HIV optimal care guidelines. Even though this was not an empirical qualitative study (87), it does suggest the importance of the temporal parameter in assessing patient uncertainty. This further supports the dynamic complexity of uncertainty and challenges the applicability of a general across-condition conceptualisation of the construct.

The variety of different conceptualisations of uncertainty in the literature reflects its complex nature but also highlights the lack of a consistent definition for the concept (82, 88). Furthermore, the multidimensional dimensions of patient uncertainty revealed in qualitative studies (34, 53-56) challenge the definition of uncertainty within the

UIT/RUIT theories (74, 79). Findings suggest that the different conceptualisations put forward are not mutually exclusive (88), and not necessarily comprehensive and applicable for all chronic conditions.

1.2.4.5 Instruments of Patient Uncertainty

1.2.4.5.1 The Mishel Uncertainty in Illness Scale (MUIS)

The MUIS (78) was the first published self-report instrument designed to specifically assess uncertainty in illness. Mishel (1981) describes how the development of the MUIS began with forty-five informal interviews with hospitalised patients (the specific illness conditions of these patients). Interviews were analysed to deduct statements reflecting uncertainty. Patient statements were judged as uncertain if they comprised any of the following: vague information, multiple meanings, a probability, ambiguity, inconsistency, lacking information, and unpredictability, or if they were unclear.

This analysis resulted in 62 statements that were reviewed by an expert group of nurses, physicians and surgical patients to confirm the wording was applicable, resulting in a final pool of 54 items. The 54-item scale was tested in a group of 259 hospitalised patients (including medical, surgical and patients undergoing diagnostic procedures). Factor analysis resulted in a two-factor structure of 30 items which was replicated in a second study of 100 patients and indicated high levels of homogeneity reliability.

The final MUIS contained 30 items relating to illness symptomatology, diagnosis, treatment relationship with care givers, and future planning, and was spread across two factors: ambiguity and unpredictability. Items from all dimensions were loaded onto the ambiguity factors, whereas only items related to symptomatology and illness outcome were loaded onto the unpredictability factor (78).

Currently, three variations of the original MUIS exist (89). The community form of the scale (MUIS-C) is used to assess uncertainty in illness for outpatients. It consists of the same items as the MUIS scale but excludes the items that are only applicable to inpatients and acute conditions. In addition, the parent form of the scale (MUIS-parent) and the family member (MUIS-family member) contain the same items as the MUIS, but are re-worded in order to be applicable to an ill child's parents or to a patient's family member. All of Michel's scales measure agreement on a five-point Likert scale.

The Mishel scales, in all their variations, are the most extensively used instrument of patient uncertainty across a vast variety of conditions in the current literature.

1.2.4.5.2 The Uncertainty Stress Scale (USS)

The USS (85) is a self-report instrument of patient uncertainty developed on the basis of the author's phenomenological work with breast cancer patients (86) and incorporating the UIT and RUIT (73, 74) conceptualisation of uncertainty. Extending the spectrum of the Mishel scales, the USS incorporates measurement of the stress, threat and positive feelings generated by uncertainty.

The USS is divided into three parts. The first part consists of 24 items requiring respondents to rate their uncertainty in relation to aspects of their specific illness. The second part requires respondents to rate their stress relating to the same 24 aspects presented in the first part. The first two parts are rated on a four-point Likert scale. The third part of the USS consists of four visual analogue scales (VAS) assessing global uncertainty, global stress, global threat, and perceptions of positive aspects of the uncertainty state against a 10-cm line ranging from very low uncertainty to very high uncertainty.

In contrast to the Mishel scales, the USS incorporates the word uncertainty in almost every item and measures both perceptions and feelings. The USS has not been very widely used, as only three quantitative studies (85, 90, 91) were identified using it.

1.2.4.5.3 Other Instruments

Two studies [38, 39] were identified using lay instruments put together for the purposes of their own research objectives. Stiegelis et al. (2004) (92, 93) used six items to assess uncertainty in cancer against a five-point agreement scale. The items concerned the need for illness information, treatment information need, illness and therapy knowledge, feelings of future uncertainty, feelings of uncertainty about handling illness, and feelings of uncertainty about the consequences of illness and treatment.

Finally, Braden (92) reported the use of three visual analogue scales (VAS) to assess uncertainty in SLE with regard to: (i) patient self-care techniques, (ii) medication effectiveness in SLE control, and (iii) medication effectiveness in pain and stiffness control. The VAS response lines used ranged from "not at all certain" to "very certain".

1.2.4.6 Quantitative Studies in Patient Uncertainty

Most quantitative studies in patient uncertainty have used the MUIS/MUIS-C instruments (78, 89). Patient uncertainty has been assessed across different illness groups, including rheumatic conditions, heart failure, cancer, asthma, and multiple sclerosis in relation to a variety of patient outcomes. The variability of research objectives and illness groups prohibits direct comparison between the studies. Findings are presented narratively firstly within rheumatic conditions and secondly within all other chronic conditions. Within each illness group findings of patient uncertainty is reviewed in relation to causes/sources and coping, and impact.

1.2.4.6.1 Rheumatic Conditions

Nine studies (29, 92, 94-100) were identified assessing patient uncertainty in rheumatic conditions (Table 1.4). Uncertainty was assessed using the Mishel Uncertainty in Illness Scales (MUIS) (78, 89) in all but one (92) of these studies.

1.2.4.6.1.1 Causes/Sources of and Coping with Uncertainty in Rheumatic Conditions

Akkasilpa et al. (2000) investigated the relationship of coping responses with fibromyalgia (FM) tender points in SLE, but no association with age sex or education. FM is a syndrome of unknown aetiology characterised by widespread musculoskeletal pain, tenderness, as well as symptoms of fatigue, stiffness, and sleep disturbance (29, 94, 101). Patients with FM suffer from an increased number comorbid conditions such as SLE and RA and are also psychologically challenged as FM is difficult to treat (29, 100, 102). In comparison with SLE and RA, there is no organic basis for FM symptoms the treatment of which is not standardised and often ineffective increasing uncertainty and unpredictability of this often called “mystery disease” (100, 103). An association of uncertainty with FM tender points was taken to indicate the relationship of poor or no coping with tender points (94).

Comparing FM to osteoarthritis (OA) which is a better understood and managed condition (100), Reich et al. 2007 further support this argument as patients with FM reported significantly higher levels of uncertainty (Table 1.4). Braden (1990) also supported the role of illness characteristics in the expression of uncertainty as illness severity accounted for 38% of the variance in uncertainty in a cohort of rheumatic patients (96). Bailey et al. (1996) on the other hand, investigated appraisal in a very small sample of RA patients (95) and reported no association between levels of uncertainty and illness duration but a cross-sectional association of uncertainty with danger appraisal.

Finally an evaluation of a self-help intervention reported a significant reduction in SLE patient uncertainty, as assessed by three VAS scales (92). Reduction in uncertainty was associated with increases enabling skills, self-efficacy and self-worth that subsequently signify potential sources of uncertainty.

1.2.4.6.1.2 Impact of Uncertainty in Rheumatic Conditions

Failla et al. (1996) reported significant strong univariate correlations between uncertainty and hopelessness adjustment in SLE; however, these were not significant on a multivariate level (97). Uncertainty showed a borderline contribution to quality of life on a multivariate level in a group of rheumatic patients (96). In comparison with the studies above indicating the increased uncertainty in FM (94, 100); Johnson et al. (2006) reported only a borderline contribution of uncertainty to symptom difficulty in FM (29) but not with coping efficacy (Table 1.4).

Reich et al. (2006) reported significant cross-sectional associations between uncertainty, pain, helplessness, anxiety, depression, affect and coping in FM but not longitudinally (98). Comparing this FM sample (98) with a sample of osteoarthritis (OA) patients, Reich et al. (2006) showed the increased uncertainty in the FM sample (99). This study reports a contribution of uncertainty in interaction with pain and disability in the levels of relationship satisfaction for both conditions (99), although uncertainty was not independently associated with relationship satisfaction in either FM or OA.

Finally, a study (100) investigated the effect of uncertainty with the FM patients` relationship with their partners showing no association with satisfaction pain or partners` behaviour. More details of the above studies are presented in Table 1.4.

Table 1.4 Quantitative Studies of Patient Uncertainty in Rheumatic Conditions

Authors	Condition	Design	Sample size	% female	Age mean (SD) or median (range)	Uncertainty Instrument	Other Patient-reported Variables	Statistical Test	Uncertainty-related Results
Akkasilpa et al, 2000 (94)	SLE	cross-sectional cohort	173	94.2	40.8 (12.9)	MUIS	Fibromyalgia tender points (TP)	Linear regression, ANOVA	1) significant association of uncertainty with FM TP (p=0.0001) 2) >11 TP Vs 1-10 Vs 0 TP significant difference in uncertainty reported 3) no association with age, sex or education
Bailey et al, 1993 (95)	RA	cross-sectional cohort	23	100	61 (29-80)	MUIS	Appraisal of Uncertainty (coping responses)	Pearson Correlations	1) No association of uncertainty with disease duration 2) Uncertainty correlated significantly (r=0.631, p<0.01) with danger appraisal but no with opportunity
Braden 1990 (96)	43% RA 25% SLE 22% OA 10% other	cross-sectional cohort	396	86%	57 (18 - 88)	MUIS	enabling skill (perceived ability to manage), dependency (reliance on others) , severity of illness, monitoring (level of information one prefers, disease characteristics	Pearson Correlation, Step-wise regression analysis, Regression equation	1) illness severity, disease characteristics, background inputs and monitoring explained 40% of the variance in uncertainty; illness severity was associated with uncertainty p<0.05 R2=0.38, diagnosis SLE also associated 2) uncertainty associated directly with QoL (beta -.17, p<0.05), self-help (beta=-.23, p<0.05) and enabling skill (beta=-0.15, p<0.05)

Table 1.4 (Cont`d)

Authors	Condition	Design	Sample size	% female	Age mean (SD) or median (range)	Uncertainty Instrument	Other Patient-reported Variables	Statistical Test	Uncertainty-related Results
Braden 1991 (92)	SLE	longitudinal - evaluation of self-help intervention (T1: baseline; T2: 7 weeks; T3: 2 months)	291 (201 in analysis)	96%	46 (13.3)	VAS uncertainty	self-efficacy, quality of life, enabling skills, self-work, SLE knowledge, depression, severity of illness (most single items)	MANOVA	uncertainty decreased between time points 1, 2, 3 (F=27.1, DF=2/428, p<0.01)
Failla et al, 1996 (97)	SLE	cross-sectional cohort	31	100	41 (10.9)	MUIS-C	Beck Hopelessness Index, Psychological Adjustment to Illness	1) Pearson Correlations Stepwise 2) Multiple Regression Analysis	1) significant negative association with BHI (r=0.46, P<0.01) PAIS (r=0.53, p<0.01) 2) uncertainty was not significantly associated with psychological adjustment on a multivariate level
Johnson et al, 2006 (29)	FM	cross-sectional cohort	51	100	52 (7.3)	MUIS-C	VAS Pain Scale, Coping Efficacy, Neuroticism, Coping with Symptoms – (all ad-hoc scales)	Multi-level modelling	uncertainty contributed to the difficulty of coping with symptoms in the presence of high pain (p<0.5) but not with coping efficacy p=0.31
Reich et al, 2006 (99)	FM	cross-sectional cohort	51 patients & partners	100	51.9 (35-69)	MUIS-C	relationship satisfaction & other-reliance encouragement ORE health controlling behaviours HCB (partners)	1) Pearson Correlations 2) Multiple Regression	1) uncertainty not associated with satisfaction, pain or partner behaviours 2) when uncertainty and pain were low, HCB and ORE were related to poorer relationship satisfaction (p<0.01)

Table 1.4 (Cont`d)

Authors	Condition	Design	Sample size	% female	Age mean (SD) or median (range)	Uncertainty Instrument	Other Patient-reported Variables	Statistical Test	Uncertainty-related Results
Reich et al, 2006 (98)	FM	longitudinal cohort (T1: baseline; T2:3 - 4 months)	51	100	51.9 (35-69)	MUIS-C	Pain & Helplessness, Anxiety & Depression, Brief Cope Scale (approach and avoidant Coping, Active), Vanderbilt Pain Coping Inventory, Positive (PA) and Negative Affect (NA), perceived stress	1) Pearson Correlations 2) multi-level regression predicting Affect	1)pain helplessness (r=0.31, p<0.5); anxiety (r=0.51, p<0.01); depression (r=0.36, p<0.01); NA (r=0.45, p<0.01), avoidance coping (r=0.40, p<0.01)passive coping (r=0.55, p<0.01); PA & coping NS correlations 2) uncertainty NS to either NA or PA at either baseline or time 2
Reich et al, 2007 (100)	FM & OA & partners	cross-sectional cohort	51 FMS, 32 OA	100	OA: 58.9(36-72)	MUIS-C	relationship satisfaction, functional disability, average pain, caregiver burden, partner supportive behaviours, pain	1) t-test 2) correlations 3) multiple regression	1) FM significantly higher uncertainty p<0.001 2) no significant association of uncertainty with any of the variable 3) under high uncertainty and pain, low levels of support related to poorer satisfaction in FMS only (p<0.05)

SLE: systemic lupus erythematosus; RA rheumatoid arthritis; OA osteoarthritis; FM fibromyalgia

1.2.4.6.2 Causes/Sources of and Coping with Uncertainty in Chronic Conditions

Cancer: A literature review (60) of uncertainty in cancer concludes that uncertainty is related to limited or lack of information, to illness progression and treatment choices, and everyday life and coping with cancer. Lower levels of uncertainty were reported in another sample of breast cancer survivors with a longer-term survival time (average 12 years) (104). This led the authors to conclude that familiarity with their illness, as well as high levels of education and social support displayed in this sample, was linked with lower uncertainty, as supported by the UIT (74).

Similar findings were reported in a study assessing antecedents of uncertainty in a very small sample of prostate cancer patients (105). Authors reported significant relationships between illness duration and education level with uncertainty levels (105). Another study assessing a sample of young patients with diverse cancers including leukaemia, testicular, ovarian, Hodgkin's, and sarcoma [55] also provided support for the UIT antecedents (74). Findings comprised a negative association between social support and uncertainty levels [55].

A study assessing women 5 to 9 years post-breast cancer treatment further supports the UIT by displaying links between education levels, and symptomatology with uncertainty (106). Similar levels of moderate uncertainty were reported in a breast cancer sample with mean illness duration of 5 years (107). The study suggested a significant relationship between older age and higher levels of uncertainty (107).

The temporal decline of uncertainty after a breast cancer diagnosis has been suggested by other studies as well. In an 8-week assessment of uncertainty before and after breast cancer surgery, findings displayed a significant decline in uncertainty in both the mastectomy and lumpectomy patients, but no significant difference in the levels of uncertainty between the two groups of patients (108).

Assessing women undergoing breast cancer diagnostic biopsies, levels of uncertainty were reportedly significantly higher upon notice and before the biopsy than after the diagnosis (109). In this study, uncertainty was predicted by various demographic variables (including age, marital status and education level), family history, religious beliefs, and perception of cancer diagnosis probability.

Assessing the impact of a self-management intervention for a group of newly diagnosed cancer patients, authors reported reduction in illness uncertainty prior to radiotherapy (as measured by a 6-item ad hoc instrument), which was linked with lower

depression levels and less tension and anger after radiotherapy (93). Finally, a study assessing the benefits of an uncertainty management telephone intervention for breast cancer survivors (5–9 years post-treatment) reported significant reduction in uncertainty 20 months post-intervention, which was associated with improvements in cognitive reframing, cancer knowledge and coping skills (110).

Diabetes: A descriptive correlational study (90) reported a negative association of patient uncertainty, as measured with the Portuguese version of the USS (85), with motivation, suggesting the high uncertainty is associated with lower motivation to adopt a healthier lifestyle regarding diabetes treatment and management.

Heart Conditions: Two studies assessed the temporal decline of uncertainty following a cardioverter defibrillator implantation. Patients with life-threatening arrhythmias displayed no significant change of uncertainty before and 6 months after receiving pharmacological and implantable cardioverter defibrillator (ICD) treatment (111). Another study assessing ICD implantation reported no significant change in uncertainty levels before and 6 months after treatment (112). Symptom severity, emotional support and education level contributed to the variance in uncertainty in a sample of atrial fibrillation patients with a relatively short diagnosis period (113, 114). Notably differential health care providers also contributed to uncertainty (113).

A comparison of coronary angioplasty and bypass surgery (115) displayed higher levels of uncertainty in the angioplasty patients, suggesting a link between the choice of treatment and uncertainty which were also inversely associated with social support in both groups.

Multiple Sclerosis: In a study assessing patients with MS (116), higher level of uncertainty was directly associated with lower social support. However, this study (116) failed to report a significant moderating effect of uncertainty in the social support-depression relationship.

Parkinson’s disease: A study assessing uncertainty in Parkinson’s disease (117) reported a significant association between patients and caregiver uncertainty, as assessed by the MUIS scales (89, 118). Notably, the study (117) reported no significant relationship between patient uncertainty and symptom distress, but rather a strong predictive relationship of patient uncertainty with caregiver depression and anxiety.

HIV: Finally, a study assessing patient uncertainty in men with HIV (119) reported a moderately negative association between uncertainty and social support and strongly

positive association between uncertainty hope.

1.2.4.6.3 Impact of Uncertainty in Chronic Conditions

Asthma: Two studies explored the impact of patient uncertainty on psychological distress in asthma patients. A moderate association of uncertainty with psychological distress was reported (120); however, this relationship was not significant when assessed via multivariate analysis. Contradictory findings were produced by another study (121) utilising the same measure of psychological distress. In this study (121), uncertainty was a significant predictor of poorer psychological adjustment after controlling for demographic and illness variables.

Higher levels of uncertainty were significantly associated with higher levels of depression; and they further suggested that this association was stronger in cases of increased illness severity, as illness severity is in turn associated with uncertainty symptom severity, emotional support and education level contributed to the variance in uncertainty (122). Uncertainty levels in another study however, did not display a significant association with depression levels but findings did reveal that uncertainty was a strong predictor of anxiety even after controlling for depression, demographic and illness variables (123).

Cancer: In a sample of breast cancer survivors of an average 5 years of survival, moderate levels of uncertainty were found to contribute to patients' quality of life (124). Findings comprised a negative association between social support and uncertainty levels and a strong positive relationship between uncertainty and psychological distress [55]. Studies assessing breast cancer survivors 5 to 9 years post treatment reported moderate levels of uncertainty (124) and suggest a significant contribution of uncertainty to psychological well-being (106) and levels of quality of life, (107).

Assessing newly diagnosed and women undergoing breast cancer treatment, heightened uncertainty levels were reported associated with anxiety (125) and emotional distress (126) in the respective studies. Levels of uncertainty in women undergoing breast cancer diagnostic biopsies, reported that uncertainty levels were moderately associated with anxiety (109). Reduction of uncertainty following a self-management intervention prior to radiotherapy was also linked with lower levels of depression, tension and anger after radiotherapy, suggesting a link between these variables (93). Uncertainty in this study was assessed with a 6-item ad-hoc instrument (93)

Diabetes: One study (127) reported a strong negative association of uncertainty with psychosocial adjustment in patients with diabetes, as uncertainty explained 43% of the variance in adjustment.

Heart Conditions: High levels of uncertainty in a sample of patients with acute heart failure were related with somatic awareness but, contrary to the study's hypothesis, were not predictive of delays in care seeking (128). Levels of uncertainty in a sample of patients with chronic heart failure presented a moderate positive association with tiredness (129).

Assessing uncertainty in a sample of atrial fibrillation patients with a relatively short diagnosis period revealed that uncertainty was only significantly associated with a threat and not an opportunity appraisal (114), which in turn contributed to mental health.

In a prospective study of patients undergoing coronary angiography (130), increased levels of uncertainty were associated with higher-anxiety depression and poorer control and quality of life, whilst baseline uncertainty independently contributed to quality of life up to 1 year post-angiography. A comparison of coronary angioplasty and bypass surgery (115) displayed higher levels of uncertainty in the angioplasty patients, whereas uncertainty was positively associated with stress levels.

Uncertainty levels in a sample of patients awaiting coronary artery bypass surgery were reportedly average (131) and associated significantly with symptom frequency and distress, but only weakly with anxiety. Discussing the lack of a strong uncertainty-anxiety link in their sample, the authors suggest that bypass surgery for many patients is a desirable treatment with probable positive outcomes and for these patients therefore, uncertainty is appraised as an opportunity. High levels of uncertainty were reported in a small sample of hospitalised patients after cardiac catheterisation (132) that were, as expected, strongly related with mood and anxiety levels.

Multiple Sclerosis: Quantitative studies assessing patient uncertainty in multiple sclerosis (MS) (116, 133-138) have indicated strong associations between uncertainty, psychological outcomes and adjustment. Two studies (136, 137) utilising multivariate statistics identified uncertainty as an independent predictor of psychosocial adjustment above and beyond the demographic, disability and illness variables.

Exploring the impact of uncertainty on depression, one study suggested that during MS exacerbations patient uncertainty levels are heightened and consequently increase depression and influence coping strategies (134). Another study reports that levels of uncertainty, together with hope and coping but not illness disability, predicted

depression in sample *of* patients with MS (135). There is, however, an estimated 88% of sample overlap between these two studies (134, 135).

High levels of uncertainty in an MS clinical trial were predictive of less hope about treatment effectiveness and poorer emotional well-being (138). In another study (116), higher levels of uncertainty were directly associated with significantly higher depression on a univariate level. Finally, a study with a very small sample size (133) reported a strong positive association between uncertainty and depression and a strong inverse association of uncertainty and optimism in MS.

Parkinson's disease: A study assessing patients with Parkinson`s disease (117) reported no significant relationship between patient uncertainty and symptom distress, but rather a strong predictive relationship of patient uncertainty with caregiver depression and anxiety.

1.2.5 Literature Review Discussion

The literature review revealed that patient uncertainty has been the subject of research across different disciplines and in many chronic conditions. However, the construct of patient uncertainty has rarely been explored comprehensively in a qualitative design, as many studies have addressed uncertainty loosely, referring to different aspects of the uncertainty experienced by patients. Despite its abstract identity, findings suggest that uncertainty is a key aspect of the illness experience worthy of further investigation, especially in complex and unpredictable conditions like SLE and RA.

The qualitative investigations indicate that patient uncertainty is concept with multiple dimensions often related characteristics specific to an illness (Tables 1.1 & 1.2). No explicit investigation of patient uncertainty was retrieved in either SLE or RA. However, findings indicate that patients with SLE and RA experience aspects of uncertainty that are specifically associated with their illness characteristics, e.g. the unpredictable flare-ups both in type and timing and the consequence of these on patient lives (31, 32, 34, 35).

Currently, the patient uncertainty literature is dominated by the Mishel Uncertainty Theories (UIT & RUIT) (73, 74) and the corresponding instruments of uncertainty (78, 89). Influenced by cognitive psychology theories (24, 75-77), the UIT and RUIT define uncertainty as a cognitive state in which a patient is unable to assign meaning to illness-related events and focus primarily on the sources and appraisal of uncertainty.

Many studies have investigated the sources and appraisal process of the UIT using the Mishel instruments (78, 89), providing significant support for the theory. Findings have identified potential sources of patient uncertainty including illness severity, health-care provider, demographic variables (e.g. age and educational level) as well as illness unfamiliarity (i.e. shorter duration of illness), social support and coping (29, 60, 94, 104, 113, 121). Findings further suggest the negative impact of uncertainty on outcomes such as psychological adjustment, depression, anxiety and quality of life (116, 121, 123, 132, 138), which is however in some cases only displayed on a univariate associational level, prohibiting any causal conclusions to be made. There is currently less evidence in SLE and RA (Table 1.4) to support these sources and impact of patient uncertainty

Less support has also been provided for the RUIT. Quantitative findings portray uncertainty as an aversive negative finding in chronic illness, hence challenging the RUIT, which argues for a reappraisal of uncertainty as an opportunity in chronic illness. Unsurprisingly, the RUIT has received less empirical support from research findings, as findings indicate the presence of high levels of uncertainty in chronic illness (44, 71, 134).

The UIT and RUIT (73, 74) constitute a very useful framework for investigating the sources and appraisal of patient uncertainty across the spectrum of any illness, acute or chronic. Nevertheless, illness-specific qualitative investigations of patient uncertainty indicate the inadequacy of these theories in capturing comprehensively what patient uncertainty means for each patient group. The UIT provides a prescriptive generic definition of patient uncertainty and does not allow for either group differences (i.e. between different illness conditions) or individual differences in the experience of uncertainty.

Even though the empirical qualitative investigations of uncertainty are limited (34, 53-56), they indicate important characteristics of patient uncertainty neglected by Mishel-driven literature. Firstly, qualitative findings offer a differential perspective on uncertainty, focusing on the construct describing the different issues patients are uncertain about, as opposed to the UIT and RUIT (73, 74) and related literature which focus on the sources of uncertainty (82).

Secondly, qualitative investigations highlight the multidimensionality of the patient uncertainty concept, as well as its variability across different chronic conditions (34, 54-56, 59). Qualitative findings display how different illness characteristics, for example,

the illness course, illness contagiousness, differential treatment advice, and mortality risk, impose different dimensions of uncertainty between different illness groups that can prevail in all aspects of life (Tables 1.1, 1.2).

Similar to the theories, the Mishel Uncertainty in Illness Scales (MUIS) (78, 89) is the most commonly used instrument of uncertainty. The MUIS has been used in studies to provide support for the UIT across different conditions and further suggested the aversive nature of patient uncertainty on patients' psychological studies. The three other uncertainty instruments (85, 92, 93) retrieved have not been used by researchers other than those who developed them.

Despite its popularity, using the MUIS for assessing patient uncertainty chronic illness has drawbacks. Importantly, all of the 23 items of the MUIS-C (89), used to assess uncertainty in outpatients suffering from chronic illness, were derived from the original MUIS (78). As such, the MUIS was originally developed and validated using interviews and data from hospitalised patients, and is an instrument developed to target acute uncertainty. The MUIS-C merely excludes the MUIS items which are specific to inpatients. In other words, the applicability of the content of the MUIS-C to chronic illness is questionable (139). This could potentially explain findings reflecting a much higher degree of uncertainty in women with an acute illness, compared with a chronic illness (79).

A variety of different definitions and conceptualisations of uncertainty are available, both across disciplines and across illness groups. These are not mutually exclusive (40, 88) and equally not comprehensive or applicable to all chronic conditions. The presence of uncertainty in chronic illness is evident, as is the multidimensional and complex nature of the construct, indicating the need for illness-specific assessment. Assessing the up-to-date literature, two gaps have been identified in relation to patient uncertainty in SLE and RA. Despite the popularity of the UIT/RUIT theories (73, 74) and the subsequent instruments, findings indicate the lack of a comprehensive conceptualisation of patient uncertainty applicable for SLE and RA and subsequently the lack of an adequate instrument to assess this construct.

Similar to all literature reviews (51), conclusions are limited to the studies identified, which are consequently a product of the search strategy and exclusion criteria. The only specific illness conditions within the search terms were SLE and RA and, thus, the review has potentially failed to identify literature specific to other illness groups. Nevertheless, the review and its conclusions are comprehensive in relation to the

literature of uncertainty experienced by adult patients with SLE and RA who are the focus of this thesis and the purpose of conducting this review. It is further acknowledged that the use of alternative search operators could have resulted in additional and/or different literature being discovered. For example, using adjacency operators could have improved the efficiency of the literature search; however, a more inclusive search strategy was considered more appropriate for the content and purpose of this review (51).

1.2.5.1 Literature Review Conclusion

There is currently no consensus on a comprehensive definition of patient uncertainty applicable to all conditions. Nevertheless, findings across different chronic conditions portray uncertainty as an aversive event and suggest its association with other outcomes in chronic illness such as mood and adjustment (42-44). Assessing patient uncertainty can therefore be useful in chronic illness research and management and specifically in SLE and RA. Achieving this requires comprehensive conceptualisation of uncertainty in these two conditions, which would lead to its appropriate quantification (82).

This is vital as the existing instruments (73, 74, 78, 85, 89) suffer from content validity limitations. Subsequent research findings (54-56, 85, 140) have challenged the sufficiency of the items within these instruments to comprehensively represent the construct of uncertainty in chronic illness. This is expected as none of these instruments was developed on an evidence based conceptualisation of patient uncertainty, whereas the MUIS (78) was developed using data from hospitalised patients which were then revised to adapt the scale to chronic outpatients with no further empirical validation.

Qualitative studies across different conditions demonstrate this unsatisfactory content validity and the lack of a comprehensive conceptualisation of patient uncertainty by the instrument developers. Contrary to the existing definitions (Table 1.3) qualitative studies (Table 1.1) reveal the multi-dimensional nature of the uncertainty construct and further highlight the differences between the uncertainty dimensions experienced across different chronic conditions. Specifically, studies in SLE and RA (Tables 1.1 & 1.2) reveal dimensions of patient uncertainty relevant to these patient groups which are not addressed by the existing instruments or conceptualisations.

An empirically developed instrument in SLE and RA would allow for the sufficient quantification of patient uncertainty further empirical assessment of patient uncertainty in these conditions to take place. In the following section, the rationale and methodology of quantifying patient variables such as patient uncertainty are outlined.

1.3 Justification for Thesis Methodology

Patient uncertainty is essentially a subjective patient-reported variable that cannot be directly observed or measured like other clinical variables of disease. Therefore, quantification of patient uncertainty is neither simple nor straightforward. The increased attention granted to patient-reported variables has led to improvements in the assessment of patient-reported variables and the advancement of psychometric methods (139, 141-144). To this effect, an overview of the history of the use of patient-reported variables is provided, followed by an overview of the "gold standard" methodology for developing and evaluating self-report instruments, which are developed to quantify patient-reported variables.

1.3.1 Patient-Reported Variables

Patient variables refer to any construct associated with a patient's health status that is reported directly by the patient without any interpretation or input by a clinician or anyone else (139). Such variables can take the form of symptoms (e.g. pain, fatigue), functionality (physical, psychosocial), feelings (e.g. worry, anxiety, depression), satisfaction with treatment/care, adherence to treatment, and patient perceptions and beliefs about their illness, such as uncertainty, which is the focus of this thesis.

In the past four decades, interest in patient-reported variables has increased dramatically for a variety of reasons. Theoretically, the narrow definition of health in terms of morbidity and mortality has long been discarded. The World Health Organization (WHO) (145) proposed a redefinition of health as a "complete state of physical, mental, and social well-being and not merely the absence of disease or infirmity". In practice, the prevalence of chronic incurable conditions (e.g. rheumatoid arthritis, multiple sclerosis, heart failure) has increased dramatically (146, 147), resulting in complex and multi-dimensional impact on patients' lives. As a result, assessment in chronic conditions has extended further from the traditional parameters of clinical morbidity and mortality to include health outcomes important to the patient.

A shift towards a more patient-centred approach in the delivery of health care (148, 149) has also taken place, focusing further attention on patient outcome variables. In the early didactic models of health care, patients were considered to be passive

recipients of medical information without the necessary knowledge or judgement to participate in their medical care. As early as the 1950s the patient-centred approach was introduced arguing for a mutual participation model of care (147, 149). In this model, patients are considered to be active processors of the information presented to them. To this effect, the didactic style of care is gradually eliminated as clinicians are advised to adopt the role of educators and facilitators whilst promoting information exchange.

This shift in health care has further led to the acknowledgement that patients are the experts of their condition, possessing unique knowledge and experience on it, especially if the condition is chronic (147, 149). Accessing patient variables can therefore provide valuable information for researchers and clinicians which would be otherwise missed, such as expectations of treatment and patients' perspective on the effectiveness of treatment (139) in clinical trials.

In line with the above and the WHO's integrative definition of health, the bio-psychosocial model of illness was proposed by George Engel in 1977 (150). The bio-psychosocial model extended the biomedical model of illness in which disease activity and adjustment were thought to be (151-153) influenced directly and only by clinical variables, which did not sufficiently capture illness according to Engel (150). Expanding this dualistic perspective, the new model postulated that health and illness are products of the interaction between a variety of variables, including biological characteristics (e.g. genetic predisposition), psychological and behavioural variables (e.g. stress, lifestyle), and social influences (e.g. culture, doctor-patient relationship). Within this perspective, patient outcome variables are considered both important outcomes as well as moderators of health and illness (147, 154, 155).

Encompassing this perspective, the bio-psychosocial model of rheumatoid conditions has been proposed (Figure 1.2) (155). It postulates that patient outcome variables such as affect, coping strategies, psychosocial functioning, and stressors dynamically impact on neuroendocrine function and consequently indirectly influence both physical adjustment but also disease activity (155). The model is supported by the literature in RA, indicating that patient outcomes such as cognitive appraisals (including stress or positive perceptions) (156-159) as well as psychosocial factors (160, 161) impact on physical functioning and indirectly on disease activity (Figure 1.2).

Reflecting on the above developments, patient outcomes are now at the heart of the agenda for clinical research, practice and trials (139, 162-164). In the 2008 Department of Health vision report for the National Health System (NHS), patient outcome variables

are explicitly recommended as a means of improving care quality (163). The report suggests that effectiveness of care should be assessed via patient well-being and outcomes such as pain, functionality, depression, and work disability, and further recommends that the patients' views on treatment success should be assessed. In the past two decades an increasing body of the literature has focused on patient outcome variables in RA and SLE. This will be discussed further in Chapter 2.

Figure 1.2 Bio-psychosocial Model of Adjustment to Rheumatic Conditions

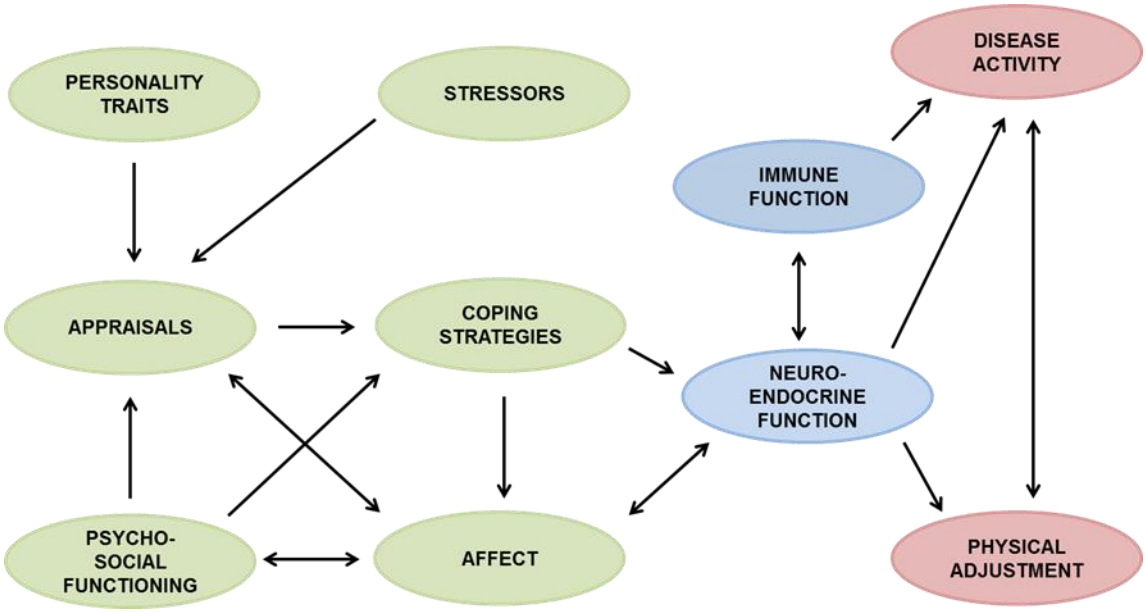


Figure 1.2: *The bio-psychosocial model of adjustment to rheumatic condition proposed by Walker et al. 2004 (155). Stressors including patient perceptions ultimately contribute to disease activity and physical adjustment through interactions between psychosocial and neuroendocrine variables.*

1.3.2 Self-report Instruments

Increased interest in patient-reported variables has also increased attention on the research and literature concerned with the assessment of patient variables. Patient-reported variables are latent unobservable constructs (165, 166). They tend to have a complex and abstract nature, as opposed to the concrete nature of the traditionally assessed clinical outcomes in health care (e.g. lab results & scanning images). As such, patient-reported variables can only be assessed indirectly through observable indicators in the form of measures, rating scales, questionnaires or instruments (141, 142, 165, 166).

Therefore, patient-completed or self-report instruments are measures of any latent variable related to a patient's health that is assessed directly by the patient, without the interpretation or guidance of a physician or anyone else, with the use of observable indicators (139). The terms *questionnaire*, *rating scale* and *measure* are used

interchangeably in the literature to refer to instruments that assess patient-reported variables (141, 142, 167). For the purposes of this thesis the term *patient-reported instrument* will be used.

Instruments comprise observable indicators (items) rated by respondents and scored to quantify variables. Single or multiple indicators (items) can be used for the quantification of variables. However, multi-item instruments are usually preferred, as single items are liable to several scientific limitations (139). Specifically, single items are liable to limited representative power over the scope of a variable, inconsistent interpretation between respondents, and limited discriminating ability between different levels of the variable, and are generally prone to random error as they fail to produce consistent responses over time, indicating they are unreliable (168).

Different rating methods can be used for scoring multi-item instruments (139) with typical response options, e.g. Likert-like scales and Visual Analogue Scales. In Likert scales, all items are scored independently on response scales comprising an ordered set of discrete terms/statements that have no right or wrong answers, with respondents being asked to choose the response option that best describes their state or experience (139). Total scores for Likert scales are then calculated by summing the scores of all individual items without weighing to produce the total score (169, 170). Less common than the Likert scales are checklists, event logs, pictorial scales, and VAS, which can also be used for assessing patient outcome variables (139).

1.3.2.1 Self-report Instruments: Type and Kind

As patient-reported variables cannot be measured directly, the process of developing self-report instruments is not clear or explicit, as different types of instrument are available, often measuring the same patient variable (141). These can be classified into two distinct approaches of patient-reported measurement (141, 171, 172): the standard needs and the psychological processes approach.

Standard needs is the most popular and conventional approach (141, 173). It is based on the notion that although patient-reported variables are unobservable, they do represent objective characteristics of an individual. The approach advocates that there is a standard set of needs that all individuals require for optimal functioning. Within the standard needs approach, therefore, it is assumed that unobservable variables such as health-related quality of life comprise a standard set of needs that are applicable to all individuals (172).

In contrast, the psychological processes approach considers patient variables as the product of individual subjective perception of life circumstances, which are influenced by an individual's psychological status. This approach operates on the assumption that patient variables vary between individuals and are the subject of subjective salient aspects of life (172).

There are different kinds of standard needs instruments that vary in relation to the specificity of their content. These include generic and disease/condition-specific instruments, site-specific (relating to a specific part of the body) and dimension-specific (relating to a specific dimension within a patient variable) instruments (141). In contrast, the psychological process approach argues against the use of instruments with pre-determined content and advocates for the use of "individualised" measure such as the Schedule for the Evaluation of Individual Quality of Life (SEIQoL) that allows individuals to nominate aspects of quality of life that are important to them (174).

Although individualised measurement achieved via the psychological processes approach could potentially benefit from higher applicability and validity, it suffers from important disadvantages, mainly a lack of practicality and comparable data between patients (141, 173). In this thesis, a standard needs approach is used for the development of a patient uncertainty instrument specific to SLE and RA.

Generic instruments, assessing variables across conditions such as the health-related quality of life MOS (SF-36) (175), benefit from comparable measurement across different illness groups. On the other hand, disease-specific instruments of health-related quality of life benefit from the inclusion of concepts that are not captured by the generic instruments. For example, the SLE-specific quality of life measure SLEQOL (176-178) covers issues of body image and sexual life that are important to patients with SLE, but are not included in the MOS (SF-36). Disease-specific instruments can therefore assess a variable more precisely (179-181).

1.3.2.2 Developing the Content of Self-report Instruments

An explicit comprehensive conceptualisation of the variable under quantification is fundamental in developing a new instrument. The so-called conceptual development approach aims to thoroughly describe a latent variable and identify the concepts and domains that are important to patients and should therefore be incorporated in the instrument (139, 182).

Guidelines for rigorous conceptual development methods (139) recommend the use of

both top-down and bottom-up approaches for developing conceptual frameworks of latent variables. Top-down approaches refer to deductive methods involving the review of existing literature and measurement methods, whereas bottom-up approaches refer to inductive methods involving the empirical exploration of the latent variable within the relevant illness populations and equivalent health care experts. Such explorations are completed within the target context and population group of a new instrument. The conceptual framework of a latent variable forms the basis of the item generation and the choice of recall period and response scale for the instrument.

Failure to achieve a sufficient conceptual framework challenges the adequacy of an instrument to quantify the latent variable it intends to measure (139, 143). This is not a unique characteristic of instruments that aim to quantify latent variables. As Hobart and Cano (2009) noted, any form of measurement, latent or direct, relies on the adequacy of the instrument used to measure it. Whether the subject of measurement is weight, height, or a health variable, measurement is achieved by the use of an instrument that reacts to the variable's measurement properties and provides an interpretable quantified outcome (142).
Upon completion of the conceptual framework and subsequent item generation, development of an instrument is completed by qualitative pre-testing of the items. Qualitative item pre-testing aims to assess ambiguities in the item wording, confirm relevance, determine acceptability, and estimate completion time (139, 183). Item pre-testing is completed within a sample and context representative of the population the instrument is intended to be used in.

The conceptual framework of a patient variable is the foundation on which the content of an instrument is based, as it underpins the item generation, the time frame and response scale choice (139, 182). An explicitly and comprehensively defined conceptual framework is therefore vital in the development of a new self-report instrument. Additionally, guidelines indicate that the target population and context of use of a new instrument should be explicitly stated and accounted for in the development process (139, 162).

1.3.3 Evaluating Self-report Instruments: Psychometrics

Self-report instruments have traditionally (165, 184) been evaluated using psychometric methodologies. The discipline of psychometrics stems from psychophysics and the assessment of subjective judgements as a form of valid measurement (185, 186). Psychometric evaluation assesses the extent to which any type of instrument successfully quantifies the variable being measured (187). Different

psychometric methods exist, each using a different range of evidence to evaluate the extent to which an instrument has successfully quantified a latent variable (141, 142). The key traditional psychometric approaches are underpinned by the Classical Test Theory; however, more recently, modern psychometric techniques have been introduced, including the Rasch Measurement and the Item Response Theories (141).

1.3.3.1 Traditional Psychometric Methods

The traditional psychometric methodology used in developing and evaluating instruments is supported by the Classical Test Theory (CTT) (188, 189). CTT is based on Spearman's 1904 definition of true and error scores for the measurement of reliability (190), and operates by testing raw scores against assumptions underlying its measurement theory (141). The role of CTT in psychometric statistical testing was only established in the 1960s (188). Steven's (191) definition of measurement as "the assignment of numerals to objects or events according to some rule" further helped cement the CTT role in psychometrics.

The CTT assumptions describe the errors of measurement that can influence the quantification achieved by instruments (142, 192, 193). The first assumption concerns the existence of a theoretical true score (T) being constant and unobservable, as well as the existence of variable random and unsystematic error (E). The CTT proposes that in measurement a person's observed (O) score is the sum of their true and error scores, i.e. O = T+E. As the true score is assumed to be constant, whereas the error varies, the observed score is expected to vary as well.

The second assumption relates to multiple administrations of the same measurement to the same person. It postulates that the mean of observed scores across the multiple measurement administrations is equal to the theoretical true score. The third assumption postulates that the error and true scores are not correlated; thus, the error is not related to the observed score. The fourth assumption suggests that error scores between scales, completed by the same person, are not related. The fifth assumption postulates that error and true scores between different scales are uncorrelated.

Psychometric evaluation is primarily achieved through the examination of the distribution of raw scores and the use of correlational analyses (188). These psychometric properties include data quality, scaling assumptions, targeting, reliability, validity, and responsiveness (194-197) and will be explained in detail in Chapter 4. If testing of raw scores derives reasonable assumptions, measurement is considered to be reasonable; if raw scores do not meet the assumptions, measurement is considered to be sub-optimal and faulty.

However useful the CTT has been in the study of psychometrics, it suffers from some fundamental limitations (142). Primarily, being that the true (T) is unobservable and theoretical, this subsequently prohibits testing of the CTT model (192). In other words, O = T+E, cannot be tested or falsified and, therefore, the criteria for success can easily be considered met by most data sets. For this reason, CTT has also been characterised as the Weak True Score Theory (142, 189), as it fails to define a mathematically testable equation of the observed, true and error scores (188), which could lead to rigorous psychometric testing of a dataset.

Another key limitation of CTT and traditional psychometric methods is that ordinal data resulting from Likert-like response scales are treated as interval level data (141, 142, 198). This results in two false assumptions: (i) that the "distance" between response categories is consistent within and across items, and (ii) that the "distance" between total scores is the same across the continuum of a scale (141, 142, 198).

Additional limitations include instruments being scale and sample dependent. A person's measurement is dependent upon the instrument used and the relative levels of the latent variable in the sample, the person is being tested within (141, 142, 199). Similarly, scale properties such as reliability and validity are not consistent, as they are sample-dependent, as are the score distributions (141, 142, 199). Due to these limitations, individual assessment is prohibited (200).

Lastly, traditional psychometric methods do not provide a scaling of items, whereby items can be mapped out on a measurement continuum of lower to higher measurement difficulty (142, 201). For example in a hypothetical instrument assessing mobility, an item assessing ability to walk for 100 meters would consistently be less difficult than an item assessing ability to walk for 300 meters. In other words, traditional psychometrics do not provide scales with specific item parameters that are consistent across samples (141).

Regardless of these limitations, traditional psychometric methods are the conventional and most popular approach in evaluating performance of self-report instruments (143, 144, 202, 203). Furthermore, traditional psychometric analyses are recommended by the Food and Drug Administration (FDA) as the minimum criteria for scientific adequacy for the evaluation of self-report instruments (204).

1.3.3.2 Modern Psychometric Methods

Following the development and extensive use of traditional psychometric methods, two new approaches were put forward: and Rasch Measurement Theory (RMT) (205, 206) and Item Response Theory (IRT) (207, 208). Both the RMT and IRT propose measurement models that define how scores generated by any sort of instrument relate to true measurement. These theories comprise testable mathematical models which can be utilised to both verify and refute the measurement properties of rating scales comprising the instruments under investigation (142). Therefore, a key limitation of the traditional psychometric methods is addressed by the modern theories that have enhanced the psychometric methodology (141, 142).

Both RMT and IRT paradigms can be traced back to Thurstone' s measurement requirements (142, 209-212) including: (i) items of a rating scale should define and be located on a measurement continuum marking different levels of the latent variable of interest; (ii) rating scales should measure clearly defined single variables of things or people; (iii) rating scales should measure a latent variable on an interval-level scale; (iv) the performance of a scale should not be influenced by the sample; and (v) the measurement of a person should not depend on the scale used, i.e. a person should present the same levels of a latent variable regardless of the means used to assess that variable.

Reflecting these requirements, modern psychometric methods postulate mathematical models that describe a person's true measurement on the latent variable measured by a scale (i.e. a person's location on an interval-level scale). They postulate that the probability of a response to an item is a function of a person's location on the measurement continuum and the scaling item parameters. In other words, modern psychometrics postulate that instruments assess latent variables which comprise different measurement levels of a trait (e.g. higher and lower levels of mobility). These traits are assessed against a range of item parameters that can be marked on a measurement continuum at different levels of difficulty with regard to the trait. For example, a "running" item would be more difficult than a "walking" item. To this effect, a person's expected response to an item is related to his/her trait levels in combination with the difficulty of that specific item. Below a brief overview of RMT and IRT is presented. As RMT is the selected modern psychometric paradigm for this thesis, it is described in more detailed than the IRT.

1.3.3.2.1 Rasch Measurement Theory (RMT)

RMT was developed by Georg Rasch, a Danish mathematician, to address individuals' reading abilities (206). Arguing that social measurements need to conform to invariant comparison, like physical measurements, Rasch proposed a simple logistic model to describe dichotomous measurement that was originally applied in education and psychology and has been known as the Rasch model (141, 142, 206). The model postulates that the probability of a positive response to a dichotomous (yes/no) item is a logistic function of the relative difference between the respondent (person) location and the item location on the measurement continuum (Figure 1.3).

Figure 1.3 Rasch Simple Logistic Model

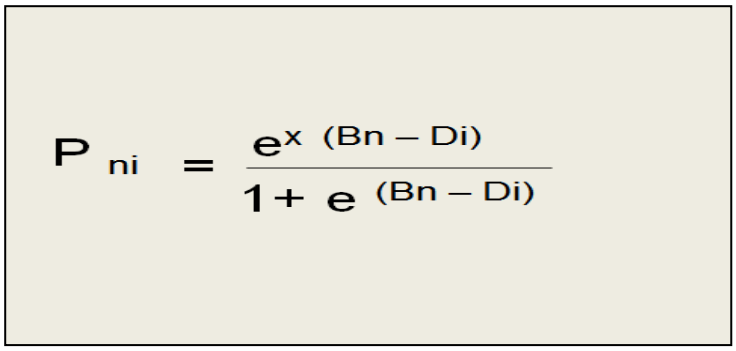


Figure 1.3: *The probability (P) of a person (n) to respond (x) to item (i), where B = the location/ability of a person; D= location/difficulty of an item and x = response 1 for yes and 0 for no.*

The model is applicable for use in polytomous data, as "x" reflecting the response option in the numerator (Figure 1.3) can be extended to values beyond 0 and 1, to reflect multiple response options, e.g. 0, 1, 2, etc. (142). In the late 1970s, David Andrich extended the Rasch model into the rating scale model (213) using odds and probabilities. In the rating scale Rasch model, the odds of a "yes" response correspond to the probability of a "yes" response divided by the probability of a "no" response. This leads to a natural logarithm where the person and item locations are additive in log-odd units (logits), thus transforming scores into an interval scale (Appendix 1.4) (142).

The RMT paradigm has two fundamental components (141, 142, 205). Firstly, within the Rasch model the probability of a response is considered to be a logistic function of the difference between the person and the item parameter. In other words, the model postulates that the higher a person's ability with respect to the difficulty of an item, the higher the probability of a positive response. The expected response is therefore defined by the location of a person and an item on the trait measurement continuum. Secondly, RMT proposes invariance in the sense that the relative location of any person on the measurement continuum should be unrelated to the items used to make

that comparison. Similarly, the location of any two items should be unrelated to the persons used to respond to the items and make the comparison.

Applying the logistic functions, RMT defines how a set of items should perform to generate reliable and valid measurements (205). Effectively, RMT analysis examines the extent to which the observed raw data (responses to scale items) 'fit' predictions of the responses expected by the Rasch model. Assessing the expected and observed scores indicates the degree to which the summing of scale items results in rigorous measurement, i.e. whether the latent variable in question has been successfully measured. Assessment is performed using Guttman (214) probabilistic scaling to define expected scores and a variety of fit statistics (215).

1.3.3.2.2 Item Response Theory (IRT)

The IRT approach (207, 208) also involves mathematical models in an attempt to explain observed rating scale data and describe the relationship between a person`s ability and his/her response to a rating scale item. The simplest logistic model within the IRT is the same as the Rasch model concerning a person's location relative to an item's difficulty. However, unlike the RMT, the IRT proposes additional measurement models with more parameters in an attempt to explain the observed data that fail to satisfy the criteria of the single (one parameter) logistic model (142). The most popular ones are the two parameter models (2P), which add the item discrimination parameter (216, 217), and the third parameter models (3P), which add the item guessing parameter (216).

1.3.3.2.3 Rasch Model vs the Item Response Theory

Despite the similarities of the two new psychometric approaches, they are characterised by a fundamental difference, which is key in scale evaluation. In theory, when observed data scores do not fit the expected ones predicted by the mathematical model, the IRT gives primacy to the data, whilst RMT analysts give primacy to the mathematical model (142, 218). With regard to Thurstone' s work, proponents of the IRT acknowledge the importance of mathematical models in social measurement, whereas proponents of the RMT paradigm acknowledge that measurement needs to conform to Thurstone' s requirements (209-212).

In practice, analyses within the IRT paradigm attempt to find a model that fits the observed data, whilst RMT proponents attempt to explore the data and construe the disparity between expected and observed scores of an evaluated scale further (142). Within the RMT paradigm, scales and/or constructs are modified and more data are

collected if necessary when evaluating the measurement properties of instruments. In this respect, RMT analysis can be utilised as a diagnostic tool for evaluating rating scales and was therefore selected as the modern psychometric methodology in this thesis, the details of which are presented in Chapter 4.

Therefore, even though both RMT and IRT operate using a mathematical testable model, the IRT is a statistical modelling paradigm which aims to find the best model to fit the data; whereas the RMT is a diagnostic paradigm which aims to find the strongest items and identify anomalies as compared to the RMT model (219, 220). Considering the exploratory nature of this data analysis, the RMT was the chosen paradigm so as to find the most meaningful items and assess their measurement properties.

Additionally, the RMT addresses all of the limitations of traditional psychometrics. Firstly, the Rasch model paradigm offers a testable model that can be utilised to verify the measurement properties of scales rigorously (141, 142, 205). Secondly, the Rasch model enables the development of linear interval-level measurement on the basis of ordinal-level raw data (221, 222). Thirdly, within the Rasch model, item and person location estimates can be provided (201) and this can lead to adaptive testing through the use of item subsets to reach measurement (223). Fourthly, RMT enables individual-level measurement (205, 224).

Nevertheless, the complexity of the RMT, in terms of understanding both the mathematical theory which underpins it as well as the additional requirements involved with gaining competence in a new technique, has challenged its popularity so far (141, 142, 225-227). Criticisms of the RMT relate to its overly restrictive and inflexible nature and its limited ability to address only one-dimensional data (141, 142, 225). Remarkably, these criticisms guarantee the scientific rigour of the RMT as a psychometric paradigm.

1.3.3.3 Evaluating Self-report Instrument Conclusions

Traditional psychometric methods have provided a useful and conventional framework of developing and evaluating self-report instruments. Nevertheless, the CTT underpinning traditional psychometrics is a theoretical non-testable theory comprising assumptions that are usually easily met by scale data.

Consequently, utilising CTT could potentially lead to weak conclusions regarding the psychometric properties of instruments. The Rasch model is more restrictive, complex and time-consuming than traditional psychometrics; but it does however, it address all

the major limitations of traditional methods and is therefore the chosen paradigm for the psychometric evaluation of this thesis.

1.4 Thesis Aims

Following these conclusions the thesis was planned around the exploration of patient uncertainty in patients with SLE and RA and the development of a patient-reported instrument to quantify it. Specifically, this thesis aimed to:

(i) develop a conceptual framework of patient uncertainty in SLE and RA using a bottom-up approach of patient and expert qualitative interviews, in addition to the top-down literature review presented in Chapter 1.
(ii) develop the content of a new patient uncertainty self-report instrument on the basis of the conceptual framework.
(iii) evaluate the newly developed self-report instrument within the modern psychometric paradigm of Rasch Measurement Theory
(iv) explore the contribution of patient uncertainty in HRQoL, mood and treatment adherence in SLE and RA.
(v) provide recommendations regarding the patient uncertainty research in SLE and RA.

Chapter 1 has presented the background and justification of exploring patient uncertainty, and further outlines the importance of developing psychometrically sound self-report instruments. Chapter 2 provides an overview of the two target patient groups, aiming to set the background of the two conditions being researched, and further justifies the exploration of patient uncertainty in SLE and RA. Three empirical phases were set up to address the aims of the thesis presented in Chapters 3 to 6. Chapter 3 presents qualitative methods and results for the conceptualisation of patient uncertainty in SLE and RA, as well as the item generation and initial qualitative evaluation of the new patient-reported uncertainty instrument.

Chapter 4 presents methods and results of the initial psychometric evaluation and scale development of the new patient-reported instrument in the first field test. Chapter 5 presents methods and results of the second field test, outlining the psychometric evaluation of the instrument revised in Chapter 4. Chapter 6 presents additional methods and results of the second field test, exploring the contribution of patient uncertainty, as quantified by the newly developed instrument, in important patient outcomes such as treatment adherence, mood and HRQoL. Chapter 7 presents a general discussion of the thesis findings and recommendations of future research.

1.5 Chapter 1 Summary

This chapter has provided a literature review, which was conducted in preparation for this thesis, and reviewed the scientific and methodological justification of this research. Findings suggest the key role and potential of patient uncertainty in the illness experience, particularly in chronic incurable conditions of an unpredictable course like RA and SLE.

Empirical explorations of patient uncertainty support its multi-dimensional nature and diverse presence in all areas of life, highlighting the diverse aspects of uncertainty experienced across different illness groups. The literature indicates the disease-specific aspects of uncertainty experienced by patients with SLE and RA. Nevertheless, the construct of patient uncertainty in RA and SLE has not been comprehensively conceptualised; therefore, no applicable instrument is available for its quantification. Investigation of patient uncertainty in RA and SLE would therefore require further exploration of the concept and the development of a quantitative instrument for its assessment.

The importance of patient outcome variables is increasingly being recognised in the field of chronic illness. The exploration of a patient perception such as uncertainty is therefore in line with the government agenda and the general trend of research. Exploring variables which are latent is complex and complicated by their latent abstract nature. However, the rising interest in patient outcomes has also increased attention in the methodologies of patient-reported instrument development and evaluation, which were reviewed in this chapter.

Gold-standard guidelines for the development of patient-reported outcomes and their corresponding instruments involve the use of both top-down and bottom-up approaches for conceptualising constructs which are latent, such as uncertainty. Assessing the ability of an instrument to quantify the construct it intends to measure involves psychometric testing. The conventional psychometric techniques suffer from some limitations that have been addressed by newer methodologies. Comprehensive evaluation of a newly developed patient uncertainty instrument would therefore require both techniques.

Chapter 2: Target Patient Groups

2.1 Chapter 2 Overview

This chapter provides an overview of the two rheumatic conditions that are examined in this thesis, presenting information on diagnosis, epidemiology, clinical features, treatment, and general impact of SLE and RA on patients' lives. The overview is brief and does not attempt to present the literature exhaustively, but rather set the background of the two conditions being researched, whilst emphasising features of SLE and RA associated with uncertainty. In line with the bio-psychosocial model of illness discussed in Chapter 1, biomedical and psychosocial aspects of SLE and RA are presented. The literature presented in this chapter constitutes the basis for the exploratory research presented in Chapter 6.

2.2 SLE Definition

Systematic lupus erythematosus (SLE) is a chronic inflammatory autoimmune rheumatic disease that is multi-system, displaying a broad spectrum of clinical manifestations involving virtually any body organ or tissue. SLE is a complex condition of diverse clinical features linked with serological diversity and characterised by periods of disease remissions and exacerbations (i.e. flares). SLE may manifest mild disease, involving mainly the joints or the skin only, or it may potentially lead to severe and life-threatening organ involvement, notably of the kidney. The heterogeneity of SLE has led researchers to suggest that it could be best described as a syndrome of related disorders rather than a single disease (36, 228, 229).

2.2.1 SLE Diagnosis and Classification

There is no gold-standard test for SLE diagnosis (229), with the diagnosis relying heavily on clinicians' judgement. The revised 1997 criteria of the American College of Rheumatology (ACR) are often used for SLE diagnosis and classification (Table 2.1). Clinical diagnosis is reached when a person develops at least four of the eleven criteria simultaneously or serially during any interval of observation (230). The diagnosis is often made by a rheumatologist, based on the history, physical examination, and diagnostic test results. Due to the variety of clinical manifestations, physicians from other specialties may also be involved, e.g. nephrologists, dermatologists or cardiologists.

Ehrenstein and Isenberg (2004) (36) note that the criteria are primarily used for classification of a disease rather than as a firm diagnostic tool, as the diagnosis and assessment of SLE are complex and often blurred due to the variable clinical and

serological manifestation of SLE. Yazdany and Dall`Era (2013) also note that many potential manifestations are not represented in the ACR criteria, and also highlight the potential confusion over SLE symptoms that mimic other conditions, e.g. skin rashes (229).

Some patients with serological manifestations fulfilling some of the criteria, primarily arthritis and leukopenia, do not satisfy the diagnostic criteria of SLE. Such patients are given the diagnosis of “undifferentiated connective tissue disease”, which in approximately 1 in 4 cases evolves into a systemic disease (231). Alternatively, some patients meet the criteria for two or more autoimmune conditions and are said to have an overlap syndrome (229).

Table 2.1 ACR Revised Criteria for SLE

	Criteria
1	**Malar rash**
2	**Discoid rash**
3	**Photosensitivity**
4	**Oral ulcers**
5	**Arthritis**
6	**Serositis:**
	(i) Pleuritis or (ii) Pericarditis
7	**Renal disorder:**
	(iii) Protenuria >0.5g/24h or 3+ persistently or (iv) Cellular casts
8	**Neurological disorder:**
	(i) Seizures or (ii) Psychosis
9	**Haematologic disorder:**
	(i) Haemolytic anaemia or
	(ii) Leucopaenia or <4.0 x 10^9/l on two or more occasions
	(iii) Lymphopaenia or <1.5 x 10^9/l on two or more occasions
	(iv) Thrommbocytopaenia <100 x 10^9/l
10	**Immunological disorders:**
	(i) Raised antinative DNA antibody binding or
	(ii) AntiSm antibody or
	(iii) Positive finding of antiphospholipid antibodies based on (a) an abnormal serum level of IgG/IgM anticardiolipin antibodies (b) a positive test result for lupus anticoagulant using a standard method or
	(iv) A false positive serologic test for syphilis known to be positive for at least 6 months and confirmed by Treponema pallidum immobilisation or fluorescent treponemal antibody absorption test
11	**Antinuclear antibody in raised titre**

SLE diagnosis when at least four or more criteria are present, serially or simultaneously during any interval of observation

2.2.2 SLE Epidemiology

SLE is a worldwide disease, with a number of epidemiological studies having been conducted principally in Europe and the United States (232). In a comprehensive review of SLE epidemiological studies, the authors (233) indicated the considerable variability of annual incidence (per year) and prevalence across countries, reporting a higher trend in Europe (annual incidence range 2.15–27.7 per 100,000) (234-236) compared to the USA (annual incidence range 1.8–7.6 per 100,000) (237-240) and the Caribbean (annual incidence range 4.6–17 per 100,000) (241-243). A higher annual incidence of SLE is reported in urban than in rural areas (228), but differential rates between and within countries cannot be taken to indicate true geographical variability, as demographic and environmental factors influence SLE occurrence (232). Worldwide, 4 to 13 times more adult women than men are affected by SLE (244), which is thought to be more common in women of a reproductive age (15–44 years of age) (238).

Ethnicity has also been associated with variable SLE prevalence. Studies have reported approximately 1 in 4,300 Caucasians in New Zealand, 1 in 1,000 Chinese, and 1 in 250 Black women in the USA and the West Indies suffering from SLE, whilst the prevalence in Africa is thought to be rare (36, 245). Population demographics such as ethnicity, age and gender have been found to contribute to the occurrence of SLE in part, accounting for differences between countries and within countries (232, 233). In addition, the variability amongst epidemiological studies can also be attributed to differential methodologies used for recruiting and classifying participants amongst the studies (233, 246, 247).

2.2.2.1 UK Annual Incidence and Prevalence of SLE

Studies report the prevalence of SLE in England and Ireland as ranging between 12.5 and 27.7 per 100,000 cases (248-252). A closer look at the UK epidemiological studies reveals comparable findings between the studies, apart from the earliest one, estimating SLE prevalence in England and Wales to be 12.5/100,000 through secondary data from general practitioner practices and possibly missing secondary care cases (249). More recently, studies in Leicester (252), Nottingham (250), Birmingham (251), and Belfast (248) have utilised the 1982 ACR criteria to define reported SLE prevalence as 39, 24.6, 27.7, and 25.4 cases per 100,000 persons, respectively, whilst the 1989 Nottingham annual incidence rate was 3.7/100,000 (250) and the 1991 Birmingham rate was 3.8/100,000 (251).

2.2.2.2 SLE Aetiology and Pathogenesis

Although the pathogenesis of SLE is thought to involve a complex interaction of genetic and environmental risk factors, the exact cause of SLE remains unclear (247). It has been suggested that exposure to risk factors in a proportion of genetically predisposed individuals leads to the development of autoantibodies that lead to the development of clinical symptoms in some individuals (247). However, genetic susceptibility and the presence of autoantibodies do not warrant SLE development.

The mechanism of disease is driven by a number of immunological abnormalities that contribute to tissue damage and inflammation in different sites of the body (228). In brief, abnormalities include apoptosis (programmed cell death), cellular abnormalities including higher numbers of autoantibodies (proteins directed against host proteins), functional defects of T and B lymphocytes (cells of the immune system), and cytokine (signalling molecules associated with inflammation) regulation (36, 232). Outlining these immunological mechanisms in detail is beyond the scope of this thesis; however, it is important to note that their exact role in SLE remains unclear.

Autoantibodies precede clinical symptoms in 85–88% of patients with SLE (253, 254), the most common of which being antinuclear antibodies (ANA). ANA antibodies are not specific for SLE and can be found in other autoimmune conditions as well as in healthy individuals. Double-stranded DNA (dsDNA) antibodies, on the other hand, are specific to SLE and were present in 55% of the patients at diagnosis in one study (253). Anti-DNA antibodies have been linked with lupus nephritis (36, 255), but they are not a pre-requisite for its development. New autoantibodies continue to be identified, but whether these immunological abnormalities are primary or secondary to SLE pathogenesis remains unclear (36).

Other multiple risk factors have been associated with SLE aetiology, the dominant one being genetic predisposition (254). Studies have suggested that siblings of patients are 29 times more likely to develop SLE than of the healthy population (256). A complex trait of several genes (36) and several different chromosomes (257, 258) have been associated with genetic susceptibility. Specifically, the major histocompatibility complex (MHC) and the human leucocyte antigen (HLA) regions have been identified as potential contributors of SLE pathogenesis (259). Importantly though, concordance for SLE in monozygotic twins is approximately 30%, indicating the importance of non-genetic factors in the development of disease (254).

Gender is an important risk factor, as it is estimated that there are nine female for every male SLE patient (254), suggesting the importance of hormonal factors in SLE. Oestrogens, which are female sex hormones, are immunoenhancing, whereas

androgens (male sex hormones) are immunosuppressive, hence explaining the higher prevalence of SLE in females of a reproductive age (36). The use of exogenous hormones in the form of hormone replacement therapy or oral contraceptives has yielded contradictory results. Hormones have been associated with increased risk of developing SLE, but not with increased flare risk in patients with stable disease (260). The pituitary hormone prolactin has also been associated with increased immune stimulation and higher disease activity in SLE (261, 262). Finally, pregnancy may be associated with increased risk of disease flares, but sex hormone levels (i.e. oestrogen of progesterone) do not seem to be associated with this risk (228). It is considered likely that prolactin levels associated with pregnancy are associated with this risk.

Several environmental triggers of SLE have also been identified that are associated with initiation of disease (36, 228). Like exposure to toxins, such as crystalline silica from farming or trades, a chemical compound has been associated with development of SLE (263). More than 100 drugs have been reported to trigger drug-induced lupus (DLI) by inducing antibodies in patients such as single-stranded DNA antibodies (264). These include biologics and antihypertensive agents such as hydralazine that often trigger disease in patients with genetic predisposition (228).

Infectious agents or viruses are also assumed to act as triggers of disease through a process of molecular mimicry, where the host immune system attacks itself by mimicking the inflammatory process caused by exogenous infections, which destroys host cells and triggers immune responses (265, 266). The Epstein-Barr virus (EBV) has been reported as a potential trigger of SLE disease through interaction with B cells (228). Lastly, ultraviolet light sometimes triggers SLE exacerbations at the disease onset as well as in established diagnosis, by stimulating skin cells to secrete cytokines and encourage apoptosis (267, 268).

2.2.3 SLE Clinical Features

The clinical features of SLE are numerous and rather diverse, involving multiple body organs and systems that are not necessarily unique to SLE (Table 2.2). The main clinical manifestations are described below in accordance with the body organ or system they involve. In addition to the organ-system manifestation, patients with SLE commonly present constitutional symptoms (269) such as fever, fatigue, weight loss, and lymphadenopathy.

2.2.3.1 Musculoskeletal

The most common manifestation of SLE is arthropathy (36, 228, 270). In contrast to RA, joint involvement in patients with SLE is primarily non-erosive and non-deforming

arthralgia, but similar to RA it mainly affects small and medium-sized joints. Arthritis involving joint pain and inflammation is a less common manifestation that usually develops during flares and in a very few patients this resembles RA. The symptomatology reported by patients (mainly pain and stiffness) is usually heightened and not in line with the objective signs of disease, such as the degree of inflammation. More information on this issue will be discussed in section 2.2.7.

Tenosynovitis involving inflammation of tendons is a less common manifestation that can in some cases lead to tendon ruptures both on the arms and lower legs. Rarely, subcutaneous nodules on the hands may be found. Myalgia, general muscle weakness and tenderness are common in the majority of patients with SLE, although myositis involving inflammation to proximal muscles is relatively rare. Osteoporosis, osteopenia and fractures are relatively common in SLE, most likely caused by a combination of risk factors including chronic inflammation, disease activity, renal dysfunction, and corticosteroid use (270).

2.2.3.2 Dermatological

Skin lesions are very common in SLE, affecting as many as 90% (271). In fact, SLE takes its name from lupus, the Latin word for “wolf”. This denotes that the destructive effects of disease are similar to wolf bites (272). Lupus-specific dermatological skin lesions are divided into acute and chronic. Approximately one third of patients with SLE develop the “butterfly” rash that is found over the bridge of the nose and malar nose, which is acute and usually triggered by exposure to sunlight. Other acute lesions involve transient rashes following sun exposure which heal without scarring (272). Involvement of the mucus membranes is also common, affecting 25–45% of patients with SLE in the form of oral lesions, ulcers and, more rarely, nasal ulcers.

Sub-acute rashes have also been described, affecting 10% of patients with SLE and presenting ring-shaped red skin lesions that affect mainly shoulders, forearms, neck, and upper body, but not the face. Up to 25% of patients with SLE develop chronic rashes and are classified as discoid lupus erythematosus (DLE) patients. DLE is a differential diagnosis and not included in the studies of this thesis (36, 228).
Finally, alopecia, which is defined as exaggerated, initially reversible hair loss, is a common feature of SLE. It can involve the skull, eyebrows, eyelashes, and facial and body hair, but primarily occurs along the front hairline during periods of exacerbated disease activity (36, 228). When accompanied by scarring, alopecia is said to be SLE-specific (272). An estimated 60–69% of patients with SLE are estimated to be photosensitive (272) REF, eliciting skin symptoms.

2.2.3.3 Cardiovascular

The heart and lungs can be affected either directly by disease or indirectly as a side effect of treatment (273), with correct and early diagnosis being challenging. There are three types of cardiovascular lupus involvement: pericardial, myocardial and valvular. Pericarditis, involving inflammation of the membrane surrounding the heart, affects almost a quarter of patients with SLE (228, 273) and is the most common cardiovascular feature. Pericarditis effusions are usually asymptomatic, but can rather quickly develop into long-term scarring and thickening of the pericardium tissue (constrictive pericarditis) (36).

Less common than pericarditis, but more common than is sometimes suspected, is myocardial involvement, which is also more symptomatic. Myocardial disease includes unexplained tachycardia, fever, dyspnoea, congestive heart failure, arrhythmias, prolongation of the PR interval on electrocardiogram or cardiomegaly in the absence of pericarditis and valvular disease (36).

Valvular heart disease has been reported, but less frequently than other cardiovascular features. It is usually asymptomatic and is usually linked with antiphospholipid antibodies (273). The mitral and aortic valves are primarily affected by diffuse thickening, vegetation and stenosis. Frequencies of systolic murmurs recorded by diagnostic echocardiograms are not always reflective of valvular defects and can reflect hyperdynamic circulation secondary to chronic anaemia (36, 228).

In addition to the above, patients with SLE face increased risk of developing premature accelerated atherosclerosis, which is one of the leading causes of SLE mortality in established disease (274-276). The exact pathogenesis of SLE accelerated atherosclerosis remains uncertain, but multiple factors such as corticosteroid treatment, chronic inflammation, and elevated lipid levels are likely to contribute (36).

2.2.3.4 Pulmonary

SLE disease activity can involve both the lungs and the walls of the thorax (pleura). Inflammation of the pleura (pleuritis) is very common, affecting 45 to 60% of patients (228), manifests in either uni- or bi-lateral pain of the thorax (36) and is sometimes accompanied by pleural effusions.

Less common than pleuritis are restrictive lung diseases such as pulmonary vasculitis, pneumonitis and interstitial fibrosis, which affect less than 13% of patients with SLE (228). It is estimated that the cause of such pulmonary lesions can be directly attributed to SLE and not to other secondary factors in less than 2% of the cases (36). Other less

common, but potentially disastrous, manifestations include acute pneumonitis, pulmonary hypertension and pulmonary haemorrhage (273).

Some patients presenting with small lung volumes on radiographs manifest with progressive dyspnoea, a condition named “small lung syndrome”. It is a purely restrictive condition (273), likely to be a secondary manifestation of diaphragmatic dysfunction, and its symptoms can be easily misattributed to other pulmonary conditions.

2.2.3.5 Renal

Approximately one third of patients with SLE have renal involvement at the disease onset but the prevalence increases significantly whilst living with SLE, affecting as many as 78% of patients (228). Renal failure is one of the leading causes of SLE mortality (36, 274, 275, 277), with renal morbidity being a major cause of patient hospitalisations. Lupus nephritis can have multiple forms, as all four renal compartments may be affected (277).

SLE renal involvement can be assessed clinically and histopathologically (277). Clinical features of renal involvement are ankle swelling, shortness of breath and frothy urine, which only become apparent at advanced stages of renal damage. It is therefore important to monitor hypertension closely, as well as levels of protein in the urine and creatinine, which are less apparent features but can signify renal involvement. The exact pathology of renal involvement can be determined through a renal biopsy that can be used to classify renal lupus into six categories (36, 228, 277). There is currently no consensus on the optimal timing and value of renal biopsy in SLE that can be accompanied by complications (36), even though this is much less of a problem nowadays as most biopsies are done under ultrasound imaging.

2.2.3.6 Nervous System

SLE affects both the central (CNS) and the peripheral (PNS) nervous system and may cause psychological manifestations. Studies have shown the prevalence of nervous manifestation to be very wide, ranging from 6–91% depending on classification and diagnostic criteria (278). CNS constitutes a major source of morbidity, affecting more than half of patients with SLE in some cases (36, 228). The diverse non-specific manifestations and multifactorial potential contributors complicated the diagnosis of nervous involvement in SLE. Some of the manifestations on CNS involvement may be secondary features of infections, medication, metabolic disturbances, and sleep apnea (278).

Currently, the ACR 1999 neuropsychiatric SLE (NPSLE) diagnostic criteria are being used. These include 12 CNS features, including migraines/headaches, cognitive dysfunction, psychosis, aseptic meningitis, movement, and anxiety disorder, and 7 PNS features, including acute inflammatory demyelinating, neuropathy, plexopathy, and polyneuropathy. Up to 70% of patients with SLE are estimated to be suffering from psychiatric abnormalities such as depression and anxiety (36, 278), which are not necessarily part of SLE but may be a secondary consequence of living with a chronic condition like SLE. These issues will be discussed in more detail in section 2.4.2.2.

2.2.3.7 Haematopoietic

Haematological abnormalities are very common features of the SLE disease which are often the signs of disease pre-diagnosis (36, 228, 279). The most frequent abnormalities are leukopenia and lymphopenia, which indicate reduced levels of white blood cells and lymphocytes. Platelet deficiency is also found in SLE; idiopathic platelet deficiency can be the first sign of disease, whilst impaired platelet production is often a secondary manifestation related to SLE treatment.

Anaemia is present in up to 70% of patients with SLE. It is associated with raised levels of disease activity but normal levels of ferritin, whilst in some cases, renal involvement and NSAIDs treatment contribute to anaemia as well (36). Autoimmune haemolytic anaemia is reported in up to 5–14% of patients (36, 228, 279), whilst iron deficiency anaemia is also an SLE manifestation.

Anti-phospholipid syndrome is a combination of the presence of anti-phospholipid antibodies and blood clots (venous and arterial) or pregnancy losses, which affects 10–15% of patients with SLE (280). Anti-phospholipid syndrome is associated with serious manifestations such as deep vein thrombosis, strokes, heart attacks, and pregnancy complications.

2.2.3.8 Gastrointestinal

Gastrointestinal involvement is reported in approximately 25–40% of patients with SLE (281), but does not necessarily reflect primary disease activity as it may be a secondary manifestation of treatment. For example, dyspepsia has been reported by 11–50% of patients, and peptic ulcers discovered in 4–21%, but such ulcers could potentially be a side effect of non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroid treatment (36, 228).

Approximately one third of patients with SLE have abdominal pain, nausea and vomiting that could be related to NSAIDs and/or antimalarial steroid treatment (281).

Liver and spleen enlargement have been reported in 25% and 10% of patients respectively but they are rarely associated with function abnormalities (36, 228). Gastrointestinal vasculitis of small arteries is usually manifested in the presence of disease activity in other organs and can lead to pancreatitis to approximately 2 to 8% of patients (36, 228). Interestingly, anorexia is common, affecting 36–71% of patients (282), but has also been linked with medications (228).

Table 2.2 Frequency of SLE Clinical Features

Clinical Feature	%	Clinical Feature	%
Musculoskeletal		**Nervous System**	
Arthritis & Arthralgia	**76 – 95**	CNS damage	**26 – 59**
Myalgia	**5 – 79**	Peripheral neuritis	**1 – 21**
Dermatological		Psychosis	**4 – 37**
Butterfly rash	**34 - 61**	Seizures	**6 – 26**
Alopecia	**21 – 58**	**Haematological**	
Oral/Nasal Ulcers	**9 – 42**	Anaemia	**30 – 73**
Cardiovascular		Leucopenia	**41 – 66**
Pericarditis	**12 – 31**	Lymphadenopathy	**10 - 59**
Myocarditis	**3 – 8**	Thrombocytopenia	**7 – 30**
Hypertension	**25 – 46**	**Gastrointestinal**	**1 – 6**
Pulmonary		**Constitutional**	
Pleural effusion	**12 - 57**	Fever	**41 - 84**
Renal		Weight loss	**27 - 51**
Proteinuria	**31 – 53**	**Raynaud**	**18 - 44**
Nephrotic syndrome	**7 - 26**		

The range of cumulative annual incidence % reported in six studies (283-288) adapted from Hinojosa-Azaola & Sanchez-Guerrero (269).

2.2.3.9 Co-morbidities

Patients with SLE often present with other co-morbid conditions (36). Raynaud's affects as many as one third of patients with SLE. It involves vasospasms that restrict blood supply to body regions, primarily the fingers and toes, causing them to change colour, and can cause gangrene in extreme cases. Sjogren's syndrome is an autoimmune condition that manifests primarily in eye and mouth dryness. An estimated 10% of patients with SLE suffer from this (289). Auto-immune thyroid disease, usually hypothyroidism, is also common in SLE, affecting 5–10% of patients (36, 228). Although exceptional, an estimated 1 or 2% of SLE patients present with erosive

arthropathy, suggesting an overlapping diagnosis of SLE and RA (36, 228).

2.2.4 SLE Prognosis and Outcome Assessment

Treatment advances have led to advances in SLE survival rates (290), which have increased dramatically from 50% in the 1950s to over 95% at five years post-diagnosis (274, 291, 292). Nevertheless, mortality in SLE is still three to five times higher compared to the general population, particularly in patients under the age of 40 (274, 291). A bimodal mortality pattern has been reported associating early mortality (<2 years) to SLE disease activity and infections, and late mortality (>2 years) to atherosclerotic complications and organ failure (274, 275).

Disease severity varies greatly between patients, but in general the flare incidence per patient has been estimated at 0.65 per year of follow-up, and the annual hospital admission incidence at 0.69 per patient (228). It is further acknowledged that the disease- and treatment-related morbidity is not always clearly distinguishable.

Similar to other chronic conditions, efficient and accurate assessment of disease is key for the management of SLE (36). Over the past two decades, improvements have been made in the development of disease activity indices specific to SLE that assess reversible clinical or laboratory manifestations (293). Four of these assessment tools — the SLAM (294) (Systemic Lupus Activity Measures), the SLEDAI (295) (Systemic Lupus Erythematosus Disease Activity Index), the ECLAM (296) (European Community Lupus Activity Measure), and the BILAG (297) (British Isles Lupus Assessment Group) — have proven to be valid, reliable and sensitive to change over time (298). They are all clinician-completed measures. The first three of these are global score systems, whereas the BILAG is a more comprehensive measure as it is rated using the principle of the “physician’s intention to treat”.

In addition to disease activity, damage inflicted either as a consequence of disease or its treatment is also assessed by clinicians (293). To achieve this, the Systemic Lupus International Cooperating Clinics and American College of Rheumatology (SLICC/ACR) damage index (SDI) (299) was developed in consultation with 25 rheumatologists. The SDI is used to assess permanent and irreversible change, or damage, occurring after the diagnosis of SLE in 12 organs or systems.

Despite the breadth of information included in clinician-completed measures, they have failed to report a consistent relationship with patient-reported health-related quality of life (HRQoL) measures, thus suggesting that HRQoL measures provide information

important for the patients which is different from the clinicians' perspective on the impact of disease (300-302). HRQoL is a multiple domain concept referring to a patient's perception of the impact of an illness and its treatment on their physical, emotional and social functioning (303). Reflecting this, the international consensus conference on outcome measures in rheumatology (OMERACT 4) has recommended that HRQoL should be one of the three assessment outcomes in SLE (304) in addition to disease activity and organ damage. Findings related to HRQoL will be discussed in section 2.2.7.

2.2.5 SLE Treatment

SLE management is very challenging (305) and there are currently no specific guidelines for the initiation, dose and duration of pharmacological treatment in SLE. Providing a detailed overview of SLE treatment is beyond the scope of this thesis, but the four types of drugs used according to the clinical manifestation and individual case (37) are briefly outlined. Non-steroidal anti-inflammatory drugs (NSAID) are administered to manage arthralgia, the most common manifestation of SLE. Hydroxychloroquine, an NSAID anti-malarial, is administered to manage arthralgia, myalgia, fatigue, and rash. Patients with mildly activated lupus disease activity can be managed with a combination of NSAIDs and hydroxychloroquine.

When NSAIDs fail to alleviate symptoms and disease progresses to severe arthritis and organ inflammation (e.g. pleuritis or pericarditis), corticosteroids are administered orally, intramuscularly or intravenously. Corticosteroid treatment is always planned in conjunction with monitoring of potential side effects that are sometimes severe. Steroid side effects include infection, osteoporosis, diabetes, hypertension, cushingoid face, and insomnia, with supplements such as calcium and vitamin D sometimes being recommended to help reduce their risk and impact. Steroid dosage is further adjusted to control the risk and severity of side effects.

Immunosuppressant treatment such as azathioprine, cyclophosphamide or mycophenolate is used when arthritis, pleuritis and pericarditis are not responsive to steroids and in combination with steroids in cases of renal and haematopoietic lupus involvement. Immunosuppressant drugs are toxic and can cause severe side effects, such as nausea, bone marrow toxicity, liver dysfunction, haemorrhagic cystitis, infertility, and increased risk of malignancy. Similar to steroid treatment, regular monitoring is conducted and additional medications may be administered to control side effects.

Recently, a biologic agent, Rituximab, which is a genetically engineered antibody, has shown beneficial effects for SLE rashes, arthritis, serositis, and nephritis (306); however, like most other SLE treatments, it is not currently licensed for use in the UK. Renal and haematopoietic stem cell transplantation is required when pharmacological treatments fail to control disease activity.

In addition to the above, non-pharmacological measures are also recommended for the management of SLE (37). As in any other conditions, patients are encouraged to maintain a healthy lifestyle, including a low-fat balanced diet and smoking cessation. Protection from excessive sunlight is considered important, particularly for the photosensitive patients but also as a precaution of disease exacerbation. Finally, patients are advised to avoid the use of contraceptive medication containing oestrogen, hormone replacement therapy and live vaccinations.

2.2.6 SLE Summary

SLE is a heterogeneous autoimmune condition with a diverse clinical manifestation and unpredictable disease course. The exact cause of SLE remains unclear, even though its SLE pathogenesis has been associated with a complex interaction of genetic, immunological and environmental risk factors. There is no explicit test for SLE diagnosis, which is reached with the collection of findings in consultation with a rheumatologist and relies heavily on clinical judgement. Patients with SLE can potentially face numerous clinical features and symptoms, as SLE-related disease activity can involve virtually any body organ or tissue. Similarly, disease severity and course can also vary greatly both between and within patients, as disease fluctuates between remissions and unpredictable exacerbations.

Even though survival rates have improved dramatically, patients with SLE are still at a greater mortality risk than the general population. SLE management is challenging and complex. Pharmacological treatment involves four types of drugs tailored to the clinical features, which are changed if they cease to be effective or if an individual patient is not responsive to them. Additionally, side effects need to be monitored because several drugs used in SLE management can cause significant morbidity, which is not always clearly distinct from disease morbidity. SLE disease severity is monitored through global disease activity and cumulative damage indices completed by clinicians. Despite the extensive information included in these indices, their association with self-report HRQoL measures is poor, indicating that the patients' perception of the impact of the disease on his/her life is an additional and independent outcome of SLE.

SLE is a complex condition with ambiguous pathogenesis, diagnosis, management, and assessment. Furthermore, patients diagnosed with SLE are faced with a diverse set of clinical features, an unpredictable disease course and, despite treatment advances, an increased risk of morbidity and mortality. The burden of living with a condition such as SLE is often reflected in the poor levels of HRQoL reported by patients, which are not always consistent with clinical markers of disease. Considering these disease characteristics, the exploration of patient uncertainty in SLE is therefore relevant.

2.3 RA Definition

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune condition of unknown cause. It primarily affects the synovial tissue of cartilage and bone of small and middle-sized joints by causing inflammatory cells to invade the synovium tissue that surrounds them. Although RA is primarily an articular condition, systemic inflammation can ultimately affect several organs including the lungs, vessels and the haematopoietic system, increasing the risk of atherosclerosis and lymphoma. The illness course and clinical manifestation of RA are diverse and can potentially include cases of mild and non-erosive symptoms, spontaneous remissions and also rapid degeneration to severe and destructive RA (38, 307).

2.3.1 RA Diagnosis and Classification

There is currently no explicit pathognomonic test for RA diagnosis. Diagnosis involves a series of clinical and laboratory tests in combination with classification criteria. Currently, the revised (308) American College of Rheumatology (ACR) 1987 criteria are used, diagnosing RA in cases where at least four of the seven listed criteria are present (Table 2.3). Early reports (309) indicated the sufficiency of the 1987 ACR criteria, suggesting a 77–95% diagnostic sensitivity (a correct positive diagnosis) and 85–98% diagnostic specificity (a correct negative diagnosis).

Table 2.3 ACR Revised Criteria for RA

	Criteria	Description/comment
1	Morning stiffness	Duration >1hour lasting >6 weeks
2	Arthritis of at least three areas*	Soft tissues swelling or exudation lasting >6weeks
3	Arthritis of hand joints	Wrist, metacarpophalangeal joints or proximal interphalangeal joints lasting >6weeks.
4	Symmetrical arthritis	At least one area of simultaneous involvement lasting >6weeks.
5	Rheumatoid nodules	As observed by physician.
6	Serum rheumatoid factor	Abnormal amounts of serum rheumatoid factor as assessed by a method positive in less than 5% of control subjects.
7	Radiographic changes	As seen on anteroposterior films of wrists and hands.

***At least four criteria must be fulfilled. No exclusions. ****Possible areas: proximal interphalangeal joints, metacarpophalangeal joints, wrists, elbow, knee, ankle, metatarsophalangeal joints.*

However, a more recent systematic review and meta-analysis of prospective studies indicated that the specificity of the criteria in early RA is very low in comparison with established disease (310), as specificity ranged from 33–76% in early and 89–93% in

established RA. This reflects the fact that the 1987 ACR criteria were developed for classification purposes through observation of patients with established disease (311). As there currently exist no accepted criteria for early RA (307), some authors suggest the importance of excluding criteria (311) to improve specificity of diagnosis. Some patients present with differential diagnosis of undifferentiated oligoarthritis involving one or fewer joints that gradually develop to meet the RA classification criteria (38).

2.3.2 RA Epidemiology

RA is also a worldwide disease, but is much more common than SLE with an approximate prevalence of 0.5–1% across different populations (307). Demographics influence RA occurrence, as more women (annual incidence: 0.2–0.4 per 1,000) than men (annual incidence: 0.1–0.2 per 1,000) are affected, whilst the annual incidence increases with age (312). There are also geographical discrepancies in the occurrence of RA, as a higher prevalence of RA is reported in North American and Northern European countries compared to Southern European (313), with the prevalence being significantly lower in developed countries and rare in China and rural Africa (312). A systematic review of RA annual incidence (per year) and prevalence across different countries also indicated a decreasing trend of RA annual incidence in the USA and Northern Europe, where rates were high.

2.3.2.1 UK Annual Incidence and Prevalence of RA

The first RA epidemiological study in the UK was conducted in 1961 (101) using the 1958 ACR diagnostic criteria (314). The study reported a prevalence of probable or definite RA in 2.1% of males and 5.2% of females, with an increasing trend in older age in both sexes as prevalence reached 6% in males over 75 and 16% in females between the ages of 65 and 74 (101). Lawrence (1961) further reported the occurrence of RA at a later age in females, in comparison to males, as no female diagnosis before the age of 35 was identified (101). In a more recent population survey using the 1987 ACR diagnostic criteria (308), Symmons et al. (2002) reported a decrease in the prevalence of RA in women, but not in men, in comparison with a study 40 years earlier (101). The extrapolated UK minimum prevalence of RA in the 1990s was estimated to be 1.16% in females and 0.44% in males (315).

The RA annual incidence rate between 1989 and 1990 using the 1987 diagnostic criteria (308) was estimated to be 35.6 per 100,000 females and 14 per 100,000 males (316). Annual incidence rates were very low in males under 45 years of age, and increased steeply with age, peaking at 61.9 cases per 100,000 persons between 75 and 84 years of age (316). In contrast, the female annual incidence rate increased up to the age of 45, plateaued at the age of 75, and dropped in the very elderly (316). In a

recent study estimating the annual incidence of RA in primary care (317) between 1996 and 1997, similar findings were reported: the annual incidence rate was 0.15 per 1,000 and 2.2 times higher in women than in men, whilst it increased with age in both sexes.

2.3.2.2 RA Pathogenesis and Aetiology

The development of RA has been linked with a variety of risk factors and pathogenic variables; however, the exact cause remains unknown. The mechanism of synovial inflammation characterising RA is driven by defective regulation of various immune cells, including T and B lymphocytes, neutrophils, monocytes, and mast cells, that consequently proliferate and produce inflammatory cytokines and chemokines (38). RA pathogenesis has been linked with two autoantibodies, although the disease can exist in their absence. Anti-citrullinated protein antibodies (ACPA) are found in an estimated 70% of patients with RA, but in hardly any other conditions displaying a specificity as high as 95–98% (38). Rheumatoid factor (RF) is another autoantibody present in 75% of patients with RA (318) and it is thought to be associated with the activation of complement (proteins targeting antigens) in the joints (38). However, part of the ACR 1987 diagnostic criteria (308) dictates that the presence of RF does not necessarily indicate a clinical diagnosis. RF is not unique to RA, as it is detected in other autoimmune and infectious diseases as well as up to 15% of healthy individuals (38). ACPA and RF can be serologically detected years before the onset of symptoms and diagnosis, with their presence being associated with a more severe course of disease (38, 319).

A UK population study failed to reveal an increased risk of RA in first-degree relatives of affected individuals (320). In contrast, studies comparing risk of developing RA monozygotic and dizygotic twins when one is affected indicate a genetic risk of RA (38, 307). With a monozygotic twin diagnosed with RA, a sibling has 15% greater chance of developing RA, which is four times as great as a dizygotic twin (321, 322). Findings in studies indicate the genetic contribution to RA susceptibility at 65% in Finland and 53% in the UK (323). The most common genetic characteristic in RA is shared-epitope alleles, associated with susceptibility as well as severity of RA (38), but importantly do not influence the risk of ACPA-negative RA.

Genetic factors predispose rather than cause RA, which is usually triggered by a variety of environmental factors in the presence of genetic risk (38, 307). Cigarette smoking is the most prominent environmental risk factor associated both with the development and severity of disease, particularly the ACPA-positive disease (38, 324). A recent meta-analysis further concluded smoking to be a risk factor for RA, and rheumatoid factors, whilst the risk was higher in heavy smokers (325). Smoking is

thought to have an inducing effect on immune cell apoptosis; nevertheless, the mechanism of association with joint inflammation remains unknown (38).

Other lifestyle factors such as diet have been linked with RA. A systematic review has concluded that higher consumption of olive and fish oil, fruit and vegetables is associated with a decreased risk of developing RA, and a low concentration of antioxidants in the blood with an increased risk (326).

Several infections have been associated with RA. Pathogens like mycobacteria, Epstein-Barr, and parvovirus are thought to increase risk of RA in genetically predisposed persons, as they cause an initial immune response that could trigger the development of RA. However, there is currently no epidemiological evidence to support the cross-reactivity pathogenesis (38).

Similar to other autoimmune diseases and SLE, one of the most important risk factors for the development of RA is the female gender, further indicating the role of sex and reproductive hormones in the development and prognosis of RA (38, 327). Multiple pregnancies (>3) are associated with a more severe course of disease (327). Although disease activity during pregnancy is significantly reduced, pregnancy itself was a risk factor to approximately 12% of women with a disease onset 12 months after pregnancy, a risk that was higher for first pregnancies (38, 328).

2.3.3 RA Clinical Features

2.3.3.1 Articular

RA is an inflammatory condition affecting joints in which inflammatory cells invade the synovium tissue. Synovium tissue offers joints nutrition and lubrication; thus, local inflammation can cause damage of the cartilage, erosion of the bone and eventually the decrease or loss of functionality of the affected joint (38, 307).
RA typically affects joints symmetrically, suggesting some neurological involvement. The joints of the hands and wrists are the most frequent clinical feature, followed by the joints of feet, knees and shoulders (38). Involvement of larger joints such as the shoulder, elbows and knees is often associated with more severe disease (307).

2.3.3.2 Extra-articular

Although joint involvement is the dominant feature of RA, extra-articular features are also reported. Constitutional symptoms such as fever, fatigue and weight loss often occur early in the disease and complicate diagnosis (307). Approximately one quarter of patients with RA present with nodules throughout the skin, and in internal organs in some cases. The cause of rheumatoid nodules is thought to be small vessel vasculitis and they are typically present in severe disease. Patients with active RA also frequently

present haematological symptoms such as anaemia and lymphadenopathy, which is often the presenting symptom of disease.

Inflammation in some patients with RA can ultimately affect several organs. Pulmonary involvement typically consists of small symptomatic pleural effusions. Other common pulmonary manifestations include pleuritis, nodules, interstitial lung disease, and obstructive airway disease. Histologically similar to pleural involvement, but usually asymptomatic, is pericardial disease. Rheumatoid nodules can lead to heart valve disease and conduction disturbances that mimic endocarditis.

Eye involvement may be very frequent in RA but is not necessarily associated with disease activity. Most frequently, patients with RA present with eye dryness (keratoconjunctivitis sicca) and less so with dryness of the eye ball (scleritis), which if untreated can rarely lead to loss of vision. Secondary Sjogren's syndrome is also common in seropositive patients suffering from erosive disease, with prevalence ranging between 11% and 62% (329).

2.3.3.3 Co-morbidities

RA is characterised by a high frequency of co-morbid conditions that typically have a negative effect on RA prognosis, outcome, and quality of life (307). Cardiovascular disease including congestive heart failure, myocardial infarction and hypertension is reported in approximately one third of patients with RA (274, 330, 331) and this is strongly related to increased mortality.

2.3.4 RA Prognosis and Outcome Assessment

The onset of RA can take an abrupt/acute (10–25%) or gradual/insidious (50%) form (332). The natural course of disease is not fully understood, as patients are invariably on treatment. Controlled studies of patients on disease modifying anti-rheumatic drugs (DMARDs) showed that 10% of patients were in remission, 40–70% displayed a chronic and progressive disease, whereas 20–40% were faced with a changing course of remissions and exacerbations (333).

In a recent review of the literature on mortality in RA (334), it was found that patients with RA had a reduced life expectancy, with standardised mortality ratios ranging from 1.16 in the community to 3 in a UK-based clinic sample. The leading causes of death in the RA sample were CVD and infections (307). Other conditions associated with RA mortality include diseases of the respiratory system, infectious and parasitic diseases, diseases of the nervous systems, and mental health disorders (335).

Accurate assessment of the disease process is highly important for its management, but this accuracy of assessment is complicated by the features of RA that may be due to inflammation, joint damage, and extra-articular involvement or medication complications. In the past two decades, progress has been made with regard to reaching consensus on the target variables in RA assessment (307). Currently, two sets of categories are assessed: process variables reflecting the actual disease activity, and outcome variables reflecting the end results of disease.

Disease activity can be assessed through joint scores rating swelling and tenderness, which are laboratory results; most frequently, ESR and CRP, and radiographic assessment of damage, are the gold-standard tools used in clinical trials (307). The Disease Activity Score (DAS) 28 (336) is the most popular validated global disease activity score. DAS-28 is a clinician-completed composite score including 28 joints, ESR, and a visual analogue scale (VAS) for general health. In addition to these measures, functional disability has also been assessed with self-report instruments (337, 338), an outcome that is of great importance to the patients.

2.3.4.1 Disability

The World Health Organization defines disability as "the outcome or result of a complex relationship between an individual' s health condition and personal factors, and of the external factors that represent the circumstances in which the individual lives" (339). It is an umbrella term used to describe function or structure impairments and/or activity limitations, as well as participation restrictions in individuals' life situations. Whilst structural impairments to the joints can be assessed radiographically, functional limitations are assessed using self-report instruments.

Various measures of disability have been developed and utilised within rheumatology, including the Arthritis Impact Measurement Scale (AIMS) (338), McMaster Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR) (340), and Functional status index (FSI) (341), whilst the Health Assessment Questionnaire (HAQ) (337) is currently the most widely used measure of functional disability in rheumatology, assessing functional status and ability to perform physical activities.

A systematic review of disability in RA concludes that significant activity limitations are reported in 15% of patients with RA within 5 years of diagnosis, and 40% after 15 years of diagnosis (342). The review further notes that average HAQ scores increase progressively with disease duration. Disability is mainly the product of disease and

demographic variables, as studies indicate that genetics, rheumatoid factor, radiological joint damage, older age, the female gender, and lower socio-economic status contribute to disability levels. However, patient outcomes such as pain, fatigue and depression have also been associated with disability and, in some cases, found to independently predict disability (343, 344).

2.3.5 RA Treatment

Providing a detailed overview of RA treatment is beyond the scope of this thesis, instead a brief outline of the drugs used is presented. Apart from pain and stiffness control, RA treatment aims to reduce inflammation and swelling, consequently minimising the risk of long-term damage to joints. Non-steroidal anti-inflammatory drugs (NSAIDs) and analgesic drugs are widely used for pain and stiffness relief from the disease onset and these have also been reported to have a beneficial effect on inflammation and functionality (345, 346).

Disease-modifying anti-rheumatic drugs (DMARDs) target inflammation and are the backbone of RA treatment, as they have been shown to improve erosions and space narrowing of joints, as assessed through radiographs (346). Therefore, when effective, DMARDs are therefore able to modify the pathogenesis of RA. Methotrexate is the "gold standard" DMARD in RA. It can be administered orally or subcutaneously, and (similar to all DMARDs) can have substantial side effects that require regular monitoring.

Initially, a sequential monotherapy of DMARDs approach was adopted for RA treatment, where drugs were used individually and were replaced when and if they became toxic or ineffective (345). Recently, this approach has changed remarkably, as patients with aggressive disease and who are resistant to monotherapy have been treated aggressively with a combination of different DMARDs. This more aggressive approach has proven beneficial but requires early and accurate diagnosis of patients, which is sometimes challenging.

More recently, biological therapies have been introduced (345, 346), including the humanised agents that target inflammatory cytokines and have been shown to improve joint symptoms and damage on radiographs. Several anti-cytokine therapies (TNF) are licensed for use in RA. Non-pharmacological treatments are also recommended in RA. According to a patient's needs, a multidisciplinary group of clinicians, including physiotherapists, podiatrists and occupational therapists, can be involved in their management (345).

2.3.6 RA Summary

RA is an inflammatory autoimmune condition which primarily affects the cartilage and bone of small and medium-sized joints. Similar to SLE, the exact cause of RA remains unclear, even though the development of RA is associated with a complex interaction of genetic, immunological and environmental risk factors. There is currently no explicit pathognomonic test for RA diagnosis reached by rheumatologists and the collection of clinical and laboratory data. Even though the primary features of RA are articular, other clinical features are also present, including constitutional symptoms. In cases of more severe disease activity, inflammation can ultimately affect the lungs and heart. The severity of disease and course of RA vary sufficiently between patients. Disease onset can be abrupt or gradual, and a disease course can likewise range from mild and non-erosive disease to spontaneous phases of remissions and exacerbations, as well as rapid progression to severe and destructive disease.

RA treatment targets the reduction of inflammation and swelling and subsequently aims to reduce the overall damage to joints. RA management is often approached through a sequential monotherapy where one drug is changed if it ceases to be effective or becomes too toxic for the patient. Alternatively, simultaneous use of different therapies has proven beneficial in more aggressive cases, but having an accurate diagnosis is a prerequisite for such an approach which is not used as often. Despite treatment advances, patients with RA have a reduced life expectancy that is greatly affected by co-morbid conditions such as cardiovascular disease, which is very frequent in RA.

RA is an autoimmune condition with an equivocal pathogenesis and no explicit diagnostic test. Assessment of disease and pharmacological management can be challenging, whereas clinical features and disease severity can vary between different patients, as RA disease features can range from mild and non-erosive to severe and disabling. The course of disease further varies unpredictably, and pharmacological treatment can be toxic and not always consistently effective. In addition, patients diagnosed with RA are at increased risk of suffering from co-morbid conditions which are often associated with an increased risk of morbidity and mortality. Even though clinical manifestation of RA appears to be less complex than that of SLE, living with RA can be challenging and unpredictable, thus constituting exploration of patient uncertainty in RA equally relevant.

2.4 Non-Clinical Outcomes in SLE and RA

The above sections (2.2 and 2.3) have briefly outlined the epidemiological, clinical and treatment features of SLE and RA. A comprehensive representation of such conditions, though, requires a more holistic description of physical, mental and social aspects affecting people with such diagnoses (145, 347). Living with SLE and RA involves several parameters in addition to the clinical and medical issues described above. People with SLE and RA are required to adapt to diverse physical symptoms that are often not congruent with clinical variables (343), various treatments and lifestyle changes, and an unpredictable disease course that challenges their life plans (25-27). In other words, the experience of SLE and RA extends beyond the clinical and medical variables to influence all aspects of life.

In line with the bio-psychosocial model of health and illness (150), this section will provide an overview of patient outcomes including: physical, psychological, behavioural, and social, which together with biological variables (discussed above) are believed to contribute to SLE and RA patients' health status. As discussed in section 1.3.1, the importance of patient outcome variables in illness management is increasingly being recognised across chronic conditions (139, 163, 164). Specifically, the adaptation of the bio-psychosocial model in rheumatic conditions (Figure 1.2) (155) proposed physical adjustment as one of the two major end outcomes in rheumatic disease, alongside disease activity. Furthermore, the dynamic impact of psychosocial, behavioural and cognitive outcomes on physical and disease outcomes has been postulated, both directly and indirectly, through neuroendocrine activity. Therefore, the role of such patient outcomes in the bio-psychosocial approach to rheumatic disease is complex, as they are considered to be both outcomes and potential moderators of disease.

In addition, there is also some degree of conceptual overlap between some of these variables and the subsequent instruments used for their quantification, further amplifying such relationships. Moreover, it is expected that the association between perceived variables assessed by the same respondent (in this case a patient Vs a clinician) will be magnified, as measurement is not solely a product of the object (i.e. variable being assessed), but also a product of the subject (respondent) (348-350). Furthermore, the majority of perceptually based instruments of patient-reported variables target constructs which are associated with dispositional attributions such as optimism which is strongly associated with subjective well-being (351), mood, quality of life (352) patient reported health outcomes in general (348), further enhancing the links between such variables, without necessarily implying causality.

This section outlines the patient outcome literature in SLE and RA in parallel, not separately, as the bio-psychosocial mechanisms outlined are applicable to both conditions; furthermore, many of the studies presented research two or more rheumatic conditions in parallel. It is important to note that classification of the patient outcomes presented into the physical, psychosocial and behavioural/social section categories is not absolute; frequently, outcomes overlap across different categories. For example, health-related quality of life has both psychosocial and physical attributes, whereas work disability has physical, behavioural and social attributes. For the purposes of this chapter, patient outcomes will be classified in line with a recent review of psychosocial aspects of rheumatic disease (343). The literature will be presented in relation to (i) the relative levels of each patient outcome in SLE and RA and (ii) what is known about the causes and contributors of those patient outcomes.

2.4.1 Physical Symptoms & Functioning

Patients with SLE and RA regularly present with physical symptoms and/or physical restrictions that are considered to be patient outcomes secondary to objective disease parameters, but are overly important for patients. There is often significant diversity between patients with regard to secondary disease outcomes that are not always consistently associated or predicted by clinical parameters (343).

2.4.1.1 Pain

Pain is the predominant symptom reported by patients with RA (353-356), a symptom that is characterised as severe and troublesome, as it limits execution of daily activities and prohibits the course of a "normal life" (343). Patients with RA usually refer to "stiffness" to describe their pain (357), a quality that, although poorly understood (343), constitutes one of the seven diagnostic criteria for RA (308). Similarly, pain is relatively common in SLE as well, as musculoskeletal pain (Table 2.2) is the most prominent clinical feature of SLE. Joint pain is reported by up to 85% of patients (354), whereas muscle pain and headaches are also very frequently reported symptoms (355, 358, 359).

The experience of pain extends beyond the physical sensation, as pain has been widely associated with other adverse outcomes such as disability (356, 360, 361), sleep difficulties (356, 362), psychological distress (356, 358-360, 363, 364), and perceived functionality (360). Unsurprisingly, pain is associated with a higher use of the health care services, and more frequent use of medication (343, 365) and greater work disability (360, 366).

2.4.1.1.1 Causes of Pain

Contrary to the traditional biomedical illness model, pain in SLE and RA is not always directly associated with organic dysfunction and physiological variables (367). Studies have shown differential reports of pain severity, intensity and quality in clinically identical conditions as well as the presence of pain in the absence of physical damage (367). Even though pain is associated with higher disease activity, it is often present during periods of disease remission, when inflammation is under control (356) and has further been found to contribute to disability more profoundly than structural joint damage (356, 358-360, 363).

Pain is now regarded as a multifaceted experience that comprises both sensory (related to intensity, location, quality, and duration of pain) and emotional (sense of unpleasantness) attributes (356, 368) that are thought to be the product of a subjective cognitive appraisal (369). Furthermore, in line with the bio-psychosocial paradigm, additional behavioural and social parameters have been assessed in relation to pain mechanisms (150, 155). For example, coping strategies have been shown to mediate the relationship between pain and disability in RA (370), whereas beliefs about pain control (i.e. self-efficacy) have been linked with lower levels of pain and better adjustment (371, 372).

RA pain has been shown to have a consistently strong relationship with depression (343, 373). Pain levels have also been shown to predict future depression levels (374). However, the bi-directional relationship between depression and pain complicates its exploration (373). A similar bi-directional relationship exists for anxiety, with studies reporting the association of pain with a feeling of anxiety related with pain-exacerbating activities (375). A number of non-clinical variables which are relevant in SLE and RA can contribute to the higher levels of pain experienced by patients.

2.4.1.2 Fatigue

Fatigue is believed to comprise both physical and cognitive features (343); moreover, contrary to “normal” tiredness, fatigue in chronic conditions is described as more frequent, persistent, unpredictable, and unresolved by resting (376-378). Currently, there is no recommended effective treatment for fatigue (378) and despite advances in treatment and survival rates, fatigue remains a prevalent and debilitating symptom in both SLE and RA. Fatigue is the predominant complaint in SLE, with a reported prevalence range between 67 and 90% in SLE (379) and (41–69%) in RA (380). Fatigue is included in three of the widely used SLE clinician-completed measures of disease activity (294, 296, 297) and has been established as a recommended outcome

in impact assessment in RA (380-382).

2.4.1.2.1 Causes of Fatigue

Despite the challenging clinical manifestations characterising SLE and RA, fatigue remains a very important aspect of the illness experience, as it is evidently associated with various patient outcomes (380). Literature reviews indicate that fatigue is predictably associated with other secondary illness outcomes, including physical functionality, sleep difficulties, pain, as well as depression levels in both RA (380) and SLE (379). Subsequently, fatigue has shown a robust adverse impact on all aspects of quality of life in both conditions (49, 379, 380, 383).

The aetiology of fatigue remains ambiguous but studies in both RA (380, 381) and SLE (379) seem to suggest a complex multifaceted causal mechanism, as fatigue may be due to anaemia, poor sleep, corticosteroid medication side effects, hypothyroidism, fibromyalgia as well as active disease. Disease variables such as inflammation and organ damage are thought to be direct but more distal predictors of fatigue, whereas other patient outcomes (e.g. pain & depression) are thought to mediate the disease-fatigue relationship and predict fatigue levels more proximally. The relationship of such patient outcomes with fatigue is confounded and intensified by the dynamic bi-directional causal relationship with fatigue.

2.4.1.3 Sleep difficulties

Sleep difficulties is another secondary disease outcome reported by patients with SLE and RA. Up to 70% of patients with RA report sleep complaints including difficulties in falling asleep, poor-quality sleep, non-restorative sleep, numerous awakenings during the night, early-morning awakening, and excessive daytime sleepiness and fatigue (384). Similarly, approximately two thirds of patients with SLE report restlessness, frequent awakenings (385, 386) and generally poor sleep quality (387). Studies have shown that clinical parameters of disease activity contribute to sleep quality in RA and SLE, whereas additional patient outcomes such as pain, depression, pain, fatigue, and physical deconditioning are also strongly associated with it (384, 385, 387, 388). Sleep has a restorative role and it is therefore unsurprising that poor sleep quality is associated with adverse outcomes in both SLE and RA.

2.4.2 Psychosocial Well-Being

In addition to the secondary physical disease outcomes, patient outcomes related to psychosocial well-being have also received attention in SLE and RA (343), primarily related to mood and health-related quality of life.

2.4.2.1 Health-Related Quality of Life (HRQoL) Concept and Measurement

HRQoL is a multidimensional concept referring to a patient's perception of the impact of an illness and its treatment as well as the patient's own perception of their physical, mental and social functionality (302, 389). Physical functioning refers to a person's ability to complete basic everyday activities; mental functioning refers to a person's ability to enjoy life and participate in social interactions, whereas social functioning refers to a person's ability to interact in society in a normal/usual way (347).

Terms such as health status, functional status and well-being are often used to refer to HRQoL (49). HRQoL is widely recognised as an important outcome of chronic conditions, particularly due to its modest association with clinical parameters of disease (180, 181). HRQoL assessment can therefore provide additional information salient to the patients and potentially useful for disease management and treatment assessment (390, 391) that would otherwise be missed.

Reflecting the wide content of the outcome, HRQoL instruments are multi-dimensional, tapping onto different aspects of patients' lives. The Short Form-36 (SF-36) scale (203) is the most commonly used measure in both SLE and RA studies. It is a generic measure (i.e. not specific to a disease) that assesses aspects of general health, physical health, bodily pain, and limitations in performing societal roles that are further classified into two overarching component subscales: physical and mental. The World Health Organization Quality of Life scale WHOQoL (392) has also been used in the SLE and RA literature. It is also a multi-dimensional scale assessing HRQoL across five scales, including: general, environmental, social, physical, and psychological.

Recently, SLE disease-specific HRQoL measures have been developed (177, 393-395) on the basis of interviews with SLE patients. The LupusQoL is a disease-specific HRQoL instrument developed and validated in the UK (396). Semi-structured qualitative interviews with SLE patients were used to develop LupusQoL resulting in a multi-dimensional instrument containing 34 items across eight domains, including physical health (assessing challenges with everyday physical activities), emotional health (assessing feelings of sadness, anxiety, worry, resentfulness and self-confidence), body image (assessing sense of attractiveness and body's interference with life), pain (assessing pain interference with activities, sleep and mobility), planning (assessing SLE interference with planning events), fatigue (assessing morning exhaustion, fatigue manifestations like lack of concentration), intimate relationships (assessing interest in sexual life) and the burden on others (assessing the extent of burden, stress and worry SLE brings to others). The LupusQoL has been increasingly

popular internationally and has been linguistically adapted for use in the USE, Canada and Spain (178, 397).

The SLEQOL is another disease-specific HRQoL instrument that was however developed in the lack of formal qualitative patient input (395). Fifty one items were suggested by rheumatology health care professionals and later reduced to 40 items by the input of patients that were asked to judge the frequency and occurrence of items in their lives. The SLEQOL operates on a total score basis but the 40 items cover a range of physical, mental and social domains of quality of life (395). The SLEQOL developed was based on previous qualitative research indicating twelve different concepts related to the SLE experience, including the uncertainty and unpredictability of SLE (35).

L-QoL is another uni-dimensional instrument (177) developed and validated in the UK on the basis of needs-based quality of life model, in other words, that improvements in HRQoL derive from the ability and capacity of a patient to satisfy his/her needs. In-depth interviews with patients resulted in a pool of 55 items that were later reduced to 25 items following subsequent validation using Rasch analysis. Authors of these measures suggested the need to develop disease-specific measures which are more sensitive than generic measures, such as the SF-36, and more comprehensive of domains that are important to patients with SLE and covered inadequately by the SF-36, such as sleep, fatigue and sexual health (177-179, 393-395).

In RA literature the AIMS (338) is a very popular instrument for the assessment of disease-specific aspects of HRQoL. The AIMS instrument assesses both physical and psychosocial aspects of quality of life and is targeted to all musculoskeletal conditions. The original AIMS was developed by building on two previous health status measures (338) and the addition of items related to social role, specific daily activities and pain. The short form of AIMS, AIMS2-SF (398) comprises 26 of the 57 original items spread across five component scales including physical (assessing physical functioning), symptom (assessing pain and stiffness), affect (assessing feelings of burden, low mood and nervousness), social interaction (assessing the amount of social interaction and sensitivity of others` to respondents` needs) and role (assessing inability or challenges with employment).

The Health Assessment Questionnaire (HAQ) (337) is the most widely used measure of functional disability in rheumatology (HAQ) often referred to as an instrument of health status. The HAQ comprises 22 items across five dimensions of disability, pain, medication effects, cost of care and mortality and is scored in three sub-scales the

disability index section (20 items), pain (1 item) and global health status (1) item.

More recently the disease-specific RAQoL instrument (399) was developed on the basis of in-depth qualitative interviews with RA patients in the UK and the Netherlands. Interview findings were used as the basis to develop 30 items related to mood and emotions, social life, hobbies, everyday tasks, person and social relationships and physical contact. All items are scored on a yes/no response scale and scored as a single total score. Regardless of the in-depth qualitative basis of the RAQoL the AIMS (338, 398) and HAQ (337) are still the most frequently used instruments of HRQoL and functional disability in RA.

2.4.2.1.1 HRQoL Levels in SLE and RA

Literature reviews (49, 400) indicate that both SLE and RA patients report reduced HRQoL compared to the general population, and are comparable to other chronic conditions like AIDS (49, 343, 400, 401). Studies comparing SLE and RA indicate similar levels of HRQoL between the two conditions, apart from the physical functioning and pain domains that seem to be more affected in RA (402) (402, 403), whereas the mental domain seems to be more affected in SLE (404). Physical functioning is a predominant aspect that is poorer in RA, in comparison with the general population (405), and is progressively impaired with disease duration (406). Studies consistently report that HRQoL scores in SLE are significantly lower than the general population, both within the physical and mental domains and particularly in the general health, role-physical and vitality (fatigue) sub-domains (404, 407-409).

2.4.2.1.2 Causes of reduced HRQoL in SLE and RA

Disease activity has not fully accounted for reduced levels of HRQoL as clinical parameters have not consistently predicted HRQoL in either SLE or RA. This is particularly true in SLE where, despite the breadth of information included in the clinician-completed measures of disease activity and organ damage, HRQoL has not consistently been shown to have a strong relationship with these disease variables (49, 391) even in longitudinal studies (410). Conflicting findings have been reported, as some studies show no association between disease activity and/or damage with HRQoL (409-415), whereas other studies (407, 416-420) designate significant links between disease parameters and HRQoL. Nevertheless, an unpublished meta-analysis conducted by the thesis` author (421) of studies utilising the SF-36 in SLE indicated that the magnitude of relationships between disease activity and organ damage with both the physical and mental component subscales was very weak.

HRQoL assessment using the recently developed disease-specific measures (394, 422) has also failed to show a strong association with disease parameters. Therefore, HRQoL in SLE, as quantified by the existing measures, seems to tap into a unique set of concepts not captured by the clinician-completed measures. In line with these findings, HRQoL is one of the three recommended outcomes for assessment in SLE, in addition to disease activity and organ damage (423).

Despite the lack of a consistent association between HRQoL and disease parameters, secondary disease symptoms and other psychosocial outcomes produce more consistent associations with quality of life levels in SLE. Higher levels of fatigue, as assessed by a variety of different measures, have been associated with reduced levels of HRQoL in both the physical and mental domains (379). Depression and psychological distress levels have displayed strong and predictive relationships with HRQoL (403, 414). Other psychosocial and behavioural variables have been associated significantly with HRQoL levels. These include coping strategies (410, 418, 424, 425) as well as lower self-efficacy, less knowledge about SLE, and less social support, which were associated with poorer HRQoL — both physical and mental (407, 426). Overall, older age and longer disease duration seem to be linked with reduced HRQoL levels, especially of the physical domain, but this is not true in all studies (300).

Fewer studies have focused on HRQoL in RA. Functional disability (427) and pain levels (361) have been reported as the most significant predictors of the physical aspects, whilst mood (depression and anxiety) and social support are the most significant of mental aspects of HRQoL in RA (343, 361, 428). Testing a bio-psychosocial model of HRQoL (390) indicated the importance of both disease parameters as well as psychosocial, behavioural and cognitive variables, proposing the role of coping strategies, perceived stress and illness beliefs, particularly in the mental aspects of HRQoL. Poor HRQoL has also been shown to be predictive of higher health care utilisation and hospitalisation (429).

The presence of consistent associations between other patient reported variables and HRQoL in comparison with the lack of a consistently strong association between HRQoL and disease parameters does not necessarily signify causal attributions. HRQoL instruments are multidimensional (176, 203) and often overlap concepts like fatigue and mood; there is therefore a conceptual overlap between such instruments. In addition, a higher association between instruments assessing variables completed by the same respondent, as opposed to a different respondent (in this case a patient Vs a clinician) is expected as measurement is not solely a product of the object (i.e. variable

being assessed) but also a product of the subject (respondent) (348-350). Furthermore, the majority of perceptually based instruments of patient-reported variables target constructs which are associated with dispositional attributions such as optimism, which is strongly associated with subjective well-being (351), mood, quality of life (352) and patient reported health outcomes in general (348).

The reduced levels of HRQoL in SLE and RA are likely to be a result of a combination of the core disease activity, secondary disease parameters such as fatigue and depression as well as aspects of the patients` response to the illness e.g. self-efficacy and coping.

2.4.2.2 Mood Levels in SLE and RA

Mood-related patient outcomes and, specifically, levels of depression and anxiety have been assessed in both SLE and RA. Depression is prevalent in chronic conditions, as chronically ill individuals are significantly more at risk of developing depression than healthy individuals (430). This is true for rheumatic conditions as well (373), where depression is reported both as a co-morbid condition or as a feature of the disease itself in SLE (36, 278, 431). Depressive symptoms often reflect the burden of living with a long-term incurable condition (432). In addition, a bi-directional relationship of depression and lupus disease activity has been suggested, postulating that depression-related stress hormones can potentially act as a trigger or accelerator of disease activity (433-435).

A systematic review of depression studies in RA highlights the significant role of the different methods of measuring depression (373). This meta-analysis signifies that the Hospital Depression and Anxiety Scale (HADs) (436) led to an overestimation of depression levels compared to other scales such as the CES-D (437). Dickens et al. (2002) further noted that different methods of measurement could be responsible for the diverse range of psychological distress reported in the literature, which was 15–66% for clinical depression and 13–70% for clinical anxiety (373). In spite of the diversity of these ranges, depression and anxiety seem to be salient aspects of RA, as even the lower bounds of these ranges (15% and 13%) are higher than the equivalent percentages of depression and anxiety in the general healthy population (12.6% and 3.6%) (373, 438). Most importantly, co-morbid clinical depression is an independent risk factor for increased mortality in RA (439).

2.4.2.2.1 Causes of Higher Levels of Depression and Anxiety in SLE and RA

Studies show that patients with SLE experience more psychological distress in the form of depressive symptoms and anxiety compared to health controls (434, 440). The SLE literature is currently inconclusive with regard to the aetiology of the depression (440, 441). Some studies suggest that depression represents SLE morbidity, as they report depression levels being associated with disease activity (431, 433, 442) even in the absence of neuropsychiatric clinical manifestations (431), where patients with SLE still report higher depression than healthy controls. On the other hand, several studies have failed to show any significant relationship between disease parameters and depression levels (443, 444). A literature review (440) suggested that patients presenting with higher levels of pain and disability experience greater psychological distress, thus supporting the hypothesis that depressive symptoms in SLE constitute a secondary consequence of living with a chronic condition (445). A causal relationship between pain and depression has been suggested (446); however, the cross-sectional design of the studies assessing depression in SLE prohibits any conclusion to be made with regard to this (441).

In RA, findings report the differential effect of disease duration on anxiety and depression levels (447), as anxiety levels were heightened in early phases of diagnosis, whereas depression levels got progressively higher with the passage of time, a finding also reported by (448). These findings could be taken to suggest the differential aetiology of anxiety and depression, with depression indicating the overall burden of living with a chronic condition in comparison with anxiety reflecting the challenge of getting diagnosed and adjusting to a chronic condition (343, 449).

Secondary disease outcomes such as pain, fatigue and physical functionality contribute to depression and anxiety levels in RA (450-452). However, these associations are more complex because such patient outcomes often have dynamic relationships; for example, depression can also contribute to pain (428) and fatigue levels. Studies have also shown the dynamic association of depression levels with beliefs about one's condition (448). As discussed in the previous section, higher depression levels are consistently associated with reduced quality of life and have further been linked with medication adherence (343, 453).

Higher levels of depression are associated with disease parameters as well as secondary disease outcomes like pain and disability which also contribute to depression; whereas, higher levels of anxiety seem to reflect the challenge of adjusting to a disease like SLE and RA.

2.4.3 Behavioural & Social Functioning

Living with SLE and RA can challenge a person's social functioning, both in terms of personal and family life as well as professional life, causing difficulties in performing activities of daily living (347). Patients with SLE and RA are further expected to follow the treatment plan suggested by their care team, which usually involves a daily addition to their regular activities.

2.4.3.1 Treatment Adherence: Levels and Causes

Adherence, defined as "the extent to which a person's behaviour — taking medication, following a diet and/or executing lifestyle changes — corresponds with agreed recommendations from the health care provider" (454), is key in chronic conditions, as poor adherence is likely to have a direct impact on clinical and physical outcomes. As Ostenberg & Blaschke (2005) stated: "drugs don't work in patients who don't take them" (455). Patients often fail to adhere unintentionally, forgetting to take their medication as prescribed, but non-adherence can also be a deliberate, conscious choice, i.e. intentional (343, 456). Similar to all patient outcomes, adherence is assessed through self-report.

Daleboudt et al. (2011) (456) assessed the extent to which patients with SLE missed any doses of immunosuppressive medication using the VAS scale and four items assessing the proportion of adherence in the past month (457). Overall, patients with SLE reported good adherence rates (86.7%), with 46.2% of the patients reporting intentional and 58.5% non-intentional non-adherence with poorer cognitive functioning and concerns about adverse effects of medication predicting non-adherence. Assessing treatment adherence in both RA and SLE, Garcia-Gonzalez et al. (2008), using a rheumatology-specific adherence instrument (458), reported that approximately one third of patients are always adherent, whereas the reasons for intentional non-adherence were the side effects for 40% and the lack of perceived treatment effectiveness for 20% (459). A recent literature review concluded that adherence to medication in RA is low, ranging from 30 to 80% (460).

Chambers et al. (2009) investigated non-adherence in SLE in a qualitative study, concluding that five general themes were responsible for patients not taking their prescribed medications regularly (461). These included: (i) the belief that SLE can be controlled by personality and lifestyle factors, (ii) the belief that continuous and long-term use of medication is not necessary for keeping SLE under control, (iii) a fear of medication side effects, (iv) poor communication and dissatisfaction with health care staff in relation to the discussion of new medicines, and (v) practical difficulties in

obtaining medications. Similar reasons have been suggested for non-adherence to RA, including beliefs about the necessity, efficacy and potential harm of medications as well as beliefs about the causes of RA flares; furthermore, the patients' self-efficacy was associated with levels of adherence (459, 462, 463). Patient beliefs have therefore been linked with intentional non-adherence in both SLE and RA.

2.4.3.2 Work Disability: Levels and Causes

Work disability, i.e. the inability to work due to an illness, has been associated with both SLE and RA. A systematic review reports that work disability ranges between 5% and 63% in SLE (464), whereas work disability in RA has been estimated between 32% and 50% 10 years post-diagnosis and 50% to 90% 30 years post-diagnosis (465). Temporary inability to work, sick leave and a reduction of working hours have also been reported in SLE, particularly in the early stages of diagnosis (347).

Disease activity, demographical variables such as age and education, and job characteristics contribute to work disability as well as patient outcome variables such as pain and physical functioning (343, 466, 467). Work disability constitutes a financial burden for patients and their families as well as an economic burden for the society as a result of productivity loss (465). Subsequently, though, work disability impacts on additional psychosocial patient outcomes and is associated with reduced quality of life (464, 467).

2.4.3.3 Relationship burden

The impact of living with SLE or RA on relationships has been investigated by some studies to assess whether such diagnoses burden interpersonal relationships due to the challenges they impose on the patient and his/her loved ones (343). Nevertheless, the literature does not clearly support this hypothesis. Rates of divorce in RA are reported to be comparable to the general population (468), and the RA diagnosis has further proven beneficial for the relationships of some patients, as they report greater appreciation to their loved ones (469). The SLE diagnosis was neither a barrier to marriage nor a cause for divorce, despite challenging childbearing within the marriage due to medical parameters (470).

Sexual functioning is an important patient outcome with significant implications on personal relationships, which is often neglected by health care professionals in rheumatic disease (343, 471). Sexual functioning is a complex aspect of life, involving physical, behavioural and psychosocial attributes, that is associated with overall well-being and quality of life (472). Both SLE and RA can have a detrimental effect on

sexuality, with as high as 26% of SLE (473) and 60% of RA females (474) reporting problems with sexual functioning. A systematic review (472) notes that stiffness and limited mobility contribute to poor sexual functioning in RA, in comparison to vaginal dryness in SLE, and further highlights the association of diminished sexual desire with other patient outcomes including depression, anxiety and body image.

2.4.4 Moderating Variables

The literature presented in sections 2.4.1–2.4.3 indicates how physical, psychosocial and behavioural outcomes in SLE and RA are not always directly associated with clinical and medical variables, as additional variables appear to influence them. Such variables included coping, self-efficacy, social support, illness beliefs, and knowledge and, in line with the bio-psychosocial paradigm of chronic illness (150, 155), moderate the outcomes of SLE and RA (Appendix 2.1).

Several theories have attempted to describe how such moderating variables can influence patient outcomes in chronic illness. Thus, the self-regulation model (17) and social cognition theory (15) describe how patient outcomes can be influenced by such non-clinical variables. In brief, the self-regulation model (17) proposes that patients are active problem solvers attempting to understand their illness. Within this attempt, illness representations are created that lead to coping strategies that can ultimately affect illness outcomes. In other words, the model postulates that the beliefs a patient holds about his/her condition influence their coping strategies (i.e. their behaviour), which in turn affects outcomes.

The social cognitive theory, on the other hand (15), postulates that behaviour (e.g. adherence to treatment recommendations) is influenced by self-efficacy, outcome expectations and socio-structural factors that all influence a person's goals. Self-efficacy refers to the confidence an individual has in performing a specific behaviour; outcome expectations refer to the beliefs about the consequences of a specific behaviour, and socio-structural factors refer to the barriers or facilitators of a target goal (147).

Therefore, according to these models, variables such as self-efficacy, coping, beliefs, and social support are associated with and can ultimately influence patient outcomes. The contribution of patient uncertainty to patient outcomes has been reported in other chronic conditions (42-44, 116, 121, 123, 132, 138) and is therefore in line with such models (15, 17, 150, 155), as patient uncertainty is a cognition. The contribution of patient uncertainty to outcomes in SLE and RA relative to other beliefs and moderating variables will be preliminarily explored in this thesis (Chapter 6). A summary of the

literature assessing moderating variables in SLE and RA is presented below to set the background for the exploratory analyses that will be presented in Chapter 6.

2.4.4.1 Beliefs

The beliefs people hold about their illness are believed to provide patients with the framework for coping and adjusting to their condition (343, 453) and are therefore considered to be of interest to research and management. Different types of beliefs have been described and assessed in the literature, including illness perceptions based on the self-regulation model (17) relating to issues of disease identity, timeline, consequence, and control (475, 476); beliefs and concerns about appearance and/or disfigurement (343), and beliefs about the disease treatment (477).

Perceptions of a stronger illness identity, control and consequence were found to significantly predict HRQoL both in terms of physical, social functioning (478) and mental functioning as well as disability (479, 480), despite being unrelated to clinical measures including ESR levels. Perceptions of negative illness consequences have further been reported to predict depression, anxiety and pain levels at approximately a 2-year follow-up (448, 481).

Multiple psychosocial, demographic, disease- and treatment-related factors influence the beliefs patients hold about their own health and illness (453). Therefore, qualitative investigations of illness beliefs about the nature, course and management of SLE indicate that although suffering from the same illness, patients with SLE hold differential beliefs about their condition (35) which are sometimes at odds with the medical opinion (482). Daleboudt et al. (2011) reported that patients with SLE hold more negative beliefs about their condition relative to other chronic patients, e.g. asthma, and further suggested that the type of treatment received influences illness beliefs (483). Another study reported that stronger beliefs about the illness having negative life consequences, an unpredictable nature and themselves having limited understanding of SLE, contributed to higher levels of depression (484).

Perceptions of appearance have been linked to depression levels in both SLE and RA (485). Concerns about hand disfigurement in particular have been linked with negative feelings of shame and body image and avoidance of social interactions in RA (343). With regard to beliefs about treatment and medication, Kumar et al. (2008) reported that patients with SLE and RA of South Asian origin hold differential beliefs and higher levels of concern about prescribed medicines compared to patients of White British origin, a difference that could potentially influence intentional non-adherence (486).

Self-efficacy, i.e. an individual's belief in their ability to undertake a specific task, has been associated with patient outcomes in rheumatic conditions (343). In a two-year longitudinal study, baseline self-efficacy scores were contributed to both generic and disease-specific quality of life, as assessed even after controlling for demographic variables (487). Similarly, in a five-year longitudinal study, baseline self-efficacy was associated with levels of pain and mental aspects of HRQoL, but these associations seemed to be affected by education level (371). Self-efficacy in relation to disease management was also associated with patient adherence in RA (488). A study investigating self-efficacy in SLE reported that lower self-efficacy in relation to disease management was associated with poorer HRQoL both in terms of physical functioning and mental health status (426).

2.4.4.2 Coping

Coping has been conceptualised as "the cognitive, behavioural and emotional efforts individuals exert to manage specific external and/or internal demands" (24). Living with a rheumatic condition exposes an individual to several stressors (155) such as accepting the diagnosis, adjusting to the medical treatment, symptomatology, and diverse consequences of living with a chronic uncertain condition (343). Coping strategies have been classified into active, i.e. taking action to remove or avoid a stressor, and passive, i.e. withdrawing and exerting passive control in relation to a stressor (343).

A literature review of coping in RA indicated links between coping strategies and physical and psychological outcomes, including higher levels of pain, depression and anxiety (489). However, the authors noted the lack of clarity with regard to coping strategies and poor design of many studies. Active coping, on the other hand, has been associated with beneficial outcomes in terms of social support, pain, disability, and depression (343, 490). Overall, coping strategies were only found to contribute to a small extent in the variance of patient outcomes (489).

A literature review of stress and coping in SLE also highlights the heterogeneity and limitation of study methodological designs (491). Nevertheless, it suggests that coping strategies are unrelated to disease activity but are significantly associated with both the physical and mental components of HRQoL. Specifically, emotional and problem-focused coping were found to have an adverse effect on HRQoL, particularly during disease flares (491).

Despite the links suggested to operate between coping strategies and patient outcomes, it is important to acknowledge that coping strategies are not static but can potentially change constantly (343), hence challenging their assessment. Furthermore, the coping literature is limited by the diversity of questionnaires used to examine coping either in a generic format or specific to symptoms such as pain or stress (489). Finally, the coping literature is limited by the poor definition of coping as a construct (492), leading to different measurement instruments.

2.4.4.3 Social Support

Social support is defined as "the process by which interpersonal relationships promote well-being by buffering stress and protecting people from a decline in health" (343). Interpersonal relationships can involve the family, friends, health care professionals, as well as patients' groups offering either practical and/or emotional support to an individual. For research purposes, social support has been conceptualised and measured both structurally, in relation to the number of people in a person's network, and functionally, in relation to a person's evaluation of the support they receive (343, 493, 494). Even though the beneficial relationship of social support with health is acknowledged, the precise mechanism responsible for this relationship is not yet completely understood (494).

It has further been suggested that patients with RA can experience both positive and problematic social support (i.e. perceived as non-supportive from the patient) without one cancelling the other (495). The authors reported that problematic support was linked with increased depression and when patients reported greater problematic support in association with low positive support, a higher level of symptoms was displayed. In a more recent study, problematic support was also found to be predictive of depressive symptoms and linked with a lower family functioning and life satisfaction in RA (496). Relative to the impact of negative social support, spousal criticism in RA was associated with anxiety in men and both anxiety and depression in women (497). Taal et al. (1993) found that instrumental, but not emotional, support was positively associated with health status in RA (488).

The role of social support in SLE illness outcomes is not very clear, as studies have produced mixed findings (440). Sutcliffe et al. (1999) reported a positive association of social support with the mental domain of HRQoL but not with the physical domain (425). Similarly, studies have displayed a significant negative association of social support with self-reported fatigue in SLE (498-500). When fatigue was assessed with a multidimensional instrument, social support was only associated with the mental

aspects of fatigue (499), suggesting that perceived social support is mostly associated with the emotional outcomes of SLE. Failla et al. (1996), on the other hand, reported no significant association of social support with psychological adjustment in SLE (97). Contrary to this, a recent review of social support literature in SLE reports a predictive role of social support on both the physical and mental aspects of HRQoL as well as a strong negative association with mood (494).

2.4.5 Non-Clinical Outcomes Summary

Living with conditions such as SLE and RA extends beyond the clinical parameters of disease to all aspects of a patient's life. Secondary disease parameters such as physical symptoms are very prevalent and important to patients. Pain and fatigue are the predominant symptoms and complaints of RA and SLE patients respectively, associated greatly with psychosocial well-being. Regardless of their profound presence, their nature, aetiology and association with disease activity and physical damage remain ambiguous, hence subsequently challenging their assessment and management.

HRQoL is widely acknowledged as an important outcome of chronic conditions, as it reflects the patient's perception of the impact of a condition on his/her life. HRQoL in SLE and RA is poor relative to the general population and not always consistently associated with clinical parameters of disease; it rather displays stronger links with physical and psychological symptoms and patient beliefs. However, this is not a surprising finding considering the overlapping content of such patient-reported constructs. In addition, dispositional attributes of an individual respondent bias measurement of such perceptual constructs, hence heightening their association as opposed to a construct measured by an independent clinical respondent.

Mood is also impaired in patients with SLE and RA who display elevated levels of depressive symptoms and anxiety. The cause of depression in these conditions remains ambiguous, as it is unclear whether it constitutes a feature of disease or a co-morbid condition reflecting the impact of living with a chronic debilitating condition.

Living with SLE and RA can also challenge behavioural and social functioning. Treatment adherence is a very important behavioural outcome, as failing to follow the recommended treatment plan can ultimately affect a patient's prognosis. Patient beliefs are thought to contribute to treatment adherence in both SLE and RA. Work disability is another important outcome, as disease morbidity and physical symptoms often restrain patients from working. Unsurprisingly, conditions such as SLE and RA can burden

social functioning; however, less evidence exists to support the detrimental effect of these conditions on personal relationships.

In line with the bio-psychosocial model of illness, the above physical, psychosocial and behavioural outcomes are not solely and consistently linked with clinical variables of disease. Other moderating variables such as patient beliefs, coping strategies and social support are thought to contribute to patient outcomes. Similar to all patient outcomes, assessment of such moderating variables is complicated by their abstract nature that consequently challenges their measurement.

2.5 Chapter 2 Summary

This chapter presented an overview of the nature of SLE and RA both in terms of the epidemiological and clinical characteristics as well as the non-clinical impact on patients' lives, highlighting potential sources of uncertainty. The exact cause of both conditions remains unknown, with diagnosis being neither explicit nor simple.

Illness trajectory is a potential source of uncertainty in both conditions particularly in SLE which is characterised by unpredictable flares and remissions, in comparison with RA which is primarily characterised by a gradual progressive course and in recent years following treatment advances with long periods of remission. Clinical manifestation is also another source of uncertainty, which similar with the illness trajectory, is more heightened in SLE. Even though clinical manifestation can vary in both SLE and RA, the systemic nature of SLE gives rise to more complexities and uncertainty as potentially any body organ can be affected, in comparison with RA which mainly affects the joints.

Uncertainty around life-expectancy and risk of mortality is further heightened in SLE, where as many as 78% of patients experience kidney manifestations whilst renal failure is one of the major causes of mortality in SLE. Uncertainty of illness progression in RA is largely focused on the extent of disability and less so on the risk of mortality. The epidemiology of SLE gives rise to further uncertainty as it primarily affects women of childbearing age, bringing uncertainty to their reproductive health both due to the clinical features of the disease and the toxicity of treatment. Such issues are less evident in RA, which is usually diagnosed later in life and therefore does not complicate reproductive health as often.

Another source of uncertainty in both conditions is the response to therapy. Pharmacological treatment is complicated by uncertain effectiveness, as well as the risk of toxicity. Despite recent advances in treatment, the predominant complaints reported by patients with SLE and RA are pain and fatigue. In addition, patients report reduced levels of quality of life and poor mood. The aetiology and management of such psychosocial and physical outcomes are uncertain, as they are not always representative of a patient's clinical state.

Uncertainty is therefore a key aspect of these conditions and particularly SLE, but it has never been comprehensively investigated. The next chapter presents an exploration of patient uncertainty in an attempt to reach a comprehensive conceptualisation applicable to SLE and RA and further develop a patient instrument to quantify it.

Chapter 3: Conceptual Framework Development, Item Generation and Pre-Testing

3.1 Chapter 3 Overview

Chapter 3 presents qualitative methods and results for the development of the conceptual framework and the development and pre-testing of a new patient-reported instrument for uncertainty in SLE and RA. The first part of the chapter presents qualitative interviews with rheumatology health care professionals and patients with SLE and RA. The second part of the chapter presents cognitive debriefing interviews conducted to pre-test the newly generated items for relevance, clarity, difficulty, acceptability, and completion time in a sample of patients with SLE and RA.

3.2 Background

Conditions with no known cause or cure, such as systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), are considered to be particularly susceptible to uncertainty (29). Patient uncertainty has been portrayed as an aversive state with great potential in chronic illness management; as its suggested causal associations with mood and adjustment (42-44) . Nevertheless, it was concluded from the literature review presented in Chapter 1, that patient uncertainty has to date not been explored comprehensively in rheumatology.

However, empirical investigations of patient uncertainty in cancer (53, 55, 56) and HIV (54, 87) revealed the multi-dimensional and diverse nature of the uncertainty concept both between and within conditions. The multiple dimensions put forward were not consistent between the two conditions, indicating the illness-specific nature of uncertainty, as unique dimensions were put forward relative to the characteristics of each illness (e.g. the contagiousness of HIV). Furthermore, these studies indicated that within each condition, patient uncertainty involves issues which are both directly and indirectly (e.g. personal relationships) associated with the illness itself.

The patient uncertainty literature is currently dominated by the UIT/RUIT theories (73, 74) and scales (78, 79) underpinned by research on hospitalised patients. The UIT/RUIT theories define uncertainty uni-dimensionally as the “inability to determine the meaning to illness-related events” and have been used extensively, particularly in conditions with acute phases, such as cancer and heart failure (43, 44). Considering the multi-dimensional and illness-specific nature of patient uncertainty displayed in

qualitative studies (53-56), the applicability and adequacy of existing theories (73, 74) and instruments of patient uncertainty for SLE and RA are doubtful.

Despite the lack of a comprehensive exploration of patient uncertainty in SLE and RA, aspects of patient uncertainty have emerged in several qualitative studies exploring well-being, beliefs and coping in these two conditions (31, 32, 34, 35). In these studies, patient uncertainty was associated with illness unpredictability and characteristics specific to these conditions, such as their illness characteristics, e.g. the diverse flare-up, thus highlighting the need for illness-specific assessment of patient uncertainty in an attempt to capture issues that are relevant to specific patient groups. In accordance with empirical investigations of patient uncertainty, these findings indicate the insufficiency of existing theories (73, 74) to comprehensively define and capture patient uncertainty. Subsequently, such findings challenge the adequacy of existing instruments (78, 79) to quantify uncertainty in SLE and RA.

As discussed in Chapter 1 (see section 1.3.2), the comprehensive exploration of a latent variable such as patient uncertainty requires both bottom-up and top-down approaches in order to develop a conceptual framework that can subsequently guide the development of a quantitative instrument. Development of a conceptual framework is the recommended approach (139, 182), as it determines the adequacy of an instrument to quantify the latent variable it is intended to measure. Developing a conceptual framework involves both top-down and bottom-up approaches, including the review of existing literature and collection of qualitative data from patients and expert opinions respectively (501-503). The purpose of a conceptual framework is to thoroughly describe an otherwise unobservable (latent) variable and further elicit the content of a patient-reported instrument using data from several sources.

3.2.1 Objectives

The purpose of the studies described below was to carry out an empirical inductive investigation, including qualitative interviews with rheumatology health care professionals and patients as well as cognitive debriefing interviews, aiming to develop and pre-test the content of the new patient uncertainty instrument in SLE and RA. Specifically, the objectives were to:

- Develop a conceptual framework of patient uncertainty in SLE and RA.
- Generate an item pool for the new patient uncertainty instrument.
- Pre-test the item pool for comprehension, acceptability, relevance, and completion time.

3.3 Qualitative Interviews

Following “gold standard” guidelines (139, 143) (see section 1.3.2.2), an inductive (bottom-up) approach towards the development of the patient uncertainty conceptual framework involved the collection of empirical data through qualitative interviews from two sources. Firstly, a series of brief structured interviews with health care professionals were conducted, followed by in-depth interviews with patients with SLE and RA.

3.3.1 Methods

The inductive bottom-up approach towards the conceptual framework development for patient uncertainty involved a two-phase qualitative investigation. The first phase constituted a consultation of expert opinion. This involved structured interviews with rheumatology health care professionals (HCPs) specialising in the care of patients with SLE and RA. The second phase consisted of in-depth semi-structured interviews with patients with SLE and RA. The HCPs interviews were conducted to: (i) inform the development of the interview guide for the patient interviews, and (ii) to broaden the validity of the conceptualisation of patient uncertainty by comparing and contrasting the findings of HCPs and patients [1]. Ethical approval both from the National Research Ethics Service and from the local hospital site was granted for this study.

3.3.2 Health Care Professional Interview

3.3.2.1 Sampling

Convenience sampling (504) was used to recruit HCPs for this consultation from the University College Hospital Rheumatology Department. Only HCPs with experience of treating both patients with SLE and/or RA were approached.

3.3.2.2 Procedure & Analysis

A series of brief structured interviews was carried out and guided by a list of specific questions (Table 3.1), which were created on the basis of the literature review (see section 1.2). Interviews were digitally recorded and transcribed verbatim. Data examination was guided by thematic analysis (505).

Table 3.1: Health Care Professional Interview Guide

Topic discussed:	Examples of Questions asked:
Understanding	What is your understanding of patient uncertainty?
Causes	What do you think causes uncertainty? (e.g. illness severity)
Timing	When is uncertainty mostly experienced by patients?
Expression	How is patient uncertainty expressed?
HCPs` perspective	Do you experience any uncertainty in treating your patients?

3.3.3 Patient Interview Methods

3.3.3.1 Sampling & Recruitment

Participants were recruited between July 2008 and March 2009 from University College London Hospital (UCH) using a convenience sampling technique (504). Upcoming outpatient clinic appointments of the consultants collaborating with this study were searched for eligible participants. Eligibility was judged on the basis of a clinical diagnosis of SLE or RA, a minimum age of 18 years, lack of significant co-morbid illness (e.g. diabetes, cancer), and fluency in English (judged on the patient's need for an interpreter). The search was completed using the UCH Electronic Patient Record (EPR) system. Participants meeting the eligibility criteria were sent a postal invitation (Appendix 3.1) and the study's information sheet a week prior to their clinic appointment. Those who attended their clinic appointment were approached by the candidate (Sophie Cleanthous, SC), presented with a participant information sheet (Appendix 3.2), and invited to participate in the study. An appointment for an interview on a date and time that suited the participants was arranged for interested participants.

3.3.3.2 Procedure

Interviews were conducted by the candidate at University College London. Informed consent (Appendix 3.3) was obtained directly prior to the interview. Participants explicitly consented to their quotations being used anonymously. Interviews were semi-structured and guided by the topic list (Table 3.2) created on the basis of our literature review and HCP interview findings. Participants were addressed with open-ended questions relative to the topics listed in the interview guide, e.g. "How effective do you think your current treatment is?" as opposed to "Is your current treatment effective?" At the beginning of the interview, participants were requested to answer questions relative to how sure or unsure they were of the issues discussed. The word "uncertainty" was deliberately not used until the end of the interview when participants were directly asked if they experienced any uncertainty related to their condition.

All interviews were digitally recorded and transcribed verbatim. Data collection and initial analysis took place simultaneously. Recruitment purposively continued until a diverse sample was interviewed and no new themes emerged (506). Sample diversity was judged upon participant age and years of diagnosis.

Table 3.2 Patient Interview Guide

Topics for discussion
Symptoms: ambiguity, course, regularity, unpredictability, severity
Casual attributions: pre and post diagnosis
Treatment: effectiveness & side effects
Patient satisfaction: satisfaction with treatment/health care; trust of medical stuff
Information: knowledge of condition; prognosis; treatment; source and amount of information
Restrictions in daily activities and role performance: interference with employment; interference with recreational activities; interference with other activities which are physically demanding; disturbance of sleep; interference with social activities; interference with eating; disturbance of other active ties
Psychosocial functioning: feelings about the condition; adjustment to condition; body image issues; feelings about the treatment and any concerns
Friends and family: family reactions before/after diagnosis; social support
Social Integration: reliability and dynamics of family & friends

3.3.3.3 Qualitative Analysis

Standard analytic techniques for conceptual framework development were used (502, 506, 507). Transcripts were analysed thematically using a detailed line-by-line coding to examine, compare and inductively develop the patient uncertainty conceptual domains (506, 508). Quotations were extracted and coded as “uncertain” if they reflected ‘a lack of certainty, or any state of limited knowledge, understanding or worry regarding an existing or future outcome’. This was decided on the basis of the literature review and HCPs consultation that informed the methodology of patient interviews.

Each quotation item was compared with the rest of the data to create analytical themes that were then grouped to form conceptual domains and sub-domains (Table 3.3). This involved an iterative process of cross-referencing between the different analytical themes closely supervised by the multidisciplinary group. Iterative constant comparison of the patient uncertainty themes resulted in the inductive development of the patient uncertainty conceptual framework.

Transcripts of the two patient groups were analysed in parallel, but independently, so that the results in SLE and RA could be compared. Qualitative analysis was purposefully performed manually and not using qualitative software as even through manual analysis is more time consuming, it allows researchers to focus on the depth and meaning of data rather than the breadth of deterministic coding (509). Acknowledging the relative disadvantage of manual qualitative analysis with regards to validity, an independent researcher (MS) re-coded 25% (n=8) of the transcripts in an attempt to minimise the interpretation bias (510, 511).

Table 3.3 Inductive Categorisation Technique Example

Patient ID	Lines	Quotations	Uncertainty displayed with regards to:	Theme	Sub-domain	Domain
SLE016	730-731	So my problem is that I don't know if I am bad enough to need it (the medication), I mean you can't know, so that's, a struggle	Judging the need for stronger medication	Necessity of medication	Treatment	Medical management
			Knowing /severity of current health status	Severity of current health status	Interpreting current health status	Symptoms & Prognosis

3.3.4 Results

3.3.4.1 Health Care Professionals (HCPs) Consultation Results

Eight HCPs specialising in SLE and RA were recruited to consult the study. The sample comprised three consultants, three clinical nurse specialists, a physiotherapist, and a clinical-health psychologist all based at University College Hospital. Findings of the HCP interviews are presented in relation to the questions that guided the interviews (Table 3.1) and are supported by quotations. The quantity of quotations reflects the breadth of data within each of the issues presented.

3.3.4.1.1 Understanding of Patient Uncertainty

The consultation suggested the multidimensionality of the patient uncertainty concept in SLE and RA. When asked to give their understanding of patient uncertainty, HCPs suggested a range of eight different uncertainty dimensions experienced by their patients (Table 3.4). The dimensions of patient uncertainty discussed by HCPs related mainly but not exclusively to the future course of the subsequent impact of illness. The dimensions comprising HCPs' understanding of patient uncertainty in SLE and RA are presented below.

The first dimension suggested by HCPs was “uncertainty at diagnosis”. This dimension refers to the period during which patients do not understand exactly what their diagnosis is and how to interpret new symptoms. According to the HCPs, all of their patients experience some diagnostic uncertainty. They further noted that diagnostic uncertainty is an inevitable part of the chronic illness experience that is mainly caused by a lack of knowledge, information and unfamiliarity with a new condition. HCPs further noted that such conditions are often accompanied by diagnostic uncertainty, affecting both clinicians and patients. This refers to an uncertain period before the establishment of a clinical diagnosis when different potential diagnostic scenarios are considered, as diagnosis can often be prolonged in rheumatic conditions as patients can face several months before getting a formal diagnosis. For the purposes of this study, diagnostic uncertainty will not be considered, as the objective is to investigate uncertainty experienced by patients with an established diagnosis.

Table 3.4 Health Care Professionals` Understanding of Patient Uncertainty

Dimensions	Explanation, patients are uncertain in relation to:
Diagnosis	(a) what their diagnosis is, (b) what their condition involves and (c) how it came about
Prognosis	(a) timing of flares i.e. when to expect a flare (b) manifestation of the illness (i.e. which joint or organ will be affected and (c) severity of the illness (i.e. how bad it will get)
Causal	(a) what is causing their condition and (b) why they got it
Treatment	their treatment, including (a) its purpose (b) effectiveness (c) future effectiveness (d) potential dosage change (e) potential side effects
Future consequences	How their condition will impact on their (a) functionality (b) productivity (c) occupation (d) finances (e) body image (f) mobility (g) potential pregnancy (h) chances of finding a partner (i) their mood
Self-management	How best to take care of themselves, in relation to exercise, diet and alternative medicine
Continuity of care	whether they will continue to be treated by the same consultant in the future
Doctor-patient relationship	whether (a) they can trust their consultant’s decision (b) their concerns are being taken seriously

The second dimension is related to “uncertainty of prognosis”. This dimension refers to the experience of not knowing what to expect of the future with regard to the clinical aspects of one’s illness. HCPs suggested that prognostic uncertainty can refer to: (i) the timing of illness flares, i.e. being uncertain about when to expect a flare; (ii) the manifestation of the illness, i.e. being uncertain about which joint or which organ/system will be affected; and (iii) the severity of illness, i.e. being uncertain about how bad it will get.

“Casual uncertainty”, i.e. the uncertainty of what is causing one’s illness and how it came about, was the third dimension suggested. HCPs explained how patients can be

uncertain about why they became ill and not someone else, what exactly caused their condition, and if and to which extent they are responsible for the onset of their condition. HCPs described how some patients speculate about the potential role viruses, infection or difficult life circumstances had in the development of their condition, particularly in the early stage of diagnosis.

The fourth dimension was “uncertainty of treatment” incorporating several sub-domains, including: (i) patients not understanding why they are being treated and taking their medication, (ii) patients not convinced that their medication is effective in treating their symptoms, (iii) patients feeling unsure about whether their treatment will continue to be effective in controlling their illness in the future, (iv) patients feeling unsure about a potential increase of their medication dosage in the future, and (v) patients who are not sure if the symptoms they are experiencing are side effects of their medication or something else they should worry about.

“Uncertainty of future consequences” was the fifth dimension put forward by HCPs. This was a broad dimension referring to every aspect of a patient’s life that can be affected by their illness. HCPs suggested that patients do not know what to expect and feel uncertain about non-clinical (personal) parameters likely to be affected by their illness, such as being able to take care of their children and continue their work (Table 3.4). The HCPs noted that these are anticipatory uncertainties of the potential restrictions their illness could lead to (e.g. physical functionality and mobility), but are often expressed with no direct reference to the illness itself. This dimension of patient uncertainty was mentioned extensively by the clinical nurse specialists and the psychologist.

“Uncertainty of self-management” was the sixth dimension put forward, referring to patients who are not sure of how best to take care of themselves in relation to their illness. HCPs suggested that there is patient uncertainty in relation to activities aiming to prevent or control the progression of one’s illness, such as how much exercise to do and what diet to follow, as well as activities aiming to cure or manage the current state of health, such as alternative treatments, physiotherapy and prescribed exercise. Uncertainty related to physical activities was particularly highlighted by the physiotherapist.

“Uncertainty of doctor-patient relationship” was the seventh dimension suggested by HCPs. This was also a multilevel dimension referring to patients who might be experiencing any of the following: (i) not feeling confident that their concerns are being

taken seriously by their doctors, (ii) feeling unsure of the interpersonal relationship and not knowing how to approach their doctors, and (iii) not being convinced that the doctor looking after them has chosen the right treatment for them.

The final dimension put forward is related to “continuity of care uncertainty”. This dimension refers to patients who are very satisfied and feel secure with their health care team and express worry and uncertainty about the possibility of a change in their health care team. Below a set of quotations relating to the different dimensions of patient uncertainty are presented.

“There’s the uncertainty about what is actually causing the problem. Why is this happening to me? And then there’s the uncertainty about what is going to happen to me in the future. So I have got pain — is it going to get better? If it’s not going to get better, how bad is it going to be? Am I going to be disabled by it? What can be done? It’s that sort of thing” Consultant Rheumatologist

“I only think of the term ‘uncertainty’ in the usual, conventional meaning of the term, i.e., lack of certainty as to the future. It's certainly one of the questions which patients ask me fairly frequently. They want to know what has happened to them…” Consultant Rheumatologist

“Patients don’t fully understand why they are being treated and in what way. I also think they are very uncertain as to the future, what to expect further down the line… people worry about how it will affect their life, especially the younger… they are very unsure as to how they are going to end up in the future” Clinical Nurse Specialist

“Uncertainty has a lot to do with how the disease will unravel… it’s likely that they would know that for every patient, lupus is different… uncertainty is to do with the disease outcome, whether they’ll still be able to keep their job” Clinical Nurse Specialist

“So uncertainty, it’s about survival functionalities… independence… socioeconomic status… whether they might still be attractive, whether they might find a partner… so it depends on what age you are and your priorities” Clinical Nurse Specialist

“It’s uncertainty about in the main the course of the illness and indeed what the future holds overall in relation to their illness and their lives, so some of the questions are around work, will I be able to continue working longer term, children; will I be able to have children start a family and how bad will it get, and it’s always around. I would say

the concept of illness uncertainty is focused in the main, not exclusively on the future and the future course of their illness" Clinical Health Psychologist

"They often talk about whether they will continue to see the consultant that they see, having built up a relationship with them or the nurse, their fear is that the staff change, so there is a notion of the lack of stability of the staff and how permanent they will be" Clinical Health Psychologist

"Some patients are unsure about how to manage and cope, if they are doing the right thing, how much to exercise, what things to avoid. They worry about making things worse" Physiotherapist

3.3.4.1.2 Causes of Patient Uncertainty

HCPs were asked to discuss the potential contribution of illness trajectory, severity, timing, age, and gender to patient uncertainty. Generally, HCPs suggested that the clinical variability and general complexity of SLE bring inherent uncertainty to patients, which is more heightened than the uncertainty experienced by RA patients. A specialist nurse pointed out that not the actual illness trajectory but the fact that most patients have no knowledge of SLE prior to their diagnosis brings differential uncertainties to them. Nevertheless, some of the HCPs noted that the uncertainty is not inherent in the disease itself but within the individual patient and how they deal with situations or events.

On the whole, HCPs argued that there is no link between illness severity and uncertainty, and suggested that coping style and personality characteristics are often more important in causing uncertainty. A conflicting set of arguments emerged, as one of the consultants proposed that illness severity can sometimes be linked with anticipatory fear of prospective flares, whereas another consultant argued that sometimes the patients with the most severe condition face minimum uncertainty, as they feel that the worse is behind them. Nevertheless, the above arguments are not necessarily mutually exclusive and could just reflect the multiple potential sources of uncertainty.

Most HCPs suggested that younger patients experience more uncertainty. This, according to the HCPs, is clearly linked with the patients' priorities, roles and responsibilities in life and whether that has to do with roles within a family environment or career goals. There was no suggestion of any gender difference in the extent of uncertainty, but HCPs do suggest that in relation to a patient's gender a different set of

issues are experienced. It was noted that female patients experience uncertainties relating to childbirth and children care-giving, whereas men tend to worry more about fulfilling their bread-winning roles and maintaining their socioeconomic status.

Additional factors were put forward by the HCPs as potential sources of patient uncertainty. Information and patient stories read on the internet were also suggested by the HCPs, as they noted that some patients focus on the worst-case-scenario stories they read online, which are not necessarily the norm. The doctor-patient relationship and the relative trust patients have in their consultants' decisions and choices over their treatment were also suggested as a potential source of uncertainty. In other words, HCPs described links between the different dimensions of patient uncertainty, e.g. one uncertainty dimension impacting on another one, and doctor-patient uncertainty causing treatment uncertainty. Most HCPs also suggested that personality characteristics are often important, as a small group of patients has trouble adjusting and experiences uncertainty regardless of the support they get and their disease severity. As the clinical-health psychologist noted, some patients display a tendency for anticipatory fear, i.e. uncertainty related with worrying about potential future aversive disease events.

"I think lupus patients are more uncertain than RA patients and the reason is that people think RA is just in the joints. Actually that's not true because RA can affect other places than the joints, but mostly it's the joints. So people have a fairly good idea of what an arthritis patient looks like, what an arthritis patient suffers. But lupus, it could be in your heart, it could be in your lungs, it could be in your skin, so people don't necessarily know. It's like there's something there, it could be hitting me anywhere at any time, so there's more uncertainty there." Consultant Rheumatologist

"Uncertainty varies with the disease because with lupus patients they tend to be quite well unless they have really bad flares, so I suppose the uncertainty for them is that they can't always see their disease, so they can't see what's affecting them" Clinical Nurse Specialist

"I haven't, I haven't noticed any difference between men and women and I'm not sure that the age affects it either. No, I don't think age affects it." Consultant Rheumatologist

"I don't think it's inherent to the disease itself, I don't think that. I think different people are different and I think it's partly to do with the way they are… So I think it's more to do with the individual than the diagnosis" Consultant Rheumatologist

"I believe RA patients are less (uncertain) so simply because their disease is slightly less complex" Clinical Nurse Specialist

"… for other people the uncertainty is because of their disposition may be I don't know being anxious, I don't know whether demographics" Clinical Nurse Specialist

"… so it depends on what age you are and your priorities" Clinical Nurse Specialist

"My view is that the range of organ involvement in lupus leads to greater uncertainty" Clinical Health Psychologist

3.3.4.1.3 Timing of Patient Uncertainty

All of the HCPs agreed on the increased patient uncertainty experienced during the period of diagnosis. However, some HCPs argued that the uncertainty experienced by the newly diagnosed patients is a different construct to the uncertainty experienced by patients with established disease and who have a greater understanding of their condition. HCPs suggested that patient uncertainty at the time of diagnosis is expected and part of the process of the chronic illness experience that is mainly caused by a lack of knowledge and a state of unfamiliarity. On the contrary, some patients with sufficient knowledge and experience of a condition still experience uncertainty. The HCPs also suggested that uncertainty varies with the course of their condition, as it tends to be heightened during the illness flares.

"Once you are 2 years into your disease say, you have probably got adjusted to what it might do to you, what the common features are in you. So I think that would be fair. There is most uncertainty at the time of diagnosis" Consultant Rheumatologist

"There is uncertainty at several phases but uncertainty varies within the course of disease" Consultant Rheumatologist

"Obviously the newly diagnosed patients are uncertain for a very different reason than those who are more affected" Clinical Nurse Specialist

"I would say everybody at the onset experiences some degree of uncertainty, but some people deal with it better… whereas other people will dwell on it" Clinical Nurse Specialist

3.3.4.1.4 How is Patient Uncertainty Expressed?

When asked to describe how uncertainty is expressed, all HCPs agreed that uncertainty is not a word patients would choose to use to describe their state of mind but that uncertainty is clearly implied by what they say. HCPs suggested that patients seem more ready to talk freely to the nurses, psychologists and the physiotherapists about issues that worry them, and less so to consultants who focus their limited time on physical assessment and treatment review. Consultants further indicated that uncertainty can often be identified even when not expressed directly through the patients' behaviour. They suggested that some patients seek constant reassurance from HCPs about the state of their health condition as well as take the initiative to request frequent medical scans and tests; checking health status by patients is a signal of uncertainty. This kind of behaviour, according to the consultants, signifies patient uncertainty.

"They seek assurance; some patients seek for assurance on a very regular sort of basis" Consultant Rheumatologist

"It's not a word that people commonly use; they would use words like "I'm worried about it" or maybe "I'm anxious about it", but no, I don't think they will say, use the word 'uncertainty'. Patients ask: So I have got pain — is it going to get better? If it's not going to get better, how bad is it going to be? Am I going to be disabled by it? What can be done? It's that sort of thing." Consultant Rheumatologist

"Particularly with the nurses, patients find us a little bit easier to open up to on personal aspects" Clinical Nurse Specialist

"You don't hear that word very much but you know that that's what they are implying, definitely" Clinical Nurse Specialist

3.3.4.1.5 HCPs` Perspective

HCPs were also asked to share any uncertainties they face when treating patients with SLE and RA. A variety of uncertainties were expressed, beginning with the uncertainty surrounding a clinical diagnosis. Consultants noted the complex process of formally diagnosing a patient, which is often unclear. HCPs further stated that they face prognostic uncertainties, as illness course, clinical manifestation and severity are often unpredictable. In addition, treatment uncertainties were expressed, such as establishing the best treatment plan, controlling potential hazardous side effects, dealing with patient responsiveness to treatment, and patient adherence. HCPs noted

that they also face interpersonal uncertainties, especially with regard to how a patient will respond to the health care professional, a key issue in the overall management progress. The specialist nurses acknowledged the uncertainty of not knowing how much information to give people regarding their condition and of knowing that they will not always be able to answer all the possible questions patients may have. Furthermore, they acknowledged the challenge of keeping up with constantly changing national guidelines for the care of patients.

"Uncertainty about treatments and that's a real thing because you don't know necessarily what's the best thing to offer; there is this whole question of evidence-based medicine, which is interesting" Consultant Rheumatologist

"So a lot of the uncertainty initially is in trying to work out their view, doctor's view, medicine, their view of the system, the interpersonal relationship that you're trying to develop" Consultant Rheumatologist

"I cannot give them (patients) absolute certainty because that's impossible in a Lupus patient because the disease is unpredictable" Consultant Rheumatologist

"Uncertainty in that you don't know sometimes how much information to give people or you don't want to overeducate them and scare them… and that you are not always going to be able to answer their questions or give them the answers they want" Clinical Nurse Specialist

"There is always uncertainty; you have no idea whether they will get better, and that's part of the excitement of doing clinical practice" Clinical Health Psychologist

3.3.4.1.5 Consequences of Patient Uncertainty

Even though it was not included in the interview guide (Table 3.1), all of the HCPs talked briefly about potential consequences of uncertainty. The most commonly suggested consequence was the sense of extensive worry and anxiety accompanying heightened levels of patient uncertainty. In addition, non-adherence to medication as well as poor attendance of clinic appointments were proposed as being linked to uncertainty, as patients are often uncertain in the effectiveness of care and the risk of treatment side effects. One of the consultants noted that patient uncertainty has a complex and often dynamic association with coping efficiency, i.e. whether efficient coping eliminates patient uncertainty or whether heightened patient uncertainty hinders

coping.

"That's often manifested in these days in wanting things like scans, which happens much more these days" Consultant Rheumatologist

"It can lead to a whole lot of things, that's non-compliance with medication, non-conformity with attendance of clinics, that sort of thing" Clinical Nurse Specialist

"Some of them are quite anxious about the future efficacy of their current treatments… they are worried about will it continue to work… another group are also worried about the possibility of having to escalate" Clinical Health Psychologist

3.3.4.1.6 Managing Patient Uncertainty

Furthermore, two general recommendations were put forward by the HCPs for targeting uncertainty. Patient information and education (e.g. using leaflets and one-on-one sessions with the nurse) were suggested as being extremely important at the time of diagnosis, as they aid the promotion of patients' adjustment, self-management as well as the reduction of potential uncertainties. However, apart from the temporal issue, HCPs also stressed the need to adjust the amount of information offered to the optimum level for each individual patient. HCPs suggested that the amount of information required or that can be handled is variable amongst patients, with the health care teams needing to be flexible to accommodate this.

On the other hand, the beneficial role of support in minimising uncertainty was acknowledged by the majority of the HCPs. The consultants argued that making yourself available to the patients so that they feel their concerns are being taken seriously minimises their uncertainty, as do the direct telephone lines of support that the nurses operate. It is therefore a matter of both interpersonal as well as the practical sense of support that is thought to minimise uncertainty.

3.3.4.1.7 HCPs` Consultation Results Summary

There was a consensus for the presence of patient uncertainty in SLE and RA. As quoted by one of the consultants: "uncertainty is simply the lack of certainty which is a given fact when dealing with conditions like SLE." Patient uncertainty was portrayed as a multidimensional concept, simply denoting the lack of certainty related to the multiple aspects of living with SLE and RA. These included clinical and medical as well as personal dimensions such as diagnostic, prognostic and causal uncertainty, uncertainty of medical treatment, self-management, and uncertainty of the potential consequences

of the condition. HCPs suggested various different potential sources of patient uncertainty based on their personal experience with treating patients. Conflicting arguments were put forward regarding the role of the different illness trajectories (i.e. SLE or RA) in the presence of patient uncertainty. Patient uncertainty was described as being a subjective perception often unrelated to objective knowledge or events but linked with anticipation of the future. Nevertheless, it was acknowledged that patients with SLE generally experience more uncertainty due to the complexity of the illness, the prevalence of the condition in younger age groups, and higher ration of females.

3.3.4.2 Patient Interview Results

3.3.4.2.1 Sample characteristics

Ninety-three patients having a scheduled outpatient appointment at the UCH rheumatology clinics were invited to take part in this study. A total of 61 patients were approached in the clinic, as the remaining 32 did not attend their appointment or were missed due to a busy clinic. Of the 61 patients approached, 20 were not interested in taking part in the study. The most frequent reason reported for a refusal to participate was the inconvenience of having to attend the interview on a different day and not on the day of their regular hospital appointment. A total of 41 patients were recruited in the clinics but 9 did not attend their interview appointment.

A total of 32 participants were interviewed (Table 3.5): 17 were SLE (mean age: 44, 20–73) and 15 were RA (mean age: 57, 29–79) patients. The younger age of SLE patients was expected, as SLE is usually diagnosed earlier in life than RA. Of the SLE participants interviewed, only one was male in comparison to five in the RA sample; these ratios are representative of the epidemiological gender difference in these conditions (36, 101, 315). Both the SLE and RA samples were quite diverse in relation to their disease duration, which ranged from 10 months to 35 years and 1 to 36 years respectively. More information on the collected sample characteristics is presented in Table 3.5.

Table 3.5 Patient Interviews: Sample Characteristics

	SLE (n=17)	RA (n=15)
Gender, n (%)		
Female	16 (94.1)	10 (66.7)
Male	1 (5.9)	5 (33.3)
Age		
Mean (SD)	44 (17)	57 (13.24)
Range	20-73	29-79
18-24	2 (11.8)	-
25-34	5 (29.4)	1 (6.6)
35-44	1 (5.9)	1 (6.6)
45-54	5 (29.4)	4 (26.6)
55-64	1 (5.9)	4 (26.6)
> 65	3 (17.6)	5 (33.3)
Years Since Diagnosis		
Mean	15	15
Range (months)	10 – 35	1-36
Marital Status, n (%)		
Married	8 (47.1)	10 (66.7)_
With partner	3 (17.6)	-
Widowed	1 (5.9)	3 (20)
Single	5 (29.4)	1 (6.7)
Divorced	-	1 (6.7)
Employment Status, n (%)		
Working (full-time)	6 (35.3)	5 (33.3)
Working (part-time)	1 (5.9)	1 (6.7)
Student	3 (17.6)	-
Retired	3 (17.6)	6 (40)
Unemployed / not working	3 (17.6)	3 (20)
Homemaker	1 (5.9)	-
Ethnicity, n (%)		
White	8 (47)	13 (86.7)
Black	4 (23.5)	-
Indian/Pakistani	2 (11.8)	2 (13.3)
Mixed race	2 (11.8)	-
Chinese	1 (5.9)	-

3.3.4.2.2 Patient Interview Results

Interviews lasted an average of 45 minutes (range, 30 to 90 minutes). The coding analysis resulted in more than 800 unique quotes selected to reflect uncertainty. Many quotations reflected more than one theme of uncertainty (Table 3.3) and were thus inductively categorised in more than one domain of uncertainty. Addressing the interview questions, patients expressed both a sense of uncertainty and certainty related to different issues discussed. When questioned openly about uncertainty, all but one male RA patient agreed that it was a significant part of living with their condition, repeating issues discussed during the interview.

Patient uncertainty emerged as a diverse multifaceted concept related to issues directly related to the illness itself and its treatment as well as to personal issues indirectly related or affected by the illness. Patients expressed uncertainty regarding on-going as well as future issues. Inductive analysis resulted in five overarching uncertainty domains that formed the basis of our conceptual framework for patient uncertainty (Figure 3.1). Both the SLE and RA patients produced quotations linked with all five of the domains; however, some differences were observed on a sub-domain level.

On cross-comparison there was an average coding an 88% coding consistency between the two coders. Importantly, the inconsistencies reflected quotations that were not chosen by either researcher so as to reflect uncertainty and not a differential coding of the same quotation. Most importantly, the inconsistencies between the two sets of codes were not linked with differential domains or sub-domains in the subsequent inductive categorisation of quotes and were therefore independent of the final findings, as the two researchers qualitatively produced the same codes. Findings are presented in reference to each of the five overarching patient uncertainty domains, and accompanied with relevant quotations from participants.

Figure 3.1 Conceptual Framework of Patient Uncertainty in SLE & RA

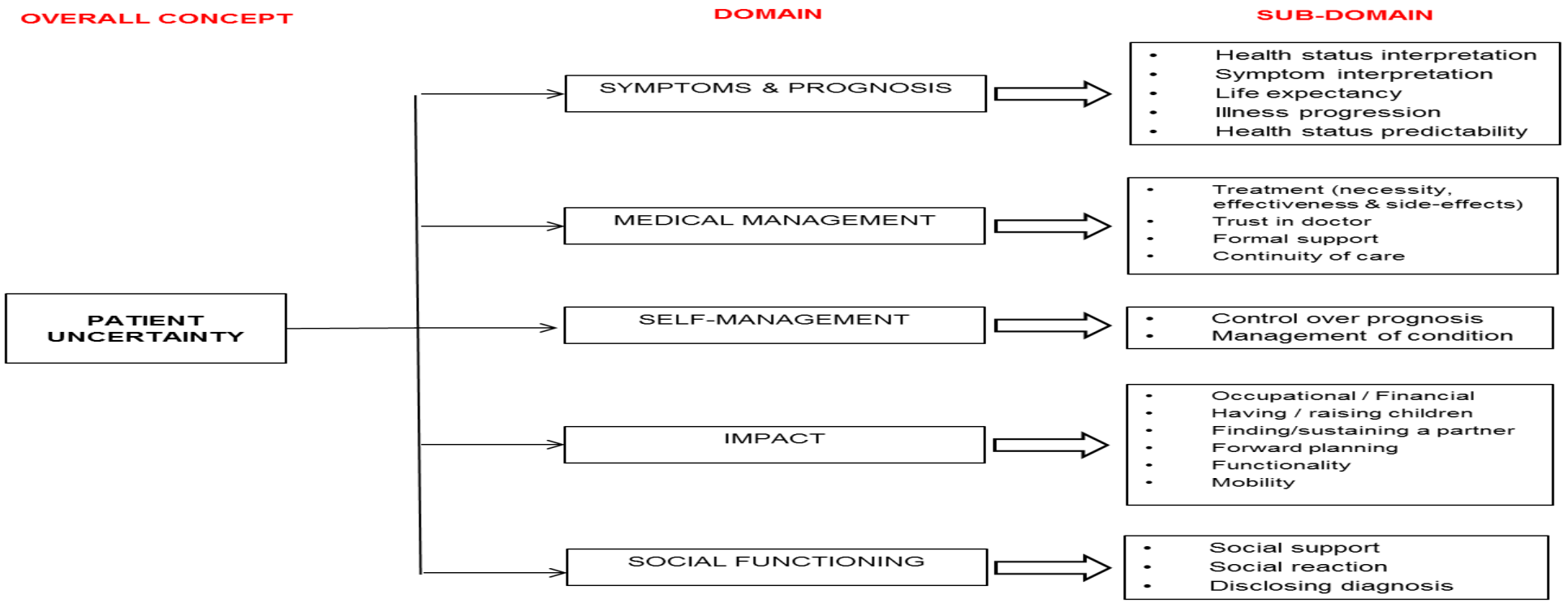


Figure 3.1: *The SLE and RA patient uncertainty conceptual framework, derived inductively by iterative constant comparison of "uncertain" quotations.*

3.3.4.2.3 Conceptual Framework: Symptoms and Prognosis Domain

Participants described uncertainty in relation to issues directly associated with their illness characteristics, course and progression. This domain comprised several sub-domains, including interpreting and labelling their physical sensations, having an overall understanding of their symptoms, judging and predicting their short-term and long-term health status, as well as predicting how their illness expression will be manifested.

Firstly, some patients reported uncertainty in relation to the interpretation of their current health status, i.e. judging how well they are, as sometimes there is disparity between the symptomatology acknowledged by the patients and the clinical markers of their condition. In addition, the dispersed and inconsistent nature of symptoms was also related to uncertainty regarding the health status, as some patients described.

"…my kidneys stopped working. I mean, I didn't know at the time I was at work and I was having these severe headaches and I hadn't even realised" SLE female, 39 years of age

"Some days I think to myself, I am like, oh I feel fine, I felt fine for a week. That might be, I haven't got it anymore and then something little will happen" SLE female, 20 years of age

"I don't know, sometimes I think to myself what if I haven't got that, perhaps it was some strange viral thing that affected my joints" RA female, 55 years of age

The symptomatology of their condition was an aspect of increased uncertainty for the patients. This uncertainty took many forms, including: judging the seriousness of symptoms, knowing what triggers symptoms, and when to expect a symptom, as well as interpreting them.

"It was very unpredictable because it, I would feel perfectly healthy one day and the next day I would, my knees would be swollen and my hands would be swollen" SLE female, 38 years of age

"Oh well I don't know what I've done, I've been in the bed the whole time I was in hospital, how can my foot be hurting" SLE female, 20 years of age

"… but I mean at the moment there are no factors that trigger, it comes any time there are no, no time of the day that comes" RA male, 58 years of age

Participants described their difficulty in interpreting all the symptoms and physical sensations they experienced and noted that it was not always easy to distinguish which symptoms were specifically related to their condition (as opposed to everyday symptoms, symptoms of transient conditions, and natural aging), as well as having difficulty distinguishing them from side effects of medication.

"I can just think well I've been busy at work and so I'm tired because everybody is tired but then there is a definite fatigue that's definitely lupus but it's their middle ground, that's tricky" SLE female, 32 years of age

"… perhaps I'm just walking up and down a lot you know. There must be a bit of loss of fluid in cartilage and all that once you're getting older anyway so you got to realise that something is going to happen at some stage, not just rheumatoid you know" SLE female, 58 years of age

Participants, especially the patients with SLE, noted the diversity of their symptoms but also the overlapping characteristics of their symptoms to everyday and transient health issues giving rise to confusion and uncertainty over their symptom interpretation. However, it was suggested that this aspect of uncertainty is often heightened at the period around diagnosis. The increased knowledge and ability to interpret symptoms are noted by a participant:

"I know if something isn't right, I know it now; whereas before you didn't know whether it's the rheumatoid that's causing the problem or was it something general aches and pains that you get" RA male, 58 years of age

Uncertainty was also described with regard to knowing what effect their illness will have on their life expectancy as well as the future severity of their condition. They did, however, acknowledge improvements in treatment and overall care of these conditions in the recent years.

"I suppose uncertainty of the future it could be, couldn't it? Whether, I suppose whether it shortens your life, that sort of thing or has it" SLE female, 47 years of age

"Well, because you assume that it might probably get worse and you don't know how much worse, and so that uncertainty is hanging over you all the time" RA male, 63 years of age

"… it's just I guess a concern and another uncertainty not that I don't know, I mean I do know because I've read about it. But in terms of life expectancy and, you know, from what I understand lupus patients nowadays and especially with rituximab these kinds of treatments have a, you know, pretty normal compared to the average person a pretty much similar life expectancy" SLE female, 27 years of age

Some differences were evident between the two conditions, as SLE patients reported heightened uncertainty related to the timing and type of future flares as well as the unpredictability of their condition both in the short and in the long run. Patients with SLE noted that their condition and state of health fluctuate constantly even within the course of a day, hence bringing them uncertainty in predicting how they will feel at a later stage. Similar to the everyday unpredictability of their health status, SLE patients revealed the uncertainty of future illness expression by discussing the various potential organ systems their condition could affect in the future.

"Lupus is an absolute uncertainty. You don't know, how you're going to be, I don't know how I'm going to be this afternoon." SLE female, 31 years of age

"I don't know what to expect. I think I generally expect it possibly to get worse, but I know that it affects different people, everybody differently. I was just reading up about kidney disease and things like that and I don't know what's going to happen" SLE female, 31 years of age

"I don't know what's going to happen, but I hope nothing's going to happen, but looking at my history… That's very hopeful I don't know, I suppose that the biggest worry in a way is my kidneys actually" SLE female, 52 years of age

3.3.4.2.4 Conceptual Framework: Medical Management Domain

The second domain consisted of uncertainty related to the different aspects of the medical management of one's illness, comprising different sub-domains. These included the effectiveness and necessity of pharmacological management, issues related to trust in the health care professionals as well as the formal support provided by the hospital. Their treatment regime was an area of great uncertainty for many participants. Participants reported being uncertain with regard to whether or not they absolutely needed the medications they were prescribed and whether they could survive without them. Similarly, some participants were unaware of the exact purpose of their medication.

"*Why am I having to take all this stuff (medication)" RA female, 48 years of age*

"… to what extent would the symptoms come back after I stop taking this medication" SLE female, 20 years of age

"I don't know quite about what the Plaquenil is for and then it was basically about my tiredness or something. I don't know why I take that though" SLE female, 67 years of age

On the other hand, patients were uncertain in judging whether or not their treatment was effective in controlling their symptoms. In addition, uncertainty was displayed in knowing whether a specific treatment regime will continue to be effective in the future.

"… doesn't necessarily mean a drug is always going to work for you" SLE female, 32 years of age

"Well I'm hoping that Humira will keep me going for a while but given everything else I suspect it will stop working" RA female, 48 years of age

Furthermore, some patients were uncertain in relation to the possibility of experiencing serious side effects as a result of their treatment regime, a theme that was often expressed with a sense of concern and worry.

"Well, as far as big uncertainties, what the drugs will do, will they shorten my life, will they complicate my body? I suppose that's the biggest uncertainty" RA male, 49 years of age

Although patients generally reported trust in their consultants, they described uncertainty in relation to the consultants' knowledge and ability to help their condition. In other words, reflecting the uncertainties put forward by the HCPs, patients were aware of the uncertainties experienced by their consultants in relation to the prognosis and treatment of their condition. Some of the participants further talked about the uncertainty HCPs faced in diagnosing them, describing long periods of testing and alternative diagnosis.

"*Obviously they (doctors) don't know if that's going to be the wonder-pill for me" SLE female, 32 years of age*

"I mean the consultant tells me that, that if I'm lucky, the medication will keep it all stable, and I think his line is that, he doesn't know any better than I do how it might develop" RA male, 63 years of age.

"… she (doctor) said it could be leukaemia, so I had to eliminate leukaemia. She wanted to eliminate lupus and then HIV because she said they all had similar symptoms or I was portraying those symptoms" SLE patient, 27 years of age

All patients reported feeling confident about the support they were receiving from the hospital, highlighting the importance of having access to emergency appointments and a direct phone line. However, some uncertainty was revealed in relation to understanding the meaning and importance of medical test results and their doctor's recommendations.

"So if I did have any worries then I obviously know that there is a team there that now I could speak to, well my GP is there as well" SLE female, 47 years of age

"Yeah, it's no good saying 'no' you need to do a blood test. I want to know why and why are the gamma globulins, you know, why are they high, how is that going to affect me…" RA female, 65 years of age

Patients also reported uncertainty in relation to being treated by health care professionals other than their regular doctor in the event that their care gets switched to a different hospital or when occasionally they get seen by a temporary registrar. Patients with SLE, in particular, also reported uncertainty in relation to needing care whilst abroad.

"*I'm just concerned that one day you (the GP) will say to me that now there are doctors who know about lupus down in Brighton and you'll say I'm not going to go on funding you to go up to UCH." SLE female, 73 years of age*

On travelling abroad: "I'd be scared that I get sick. I'm just worried about the treatment and healthcare in a different country" SLE female, 31 years of age

3.3.4.2.5 Conceptual Framework: Self-Management Domain

Patients appeared to be very knowledgeable on the issues related to managing their condition and their symptoms. As they noted, their knowledge was built both on the information they received from the hospital and also on the everyday experience of living with their condition. Participants described growing familiar with their bodies and knowing their limits, especially with regard to fatigue and pain.

"Yeah, I mean I have my days where I don't do anything and I'll just lie down and sit and relax, and I know that my body wants it and that's what I do. I listen to my body" SLE female, 20 years of age

"You know your body, I think, I know when, when I get, you know, when the body is saying when that's enough sort of thing." RA male, 58 years of age

However, some patients described uncertainty in relation to knowing how much control they have over their illness progression and whether there is anything more they could do to help control it, i.e. speed up recovery and prevent future flares.

"I try to be good with my kidneys then something else happens. So it's like you try to prevent other things happening but it doesn't make any difference." SLE female, 49 years of age

"Because I am realistic, I cannot change nothing" RA female, 54 years of age

Nevertheless, some patients were adamantly positive about things they can do to help control their illness progression and symptomatology.

"I think it's important that one is active, exercises, doesn't get overweight because that just puts more, if you're, if you are overweight it puts more strain on your body and your bones I think" RA female, 71 years of age

In addition, uncertainty was reported in relation to behavioural aspects of self-management, mainly associated with the types of physical activity patients should or should not do, and how much to push themselves without jeopardising their health.

"Just thinking about not overdoing it and my partner really wants to go to Peru and do this big hike, and I just don't know if this is something that I could do or should do and just things like that" SLE female, 32 years of age

3.3.4.2.6 Conceptual Framework: Impact Domain

Apart from the aspects directly related to the illness itself or its management, patients described uncertainty related to the potential impact of their illness on their lives. Uncertainty was identified in relation to whether or not and to which extent their illness would impact on a diverse range of personal issues that were closely related to the demographics of each participant. These included sub-domains closely associated with their illness, such as physical functionality, but also indirect sub-domains such as career development, personal relationships and family planning. Uncertainty in this domain mostly referred to future outcomes or issues and was expressed with an evident sense of concern or worry.

Many participants reported having to change profession, reduce their working hours or even to quit their job as a consequence of their condition. Consequently, some participants reported being uncertain in relation to maintaining or finding a job in the future as a result of their illness and the subsequent effect of this on their financial stability.

"I have one good day a week where I can be good from morning till afternoon, who is going to employ someone like that?" SLE female, 31 years of age

"I was panicking about my job because I was a trainee solicitor. I thought well, how am I going to go back (to work) and my condition was just becoming worse and I was panicking" RA female, 29 years of age

Both SLE and RA patients reported uncertainty in relation to their physical ability and having enough stamina to raise their children. Patients with SLE, in particular, reported uncertainty in relation to their ability to get pregnant, the effect of SLE on their pregnancy as well as the potential effect of the pregnancy on their own health.

"I still end up thinking well how am I going to manage other things. I don't know how I'm going to have kids" RA female, 29 years of age

"You've got lupus and that's something which in terms of especially in relation to having children and getting married worries me a little bit in terms of, you know, I don't want to leave children un-mothered" SLE female, 31 years of age

"I think a third of women who become pregnant who have lupus miscarriage, which is, you know, obviously another concern" SLE female, 29 years of age

"… you know I have got an illness and stuff and I don't know it can affect your chances of having children and things like that and some of the medication can affect you that way" SLE female, 31 years of age

Furthermore, participants described uncertainty in relation to the effect of their condition on their ability to find a partner or sustain a relationship. There was a general consensus on the burden/risk chronic illness can place on a personal relationship, even if both parties have good intentions. In addition, some patients reported uncertainty as to finding a partner because of their diagnosis.

"You know especially with arthritis you know with age it does get worse. So I'll get worried like would that be a hindrance on your relationship" RA female, 45 years of age

"You got to think to yourself, well is this person going to stay with me and support me or are they going to run away?" SLE female, 21 years of age

"I thought, because I am not married, I don't have boyfriend and I don't have kids, I just thought who is going to have somebody who is ill" SLE female, 31 years of age

Patients with SLE reported uncertainty in the general planning of their lives as a result of the unpredictability of their condition. This planning uncertainty stretched from everyday short-term activities, such as shopping and cooking, to longer-term social activities, such as attending family weddings and planning holidays.

"It does mean I could be in the hospital, you know next week and next month so how can I plan anything?" SLE female, 31 years of age

"I'm aware that there's a huge amount of uncertainty so much so that when it comes to planning holidays and things of that nature and big event" SLE male, 48 years of age

Finally, their future physical functioning was also an area of uncertainty, but was expressed rather differently between the two conditions. Patients with RA reported a sense of fear of disability and often expressed uncertainty in relation to predicting future mobility in the longer term. Patients with SLE, on the other hand, expressed a constant uncertainty of predicting the potential restriction of activities, ranging from everyday things like cooking dinner to completing an educational degree.

"My first concern was, am I going to end up in a wheelchair?" RA female, 79 years of age

"Is this thing ever going to be fixed, am I going to be able to walk again, am I going to be able to do simple things" RA female, 31 years of age

"The more uncertainties are the smaller things like I said what am I going to be able to cook for dinner tonight…" SLE female, 31 years of age

3.3.4.2.7 Conceptual Framework: Social Functioning Domain

Another uncertainty domain, which was not directly associated with the illness itself, was related with social relationships and behaviour in light of their illness. Some patients described being uncertain in terms of the support they can expect from their family and loved ones, i.e. whether or not they could count on their loved ones' care.

"I am scared because my daughter might leave London next year and I hope my son should come here, but I hope she will decide to stay here in London" RA female, 59 years of age

"… so I imagine if I get to a stage where I can't look after myself and she will face this, she's got her own life to live and she has, no I'll go into a home" SLE male, 48 years of age

Patients further reported being uncertain about whether their loved ones fully understand what they are going through in relation to the range and severity of their symptoms. SLE patients, in particular, talked about the invisibility and inconsistency of some of their symptoms, which brings uncertainty to others in relation to understanding their condition.

"I don't think he (partner) can really understand (the fatigue) because he can't physically see it" SLE female, 38 years of age

"It's just hard when people don't understand what you're going through. They see you yesterday, you're smiling. They see you today, well what's got in, they look at you like what's wrong with you. And it's just, the, the lack of knowledge they have of it is hard" SLE female, 21 years of age

Both patient groups reported uncertainty in terms of disclosing their diagnosis to potential employers, but patients with SLE also reported being uncertain about disclosing their diagnosis within their social circle and to potential partners. This uncertainty was associated with the expectation of negative implications following the disclosure of diagnosis.

"Now with a potential partner is hard… and I just don't know when to tell them (tell them about SLE)" SLE female, 21 years of age

"I wasn't sure how it would work out. I wasn't sure how long I was going to be there and, and I was thinking well I could be fine… but yeah my boss knew, eventually I told them because I have yeah, take time for doctor's appointments and stuff" SLE female, 31 years of age

3.3.5 Conceptual Framework

Patient uncertainty quotations deducted from the interviews were inductively categorised into five overarching domains: symptoms and prognosis, medical management, self-management, impact, and social functioning relevant to both SLE and RA patients (Figure 3.1).

This work has been published in a peer review journal (20). The domains were relevant to both SLE and RA but some differences were observed on a sub-domain level. Specifically, heightened patient uncertainty was displayed with regard to illness progression and unpredictability, forward planning social reaction, and disclosing diagnosis in the SLE sample, which produced a greater breadth of quotations in these sub-domains. The breadth of quotations was also different between the five domains across both conditions, as self-management and social functioning do not cover as many sub-domains and themes of uncertainty as the remaining three domains.

There was overlap between the conceptual framework domains (Figure 3.1) and the HCPs' understanding of the patient uncertainty (Table 3.4), even though the patient interviews were richer in information and provided more detailed description of the patient uncertainty domains and sub-domains. The dimensions of diagnosis and causal patient uncertainty suggested by HCPs were not replicated in the patient interviews and, thus, were not included in the conceptual framework.

Considering that HCPs suggested that these dimensions are particularly prevalent in the early stages of a person's diagnosis (see section 3.3.4.1), it can be assumed that they were not of great relevance to this specific patient group, the vast majority of which had established disease of longer than one year of diagnosis. In addition, although patient findings did not reveal any causal uncertainty similar to that suggested by HCPs, patients seemed to be well informed of the unknown cause of their condition and further indicated their awareness of the uncertainties HCPs face in treating them (see section 3.3.5.2 *medical management*). In view of the above, the HCPs findings were considered to be consistent with the final conceptual framework of patient uncertainty.

3.3.6 Qualitative Interview Conclusions

Reflecting previous findings (29, 78, 79), patient uncertainty was manifested as a subjective perception that took many forms, including lack of absolute knowledge or understanding, difficulty in interpretation or judgement, unpredictability, and expectation of potential consequences or risks, and often expressed with a feeling of worry. The findings portrayed patient uncertainty to be a complex outcome of multiple sources within the context of each individual and sometimes inherent in the presence of SLE and RA.

Despite the differences between the two conditions, findings suggested that patients with SLE and RA experience uncertainty across the same five overarching domains, whilst differences between the two illness groups were only observed on a sub-domain level (Figure 3.1). Although the domains are conceptually independent, they could potentially be dynamically associated. For example, increased uncertainty in the symptoms and prognosis domain could potentially be linked with increased future uncertainty in the impact domain. However, such conclusions cannot be drawn from qualitative data.

Aside from these five domains, different sources of uncertainty were suggested, linking the different domains of patient uncertainty (82). These included issues extrinsic to the patient, such as characteristics of illness trajectory (e.g. multi-organ involvement), unfamiliarity with diagnosis, and limited information and knowledge, but also issues intrinsic to the patient, such as age, gender, work, and personal situation. Most importantly, uncertainty appears to be the result of a subjective appraisal process, often expressed in an abstract and emotional manner and not as the objective calculation of probability or risk (2, 3, 24).

These findings extend previous theories of patient uncertainty with the inclusion of domains such as the “impact” and “social functioning”, displaying how patient uncertainty goes beyond the purely medical aspects of a condition (73, 78). In addition, findings provide a more thorough account of the illness-specific uncertainty experienced by patients. Themes within the symptoms and prognosis domain, such as uncertainty of illness expression (e.g. organ involvement) and illness course (e.g. unpredictability of flares), have not been reported in previous conceptualisations of uncertainty and demonstrate the diversity of SLE clinical expression and an unpredictable illness course. Such themes were previously suggested sporadically in qualitative SLE (31, 35) and RA (32, 34) studies, but not conceptualised comprehensively.

The increased complexity of SLE was also demonstrated in the heightened uncertainty in the “impact” domain, especially within the “occupational” and “having children” sub-domains. This could potentially be related to the heightened uncertainty reported by SLE patients with regard to aspects of their illness (i.e. the “symptoms & prognosis” domain), an implication which requires further exploration in subsequent studies. Another explanation of the differential uncertainty in the “impact” domain could be the demographical differences between the two patient groups (Table 3.5), as a larger proportion of young (<35 years of age) SLE patients were recruited. As suggested by the HCPs, there are different sources of uncertainty across the life-span and this can arguably cause uncertainty to younger patients with regards to issues such as finding a partner, family planning, and building a career which are not that relevant to patients of an older age.

It is important to note that the youngest female RA patient (29 years of age) reported “impact” uncertainty comparable to the SLE data, indicating the potential primacy of demographic variables in uncertainty and further indicating that illness characteristics are not the sole source of uncertainty. Therefore, it is likely that the heightened uncertainty reported by patients with SLE can be attributed to both the different characteristics of the illness trajectories as well as the typical demographic differences between the two patient groups. Similarly, males and females expressed different dimensions of impact uncertainty, as family planning and “maritability” were only mentioned by females, further signifying the causal role of demographic variables in patient uncertainty.

Overall, HCPs appeared to be aware of the different aspects of patient uncertainty as well as the multiple and complex potential sources of uncertainty that were subsequently indicated by the patient findings. Comparatively, patients were aware of the uncertainties HCPs face in treating them. HCPs acknowledged both the importance of illness trajectories and demographic characteristics in bringing about uncertainty, a finding validated by the patient interviews. In addition, HCPs highlighted that although patient uncertainty is heightened around the diagnosis period, some patients remain highly uncertain even after the passage of time and acquisition of knowledge around their condition. This emphasises the distinction between the subjective perception of uncertainty and the objective lack of information or knowledge about an event or situation.

These findings also supported the potential negative effect of patient uncertainty on both behavioural and psychological outcomes (24, 29, 43, 44). Both patients and HCPs suggested that patient uncertainty can have a negative impact on their emotional well-being, quality of life and overall adjustment to their condition. This was particularly evident in quotations related to uncertainty of “impact”, “social functioning”, as well as the sub-domain of “side effects”, which were expressed with an evident sense of concern and worry portraying uncertainty as a significant cognitive stressor (24). Treatment non-adherence, non-attendance of clinics and reassurance seeking were suggested by HCPs as potential consequences of patient uncertainty. These behavioural issues can be inferred from uncertainty around treatment necessity and effectiveness and uncertainty around future side effects associated with thoughts of deliberate non-adherence. In addition, uncertainty around health status and symptoms interpretation, i.e. the patient’s ability to distinguish whether a symptom is linked with their illness and judge how serious it is, has important implications on self-management and care.

3.3.6.1 Qualitative Interviews Summary

The qualitative findings have expanded previous patient uncertainty literature and comprehensively revealed multiple and different aspects of patient uncertainty experienced by patients with SLE and RA. Uncertainty related to the unpredictability of illness expression in SLE and RA suggested by previous studies (31, 32, 34, 35) was confirmed and expanded by this study. Despite the differences between SLE and RA findings revealed that patients with SLE and RA experience the same overarching uncertainty domains including; symptoms and prognosis, medical management, self-management, impact, and social functioning (Figure 3.1) with some differences observed on a sub-domain level. The findings confirm the importance of illness-specific assessment of patient uncertainty (54, 55, 82) and further indicate the insufficiency of a generic definition (78) of patient uncertainty to comprehensively capture the concept in SLE and RA.

3.4 Item Generation

The patient uncertainty conceptual framework and the patient quotations coded as uncertain were used for developing the content (139, 182) of a new patient-reported instrument to assess uncertainty in SLE and RA. Items for the new patient uncertainty instrument were generated on the basis of uncertainty domains and guided by qualitative investigation comprising the literature review, HCPs and patient interviews. Items were generated using an iterative process under the supervision and guidance of a Psychometrics expert (Dr Stefan Cano) and cross-referenced with Prof. Stanton Newman, an expert in Health Psychology. Similar to qualitative analysis item generation was performed in parallel but independently for the two conditions and resulted in qualitatively the same content of items.

Although the initial intention of assessing patient uncertainty across the two conditions in parallel was for RA to act as a comparator to SLE in an attempt to contrast the illness-specific differences of uncertainty, the final item pool was mutual for both SLE and RA. This was due to the fact that the qualitative analysis performed in parallel but independently in SLE and RA, led to the same five overarching uncertainty domains comprising the conceptual framework consistent across the two conditions. Furthermore, even though the volume of uncertainty quotations in the SLE sample was greater, the youngest female patient with RA revealed issues of uncertainty analogous to the SLE sample and hence relevant items had to be included in the RA pool to cover this patient. To this effect, the items related to SLE and RA patient uncertainty were qualitatively mutual.

3.4.1 Item Construction & Phrasing

Items were constructed using as many of the patients' own words as possible; where possible, verbatim quotes were used. Language was purposefully kept lay, with items being worded in a positive direction where possible. Items were written in the first person and the majority of them contained direct reference to the individual's condition, i.e. SLE or RA. For items where this attribution was not possible, direct reference to the condition was made in the equivalent instructions.

Following principles of item construction (512), we aimed to have an adequate range of items to cover the breadth of content within each of the five conceptual domains, as well as to have items to cover all levels of uncertainty within each domain. Brevity was aimed,

as items were constructed with the minimum numbers of words possible in conveying a concept. Additional semantic overlap between items was kept to the minimum, as each item was directly targeting a single concept (512).

3.4.2 Response Categories

Response categories of a Likert-like format were chosen so as to reflect the extent to which respondents were uncertain or certain in relation to the item statements (139). In an attempt to keep the response scale as proximal as possible to the intended measurement trait which is otherwise quite abstract as well as to maximise clarity within the measurement, the word uncertainty was explicitly included in the response categories. Four response options were included: “Very Uncertain”, “Somewhat Uncertain”, “Somewhat Certain”, and “Very Certain”, giving them a score from 1 to 4.

The choice of four responses was purposeful so as to avoid respondents choosing the middle “neutral” category (512) whilst offering them an exclusively positive (i.e. Very Certain) and negative (i.e. Very Uncertain) category, as well as two middle categories which differentiate between those who are unsure but leaning towards a positive response (i.e. Somewhat Certain) and those who are unsure but leaning towards a negative response (i.e. Somewhat Uncertain). In addition, the future “impact” sub-section included a “Not applicable” response option, as it included items specifically relevant to respondents’ gender or age (e.g. pregnancy).

These response categories were chosen on the basis of discussions within the multi-disciplinary research team but in line with the PCQ items require empirical validation both qualitative and quantitative.

3.4.3 The Initial Patient Certainty Questionnaire (PCQ) Items

A total of 82 items were constructed for the new patient uncertainty instrument, reflecting the five overarching domains of the conceptual model (Figure 3.1). The instrument included: 26 items referring to symptoms and prognosis, 27 items referring to medical managements, 5 items referring to self-management, 18 items referring to impact, and 6 items referring to social functioning (Table 3.6).

Although the new instrument was developed to quantify uncertainty, it was decided to name it “Patient Certainty Questionnaire” and further score all items in a positive direction, allowing for higher scores to reflect higher levels of certainty and subsequently lower levels of uncertainty. This was done in an attempt not to pre-empt, imply or reinforce uncertainty to respondents. The initial items of the PCQ were divided into a current (49 items) and future section (40 items) across the five conceptual domains to reflect the timeframe of each item. An SLE and an RA version of the PCQ were designed. They both comprised exactly the same items (Table 3.6) but eliminated the equivalent reference of lupus/arthritis from the item strings.

3.4.3.1 Relevance of Items to the Conceptual Framework

Items were generated to reflect themes of the conceptual framework. To this effect, the range of items covering each domain was related to the breadth of the uncertainty content within each domain. Therefore, the number of items generated was relative to the amount of sub-domains comprising each domain (Figure 3.1), leading bigger domains such as symptoms and prognosis to generate a greater number of items than social functioning. Items were further generated to cover all potential levels of each uncertainty theme whilst aiming for minimal or no content overlap between items.

Table 3.6 Item Generation

Domain	Sub-domain	Items
Symptom & Prognosis	**Health status interpretation**	My lupus/arthritis is under control at the moment.
	Symptom Interpretation	I can tell which symptoms are specific to lupus/arthritis.
		I can tell apart lupus/arthritis symptoms from the natural symptoms of getting older.
		I can tell lupus/arthritis symptoms apart from side-effects caused by the medication.
		I can tell apart everyday lupus/arthritis symptoms from flares.
		I can judge how serious my lupus/arthritis symptoms are.
		I know that my lupus/arthritis symptoms are not in my head (i.e. not imaginary).
		I can tell straight away when I am experiencing a lupus/arthritis symptom.
		I know when to expect a lupus/arthritis symptom.
		I know how long my lupus/arthritis symptoms last.
		I know what triggers my lupus/arthritis symptoms.
		I know all the different symptoms related to my lupus/arthritis.
		I am experiencing side effects because of the medication I am taking.
	Life expectancy	Lupus/arthritis will NOT affect my life expectancy.
	Illness progression	I know what may cause my symptoms to get worse.
		I know that my lupus/arthritis will flare-up at some time in the future.
		I know what type of flare-ups I will experience.
		I can predict when I will experience a flare-up.
		I can predict how often I will experience a flare-up.
		I can predict how lupus/arthritis will affect me in the future.
		I can predict how severe my flare-ups will be.
		The state of my lupus/RA will stay the same in the future.
	Health status predictability	I can predict how well I will be in six months.
		I can predict how well I will be next month.
		I can predict how well I will be next week.
		I can predict how well I will be tomorrow.
Medical Management	**Treatment**	I understand how my lupus/arthritis is treated.
		I understand why I am being treated.
		The medications I am taking are helping my lupus/arthritis symptoms.
		The medication I am taking is controlling my lupus/arthritis.
		I need the medication I am currently taking for my lupus/arthritis.
		I need a stronger dose of medication for my lupus/arthritis.
		I need additional medication for my lupus/arthritis.
		I need alternative medication for my lupus/arthritis.
		The medication I am taking will continue to control my symptoms…
		I will NOT need to have surgery related to my lupus/arthritis in the future.
		The medication I am taking will NOT cause any side effects…
		The medication I am taking will NOT cause any severe side effects…
		The medication I am taking will continue to control my symptoms in the future.

Table 3.6 (Cont`d)

Domain	Sub-domain	Items
Medical Management	**Trust in Doctor**	My doctor(s) know exactly what caused my lupus/arthritis.
		My doctor(s) know exactly how physically active I should be.
		My doctor(s) know which medication(s) and dose(s) are the best for me.
		My doctor(s) know which medication will work best for me.
		My doctor(s) know exactly how my lupus/arthritis will progress in the future.
		My doctor(s) know exactly what's wrong with me.
		My doctor(s) know how to help me control the physical aspects of my lupus/arthritis.
		My doctor(s) know how to help me with the non-physical aspects of my lupus/arthritis (e.g. feeling low).
	Formal Support	I have the continuous support of the hospital team
		I understand what my medical test results mean.
		I understand my doctor's/nurse's questions, comments and recommendations.
	Continuity of care	I would feel confident if a doctor other than my personal consultant saw me in the clinic.
		I would feel confident moving my lupus/RA care to a different hospital.
		I would feel confident receiving healthcare whilst abroad (outside the UK).
Self-management	**Control over prognosis**	There are things I can do to help control my lupus/RA (e.g. avoid or recover from flares).
	Management of condition	I know exactly how to manage my lupus/arthritis.
		I know which symptoms I need to report to my doctor.
		I know which types of physical activity I should avoid.
		I will be able to manage my lupus/arthritis in the future.
Impact	**Occupational/ Financial**	Lupus/RA will affect my ability to keep a job.
		Lupus/RA will affect my ability to find a job.
		Lupus/RA will affect my finances.
	Having /Raising children	Lupus/RA will affect my ability to care for my children.
		Lupus/RA will cause problems to my pregnancy.
		Lupus/RA will affect my ability to get pregnant.
	Finding/Sustaining a partner	Lupus/RA will burden my relationship with my partner.
		Lupus/RA will affect my ability to maintain a relationship with my partner.
		Lupus/RA will affect my ability to find a partner.
	Forward planning	I can plan everyday things e.g. work, grocery shopping & housework, exercise.
		I can plan social events in advance e.g. attending a wedding.
		I can plan holidays in advance.
		Lupus/RA will affect my ability to complete my education.
	Functionality	Lupus/RA will affect my ability to exercise.
		Lupus/RA will affect my ability to cook.
		Lupus/RA will affect my ability to dress myself.
	Mobility	Lupus/RA will affect my ability to travel abroad.
		Lupus/RA will affect my mobility (e.g. my ability to walk).
Social Functioning	**Social support**	My family and loved ones are supportive of my lupus/RA.
		My family and loved ones will be supportive of my lupus/RA.
		My family and loved ones will help me manage the day-to-day issues of my lupus/RA.
		My family and loved ones will care for me if necessary.
	Social reaction	My family and loved ones understand the variety and severity of lupus/RA symptoms I am experiencing.
	Disclosing diagnosis	I can confidently reveal my lupus/RA diagnosis to others.

3.5 Pre-Testing of the Initial PCQ Items

It is recommended that once a new instrument is developed, cognitive debriefing interviews (183) should be carried out to qualitatively assess the newly developed items. The purpose of this assessment is to identify any items or instructions that respondents have difficulty in understanding, responding to, or interpret differently from intended as well as assess the applicability of the response scale categories (139, 503, 513). In addition, pre-testing helps identify ambiguities in the wording of items, confirm relevance, determine acceptability, and estimate completion time for the measure in question. Cognitive debriefing can further enhance the reliability and validity of an instrument by gaining insight into how respondents understand the items (139, 183). Analysis of the pre-testing cognitive interviews leads to appropriate modifications of the questionnaire.

3.5.1 Pre-Testing Methods

3.5.1.1 Pre-Testing Sampling and Recruitment

There are no specific sample size guidelines for pre-testing procedures, though studies have traditionally conducted 15–25 interviews for this purpose. Participants recruited should, like other qualitative methods, be representative of the target population. All but one of the patients participating in the qualitative interviews of this study were re-invited to participate in the pre-test study. It was not possible to re-invite one of the existing patients with SLE, as his sight problems restrict his reading ability completely. As pre-testing of the PCQ required participants to read through the new measure, it was not possible to recruit this patient.

3.5.1.2 Pre-testing procedure

A total of 31 existing participants (16 SLE and 15 RA) were invited to participate (Appendix 3.4). Patients were sent a letter by the candidate (SC) who interviewed them in the first phase of this study, inviting them to participate in the pre-testing phase along with an information sheet (Appendix 3.5). Patients were then contacted by the candidate (SC) who went through the study information with them and answered any questions they had. Interested patients scheduled an appointment to meet the researcher face to face.

During the face-to-face appointments, which took place at University College London, patients were asked to fill in the consent form (Appendix 3.6). Participants were instructed to complete the initial PCQ items (Appendix 3.7) whilst thinking aloud. Specifically, participants were asked to verbalise their thought process whilst noting

any queries or problem questions and discuss these with the interviewer (183). Cognitive debriefing interviews were digitally recorded and timed to examine patient burden and completion time.

3.5.1.3 Pre-Testing Analysis

Transcripts were reviewed, with issues related to items, instructions or response options being identified. Summary tables were created, outlining all of the issues identified, and were presented and discussed within the supervisory team. Revisions were made to the initial PCQ items on the basis of the results of the pre-testing and in consultation with the research group team.

3.5.2 Pre-Testing Results

3.5.2.1 Participant Characteristics

A total of 20 patients, 10 SLE and 10 RA, were recruited for this study. All of these patients had previously participated in the qualitative interviews (Table 3.5).

3.5.2.2 Participant Comments/Remarks

The initial PCQ items were well received by participants. No items were omitted, and participants generally praised the relevance and importance of the issues covered by these items. Issues and problems were highlighted for thirty-eight items and two sets of instructions. Four types of problem were identified, including problems with item relevance, comprehension and acceptability as well as problems with the item response categories. A summary of the items highlighted by participants is presented in Table 3.7.

The majority of comments related to the items' relevance to individual participants, as some of the issues covered by items were reportedly not applicable to all respondents. Items were acceptable on the whole, as only two items were highlighted as too sensitive for respondents. The majority of the patients identified a problem with the response categories of 15 impact items and 3 items related to medication.

Although none of the patients raised any issues relating to question 20c (Lupus/arthritis will NOT affect my life expectancy), SC purposefully asked participants if they found this item to be sensitive or upsetting. On the whole, participants admitted that this was something that had crossed their mind before and they understood that it had a purpose in such a survey.

Table 3.7 Pre-Testing: Problematic Items

Index	Item	Comment / Remark	Type of Comment	n
1b	I can tell apart lupus/RA symptoms from natural symptoms of growing older.	Not relevant – I am not old	**relevance**	1
1f	I know that my lupus/RA symptoms are not imaginary.	I am sure they are not imaginary!	**acceptability**	2
1h	I know when to expect a lupus/RA symptom.	if you`ve got arthritis you`ve got arthritis - I`m just wondering whether that`s relevant	**relevance**	1
2	I am experiencing side effects because of the medication I am taking	Not applicable – not currently on medication	**relevance**	3
5a	The medication I am taking is helping my lupus/RA symptoms.	Not applicable – not currently on medication	**relevance**	2
5b	The medication I am taking is controlling my lupus/RA.	Not applicable – not currently on medication	**relevance**	2
5c	I need the medication I am currently taking for my lupus/RA.	Not applicable – not currently on medication	**relevance**	2
5d	I need stronger or more medication for my lupus/RA.	Not applicable – not currently on medication Problematic response option	**relevance** **confusion with response scale**	2 2
5e	I need additional medication for my lupus/RA.	Not applicable – not currently on medication Problematic response option	**relevance** **confusion with response scale**	2 2
5f	I need alternative medication for my lupus/RA.	Does this mean alternative or other medication? Problematic response option	**comprehension** **confusion with response scale**	1 2
9b	My doctor knows exactly how active I should be.	I find this difficult to answer	**comprehension**	1
9h	My doctor knows how to help me with the non-physical aspects of my lupus/RA (e.g. feeling low).	I don`t have any non-physical problems	**relevance**	1
9a-9h	How well do you think your rheumatology doctor knows your lupus/RA? Please **circle** the option that best describes **how certain** you are about the following statements.	I don`t have a personal doctor	**relevance**	1
13	I know which types of physical activity I should be doing and which I should avoid.	I don`t know maybe you wanted to say how long someone should be doing it as well	**comprehension**	1
15a	My family and loved ones are supportive in helping me to manage my arthritis.	I have no close relative left - could add "close friends" in the question	**relevance**	1
15b	My family and loved ones understand the variety and severity of arthritis symptoms I am experiencing.	what could be another questions for that is how much do members of your family or loved ones either accompany you on your consultations	**relevance**	1

Table 3.7 (Cont`d)

Index	Item	Comment / Remark	Type of Comment	n
16	I can confidently reveal my lupus/RA diagnosis to others	useful to add a question specifically about potential employer and job interviews, perhaps you could have a question for those people that are working or that are seeking work, how confidently they are in revealing their lupus to an employer…	**relevance**	2
17	I know what could cause my symptoms to get worse.	Not sure how to answer this	**comprehension**	1
20a	The state of my lupus/RA will stay the same in the future.	What do you mean by state?	**comprehension**	1
21	The medication I am taking will continue to control my symptoms in the future.	Not applicable – not currently on medication It`s quite a medical questions, maybe I am reading too much into the question, I don`t really know if I can answer it	**relevance** **comprehension**	1 1
23a	The medication I am taking will NOT have any long-term side effects.	Not applicable – not currently on medication	**relevance**	2
23b	The medication I am taking will NOT have any severe long-term side effects.	Not applicable – not currently on medication	**relevance**	2
24a	I would feel confident if a doctor other than my personal consultant saw me in the clinic.	problematic response category	**confusion with response scale**	2
24b	I would feel confident moving my lupus/RA care to a different hospital.	problematic response category	**confusion with response scale**	2
24c	I would feel confident receiving healthcare whilst abroad (outside the UK).	I am not sure I understand the purpose of this is, is this for when you`re on holiday? problematic response category	**comprehension** **confusion with response scale**	1 2
26a – 26o	All Items of the Impact Domain	I think these are important, but I think if you need to ask these questions then I think you just need to word them correctly. Yes, I don`t understand, what I`m trying to say it doesn`t affect my finances, do I mean very uncertain or do I mean very certain?	**confusion with response scale**	14
26k	Lupus/RA will affect my ability to maintain a relationship with my partner.	k & l are quite sensitive, and because I think if you`re feeling low and you`re on your own the last think you want to know is that because you`ve got lupus...	**acceptability**	1
26l	Lupus/RA will affect my ability to find a partner.			

3.5.2.3 Completion Time

The completion time ranged from 8 to 30 minutes. The mean time was 18.75 minutes (SD=6.84). This time included the completion of the PCQ as well as the comments and discussions regarding the items, the length of which varied greatly between participants.

3.5.2.4 Implications – Modifications

Following a review of the pre-testing results, modifications were made to the initial PCQ items (Appendix 3.8). Modifications involved item wording and response categories. Eighteen positively worded item strings (5d, e, f and 26a–26o) were re-worded in a negative direction in order for the response options to be applicable and higher scores to reflect lower uncertainty, aid item comprehension as well as to make items more sensitive for respondents, i.e. avoid implication of negative illness outcomes.

An additional item was added to question 16 (which previously addressed disclosing diagnosis specifically to a potential employer or at the workplace) to include disclosing of diagnosis to others in general (e.g. in a social setting). A “Not Applicable” response category was also included for those patients not in employment. Individual words were altered in the wording for items 1b, 17, 20a, 23a and 23b. Instructions to items 24a–c and 9a–h were altered to make items more easily comprehendible and relevant.

A “Not Applicable” response option was added to questions 2, 5a–f, 21 and 23a–b so that they would be relevant to patients who are either not prescribed any medication or they choose not to take any medication. A “Not Applicable” response option was also added to questions 9a–9h that are related to trust in doctors, to address a participant’s comment (Table 3.7).

3.5.3 Pre-Testing Conclusions

Pre-testing methods indicated that the initial PCQ items were relevant and acceptable by SLE and RA patients. Sub-optimal phrasing and problems with some of the items’ response options were indicated, all of which were appropriately modified to improve the items. These changes did not impact on the initial content and structure of the PCQ. The PCQ items reflected the patient uncertainty conceptual framework covering a range of domains suggested by SLE and RA patients themselves, which were not included in pre-existing patient uncertainty instruments.

3.6 Chapter 3 Summary

This chapter presented qualitative methodology that led to the development of a patient uncertainty conceptual framework, item generation of a new patient-reported instrument as well as qualitative pre-testing of the new instrument. Patient interviews and consultation with health care professionals led to the conceptualisation of patient uncertainty in a five-domain framework. These domains related to symptoms and prognosis, medical management, self-management, impact, and social functioning, which were relevant to both patients with SLE and RA. On the basis of this conceptual framework, the patient-reported instrument PCQ was developed using items generated directly from the patient qualitative data. Cognitive debriefing interviews were conducted to qualitatively assess the initial items of the PCQ that proved to be relevant, acceptable and comprehensible to the patient groups. Prior to utilising this new patient-reported instrument, its measurement properties and scale development need to be psychometrically evaluated extensively. This evaluation will be described in Chapters 4 and 5.

Chapter 4: Psychometric Evaluation of the Patient Certainty Questionnaire (PCQ): 1st Field Test

4.1 Chapter 4 Overview

This chapter presents the methods and results of the first of the two quantitative field tests which were conducted in order to psychometrically evaluate the first draft of the Patient Certainty Questionnaire (PCQ) instrument, the development and pre-testing of which were presented in Chapter 3. A Rasch Measurement Theory (RMT) psychometric analysis was performed on the PCQ scales. Review and interpretation of the RMT results led to the formation and modification of the scales and the second draft of the PCQ. RMT analysis was performed for the second time in order to evaluate the revised PCQ. This chapter describes the methodology and results of the RMT psychometric analysis.

4.2 Background: the Purpose of Psychometric Evaluation

The Patient Certainty Questionnaire (PCQ) is a self-report instrument that is comprised of five scales aiming to quantify patient uncertainty in SLE and RA. The quantification is achieved indirectly through observable indicators in the form of items that are completed by patients (141, 166). Considering this, necessary steps need to be taken to evaluate and ensure the adequacy of an instrument to quantify an unobservable latent variable such as patient uncertainty.

First and foremost, outlining and defining the content of an instrument, or in other words conceptualising the latent variable that an instrument is expected to quantify is neither simple nor straightforward (139). Secondly, observable indicators are subsequently scored and added to produce a quantification of a latent variable in multi-item instruments like the PCQ (139). It is therefore fundamental to evaluate such indicators and the legitimacy of adding them in order to produce a total score representing a latent variable. Furthermore, it is essential to examine whether the scores generated by instruments possess reliable and valid measurement properties (141, 142).

This is achieved by the use of psychometric analysis. In essence, psychometric assessment evaluates the extent to which an instrument has successfully quantified a latent variable. Currently three of the main psychometric paradigms used for developing and evaluating scales include the traditional Classical Test Theory (CTT), the Item Response Theory (IRT), and the Rasch Measurement Theory (RMT).

As described more fully in Chapter 1, traditional psychometrics underpinned by CTT evaluate the extent to which raw data satisfy the assumptions of the CTT (144, 168, 204). Traditional psychometric methods are popular (141, 225, 227), however as outlined in Chapter 1 traditional psychometrics are restricted by the theoretical and untestable nature of the CTT which prohibits rigorous testing of measurement properties. The assumptions of the CTT and consequently the measurement criteria within the CTT paradigm are relatively easy to satisfy.

Modern psychometric theories have addressed these limitations and put forward testable mathematical models that can be used to assess measurement properties of scales rigorously. As such, RMT is the chosen paradigm for this thesis as it gives primacy to the data and postulates invariance (141, 142). The RMT provides a template which is underpinned by the axioms of physical measurement that can be used to evaluate a scale`s measurement properties and also provide a linear transformation of ordinal raw scores. The RMT paradigm can be restrictive and more complex, but it addresses all of the limitations of the CTT paradigm by adding scientific rigour to the psychometric evaluation, and consequently the properties of a rating scale.

4.2.1. Aims

In the first field test study reported in this chapter, the Andrich (1978) polytomous Rasch model (213) was used to evaluate and revise the first draft of the PCQ sub-scales. Multiple tests were conducted to examine the extent to which observed scores matched the expectations and criteria of the RMT. The broad aim of these tests was to assess the extent to which observed scores fit the Rasch model in relation to the following:

- How adequate is the scale to sample targeting?
- To what extent has a measurement continuum been constructed successfully?
- How has the sample been measured?

4.3 Method

4.3.1 Study Design

A cross-sectional observational field-test study was set up across five hospitals in England: University College Hospital (UCH), Kings College Hospital (KCH), Royal Blackburn Hospital (RBH), Robert Jones and Agnes Hunt Orthopaedic Hospital (RJAH) and Leicester Royal Infirmary (LRI). National Research Ethics Committee (REC) approval was obtained for this study as well as local approvals issued by the Research & Development (R&D) offices at the five hospital sites. The study was further registered on the National Institute for Health Research (NIHR) portfolio database.

4.3.2 Participants – Sample Size

No explicit guidelines exist for sample size calculation in psychometrics. However, "a rule of thumb" recommendation for evaluating new scales of summed items is for the sample to comprise five to ten subjects per scale item (168, 514). In line with this recommendation, a minimum sample of 135 to 270 participants would be required to allow for 5 to 10 subjects for each of the 27 items of the longest scale.

4.3.3 Participants – Eligibility

Criteria of participant eligibility included a clinical diagnosis of SLE or RA, fluency in English and a minimum 18 years of age. Participants having more than one clinical diagnosis of an illness, i.e. a significant co-morbid condition such as cancer, were excluded from the recruitment process. This was done in order to avoid bias in the assessment of patient uncertainty, as additional diagnosis could potentially increase or change the reported levels of patient uncertainty.

4.3.4 Participants – Sampling and Recruitment

Participants were recruited between May 2011 and February 2012 using two different methods of convenience sampling.

(i) Eligible participants were identified through forthcoming rheumatology appointment lists using the local NHS electronic databases. A postal survey was set up for elegible participants who were sent a package comprising a personalised letter of invitation to the study from their lead consultant, the participant information sheet and consent form, the first draft of the PCQ and a stamped addressed return envelope (Appendices 4.1-4.3). Participants interested in taking part were instructed to complete the consent form and questionnaire booklet and return them as soon as possible using the return envelope provided. They were also asked to contact the study`s researcher if they had

any queries or concerns regarding the study. Personalised reminder letters were sent to participants who had not completed the study three weeks after the initial posting. This is a standard technique used to ensure better response rates in postal suveys (515). This method was used by three Hospital sites; UCH, KCH and LRI. Participant eligibility was based on records information available through the NHS sites` electronic databses. The candidate (SC) carried out the sampling for UCH and KCH, and a local research collaborator for LRI. Recruitment continued until a satisfactory number of participants completed the study.

(ii) In addition to the above, eligible participants were also identified during outpatient clinic appointments. At the completion of the appointments local consultants running the clinics directed eligible participants to the study researchers who presented them with the study documents (letter of invitation from their lead consultant, the participant information sheet and consent form, the first draft of the PCQ and a stamped addressed return envelope). Interested participants were given the study documents to take home with them. They were instructed to complete the consent form and questionnaire booklet and return them as soon as possible using the return envelope provided. They were also instructed to contact the study`s researcher SC if they had any queries or concerns regarding the study. Clinic recruitment was used in two sites, RBH and RJAH, where it was not logistically possible to set up a postal survey or the reminder technique used in the postal surveys. Participant eligibility was determined by local consultants in clinic recruitment.

4.3.5 Materials

The first draft of the PCQ (Appendix 4.4) was administered in this Field Testing study. The instrument consisted of 83 items developed on the basis of a thorough qualitative exploration of uncertainty in SLE and RA (20). Items were constructed using as many of the patients` own words as possible and inductively categorised into five scales, constructed to mirror the five overarching domains of the uncertainty conceptual model (20). The first draft of the PCQ scales included "***symptoms & prognosis***" (27 items), "***medical management***" (26 items), "***self-management***" (5 items), "**i*mpact***" (18 items), and "***social functioning***" (7 items). Items are scored against a 4 point Likert-scale ranging from "very uncertain" to "very certai**n**". A "not applicable" response option was added in three of the scales (Appendix 4.4) which was coded as missing in the scale analysis. Responses were analysed on a total (summed) score for each scale, with higher scores reflecting more certainty/less certainty. A short demographics questionnaire was also administered to participants. Details of the participant age, year

of diagnosis, gender, ethnic group, employment status, living status and highest level of education were recorded (Appendix 4.4.1).

4.3.6 Data collection and monitoring

Participants were consented by the candidate (SC) at all sites apart from RJAH and some of the RBH, where local researchers recruited participants along with SC. Study questionnaire booklets were returned to the UCL Centre for Rheumatology Research and collected by SC, who monitored and co-ordinated the study processes and updated the NIHR portfolio with accrual data. Data were entered onto an SPSS dataset and transferred onto RUMM2030 software (516) in order to perform the RMT data analysis.

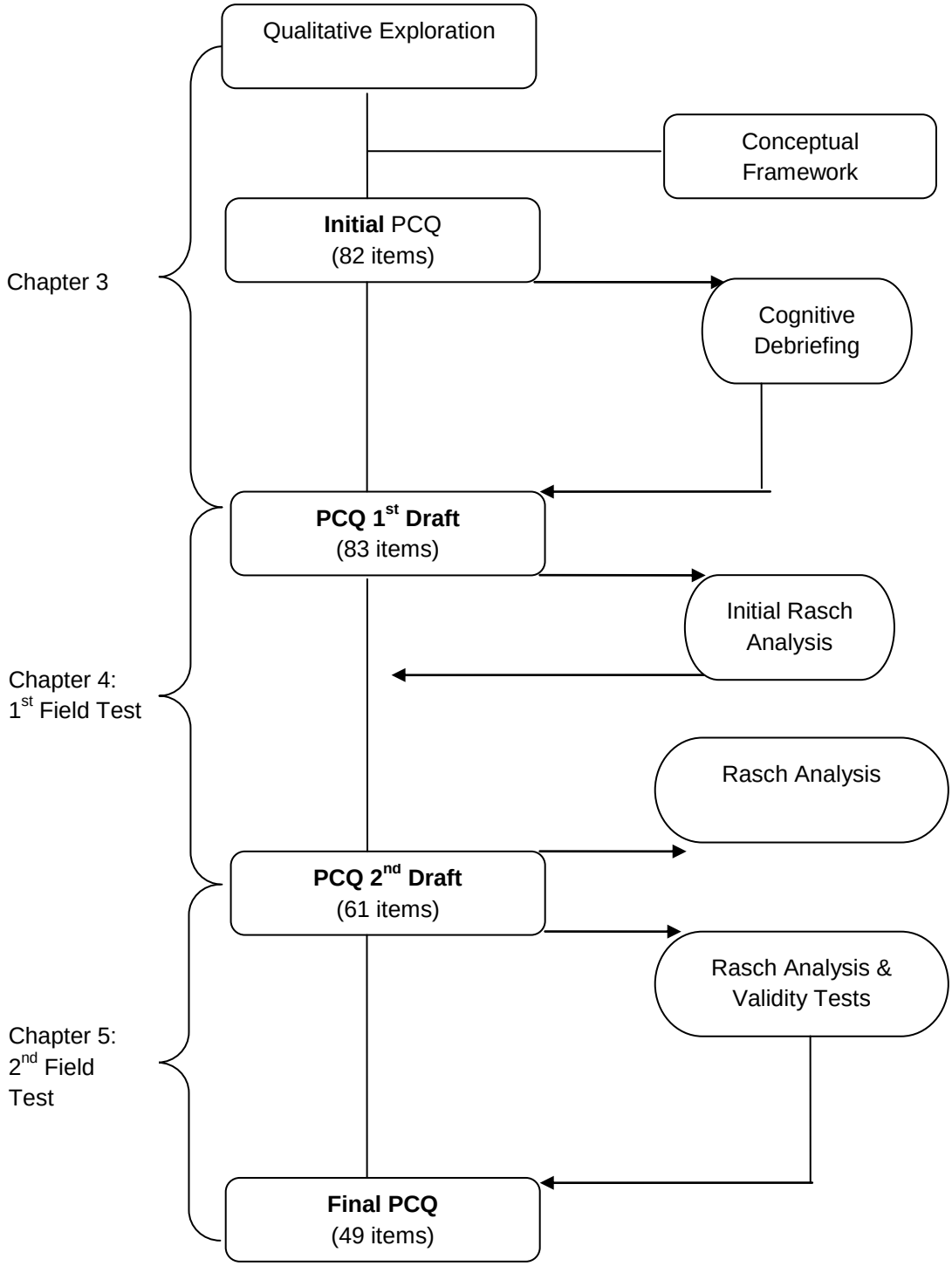
4.4 Psychometric Analysis

Modern psychometric techniques (RMT analysis) were used to evaluate the first draft of the PCQ scales (Table 4.1). Examination of these results (i.e. the extent to which observed scores fit the expectation of the Rasch model) led to the revision of the scales (Figure 4.1). Revision of scales was conducted under the supervision of a Rasch Analysis Expert, Dr. Stefan Cano, and in consultation with the research group, Stanton Newman Professor of Health Psychology, and David Isenberg, Professor of Rheumatology. Measurement properties of the revised scales were then reassessed using RMT analysis (Figure 4.1).

4.4.1 Modern Psychometric Analysis: Rasch Measurement Theory (RMT)

A series of different tests were performed using the RUMM2030 software (516) to integrate evidence towards the evaluation of the PCQ measurement properties. Each of the five PCQ scales was evaluated independently. Observed findings were compared against the stringent measurement criteria of the RMT, acknowledging the expectation of some anomalies (142, 517). Findings and discrepancies were reviewed and interpreted with professional judgement within the research team, and revisions were made where necessary to the PCQ scales. Analysis and interpretation was guided by the three broad aims of the RMT analysis; the evaluation of the scale to sample targeting, the evaluation of the measurement continuum and the evaluation of the sample measurement. The tests and information used to address these aims are explained in detail below.

Figure 4.1 PCQ Development Procedure



4.4.1.1 How adequate is the sample to scale targeting?

Scale to sample targeting refers to the comparison between the range of uncertainty/certainty measured by the scale and the range of uncertainty/certainty measured in the study sample. Targeting was evaluated through examination of the person, in other words, the distribution of individual person estimates on a measurement metric, as opposed to group level statistics and item distributions (142, 201, 518). The relative distributions inform the adequacy of the sample for evaluating the scale and the adequacy of the scale for measuring the sample.

RUMM2030 provides paralleled histograms of person locations, item locations and item thresholds. Thresholds reflect the difficulty of each of the multiple response options to each item for polytomous scales. The mean location of all of the thresholds to each item is used to indicate the item location. These histograms are plotted against the same metric scale of logits (see glossary). Logits constitute logistic transformation of the probability of a response by a person to an item. Higher logits reflect higher person locations, and similarly higher item difficulty in relation to the trait. As higher scores on the PCQ scales reflect lower levels of uncertainty, and consequently higher levels of certainty, for simplification purposes certainty will be referred to as the trait (i.e. instead of lower uncertainty). These histograms were examined for each of the scales in order to assess targeting. A scale with adequate targeting is expected to comprise item thresholds that span across the full range of person locations, and equally a sample with adequate targeting is expected to have a distribution that closely matches the item distribution (142, 517).

Comparison of the person and item mean locations was also used to assess targeting. The item location and threshold mean is always set at zero logits by RUMM2030. Precision of the person location mean to the item mean indicates adequate targeting (519). A positive person location mean indicates the sample is located at a higher level of the trait (e.g. certainty) than the range of the trait that the scale is measuring. Alternatively, a negative person location mean indicates that the sample is located at a lower level of the trait (e.g. certainty) than the range of the trait the scale is measuring (142).

The RUMM2030 further provides the information function curve for the scale plotted in green colour on the upper histogram displaying the person locations. This curve represents the inverse of the standard error at every location across the measurement continuum. The higher the curve line the lower the representing standard error, and

hence, the greater the precision of the scale measurement at that location. In other words, the information function displays the location on the measurement continuum a scale performs at its best (142).

4.4.1.2 To what extent has a measurement continuum been constructed successfully?

Information from five different tests was gathered in order to address this question (517).

4.4.1.2.1 Do the response categories work as intended?

The PCQ items were scored on a four-point response scale. Response categories ranged from “1; very uncertain” to “4; very certain”, suggesting a continuum of increasing certainty. It is therefore assumed that respondents with higher levels of the trait (i.e. higher certainty) would endorse the higher response categories, whilst respondents with lower levels of the trait (i.e. lower certainty) would endorse the lower response categories.

RUMM2030 produces a threshold map for each individual item. Thresholds represent the point between two response categories where a person with a specific location is equally likely to choose either of the two response categories. Response thresholds should be ordered in a successive manner (i.e., “1”, “2”, “3”,”4”[2]), with no crossovers between adjacent response categories (142, 517).

Disordering can denote respondents` difficulty in distinguishing between the different response categories (519). This can be caused by either the availability of too many response categories or by the confusing labelling of categories (520). Response category thresholds for all scale items were examined for disordering.

4.4.1.2.2 Do the PCQ scales map out a continuum?

PCQ scales comprise different items defining the uncertainty domain (i.e. trait) they intend to measure. An optimal scale is expected to comprise items located at different logits of the measurement continuum, thereby covering the range of the trait it is intended to measure and equally representing all different levels of that trait (517, 521).

The sufficiency of the item distribution along the measurement continuums was

[2] RUMM2030 transforms response category integers to 0-3 from 1-4

examined for each scale. Item locations were assessed for their range and spread on the metric scale logit continuum provided by RUMM2030 (167). The measurement continuums were further examined for their item location spread, proximity and precision through the evaluation of item threshold distributions, item location logits and their standard errors (201, 517). The smaller the standard errors the greater the precision of the item location estimates and of the overall analysis. There are no specific criteria used to assess the spread of item locations and standard errors, which are assessed descriptively (142).

4.4.1.2.3 Do the PCQ scale items define a single variable?

Measurement within PCQ scales is based on total scores achieved by adding the responses to individual items. Item responses need to be examined in order to assess the cohesiveness of the measurement continuum and therefore the legitimacy of the scale (517, 521). Three “fit” indicators were examined to assess the above, two statistical ones; fit residuals and chi squares, and a graphical one (item characteristic curves) (142). Item responses within the RMT expected fit indicators would suggest that the PCQ scales components work well together to define a single measurement continuum.

Item fit residuals are used to examine whether the item-person interaction is in line with the RMT. In other words, the fit residuals represent the difference between the observed and expected scores for each item by each and every person in a study sample. Fit residuals are derived by subtracting the response expected by the RMT from the observed responses (i.e. observed-expected=residual). The residuals of the entire sample of persons are squared, summed and transformed in order to produce the fit residual for each individual item in a scale. Fit residuals are then transformed to approximate a normal distribution and are therefore expected to have a mean of zero and a standard deviation (SD) of 1.

Therefore, according to the RMT it is expected that fit residuals should be distributed between -2.5 to +2.5 with a mean proximal to zero and SD close to 1. An observed fit residual of 0 indicates perfect fit (i.e. observed = expected). The greater the departure of a residual is from zero in either the positive or negative direction, the greater the misfit. High negative fit residuals indicate over-discrimination of the trait , whilst high positive fit residuals indicate items that are under-discriminate the trait (142). Over-discrimination refers to items where the observed score is greater than expected at higher levels of ability on the measurement continuum, and lower than expected on lower levels of ability. Under-discrimination on the other hand, refers to items where the

observed score is lower than expected at higher levels of ability on the measurement continuum and higher than expected on lower levels of ability.

Chi-square statistics are used to assess the item-trait interaction, or in other words assess whether items behave in line with the RMT at each level of the trait. Chi square is a summary statistic computed by dividing the sample into six groups (class intervals) based on their trait (i.e. level of certainty). For each item a chi square value is computed by summing the mean person locations and mean scores within each sample group (class interval). Therefore, for each Chi square value degrees of freedom are equal to the number of class intervals in the sample minus 1. For items to fit the RMT, it is expected that the chi-square probabilities would not be significant (>0.05) (142). Significant chi square probabilities signify scores which are significantly different from the expected ones. The Bonferroni adjustment is calculated by RUMM2030 in order to adjust the significance levels when multiple tests are performed on the same data (522, 523).

Item characteristic curves (ICC) are graphical indicators of fit which are used to complement the interpretation of the fit residuals and chi square probabilities (142, 201). RUMM2030 provides a line graph for each item, where the scores expected by the RMT are plotted on the y-axis against the person locations on the x-axis. The ICC is therefore the expected scores for each item. Additional to the curve line of expected scores, RUMM2030 also plots dots on the graph. These dots represent the intersection between the mean observed scores for each of the class intervals (y-axis) against the mean person location for that interval. For items that fit the RMT it is expected that class-interval dot plots would lie close to the ICC curve. Dot plots steeper than the ICC indicate items that over-discriminate the trait, and similarly dot plots flatter than the ICC indicate items that under-discriminate (142). Fit residuals, Chi squares and ICCs of each item within the PCQ scales were examined using the above criteria.

4.4.1.2.4 Do responses to one item bias responses to others?

Item responses are expected to display association in relation to person locations. However, response to an individual item should not directly influence one response to another as this will bias measurement estimates (inflate or deflate). The RMT therefore expects item independency. The extent of response dependency is assessed via residual (i.e. observed - expected = residual) correlations. As the RMT model expects local independence for items, it is also expected that item residuals should reflect random error.

Residual correlations are therefore used to examine the association, if any, between item residuals (201, 518). The Rasch model expects item residuals to be independent, i.e. display random error and no significant association as assessed by a correlation test. Item pairs displaying positive residual correlations (r) above 0.3 are set to have a 10% shared variance, and this suggests they are locally dependent (142, 517). Response bias was assessed in line with the r>0.30 rule of thumb, but residual correlations below <0.4 were considered as acceptable (218).

4.4.1.2.5 Is the performance of the scales stable across relevant groups?

The RMT expects the measurement continuum to be consistent and stable across different sample groups. The extent to which items are stable across different sample groups is assessed through differential item functioning (DIF) (142, 517, 520).

DIF refers to item bias displayed between groups chosen on the basis of clinical or theoretical consideration and relating to how the trait under assessment (e.g. certainty) could potentially have a different conceptual meaning across these groups (142). DIF explores the relationship between item responses and group membership by examining the observed response differences between class intervals within groups (524). In RUMM2030, DIF is detected statistically for each item using analysis of variance (ANOVA) assessing item scores between the sample groups and across the different class-intervals. Items that fit the RMT are expected to display no DIF and produce a statistically non-significant ANOVA test result.

Items in the PCQ scales were tested for DIF by condition group (SLE/RA), age and disease duration categories. As multiple tests of DIF can inflate the type 1 error a significance level of p<0.01 with Bonferroni adjustment was taken to indicate DIF (142, 517, 522, 523). DIF was not examined by gender as the number of male participants was very small compared to the number of females in the sample.

4.4.1.3 How has the sample been measured?

Three indicators were used to examine measurement of the specific sample.

4.4.1.3.1 Is the sample separated by the PCQ scales?

A scale is expected to detect differences in the levels of trait within a sample and also detect changes in trait levels over time. Within the RMT paradigm the person separation index (PSI) is calculated to assess this (142, 517). The PSI is a numerical indicator ranging from 0 to 1 which is computed as the ration of variation of person estimates relative to the estimated error for each person (525). In other words, the PSI

displays how much of the variation in person-location estimates can be associated with random error, where a 0 score indicated all error and a 1 score no error at all (142). It is highly comparable to Cronbach's alpha (526), however the PSI signifies a property of the scale in relation to a specific sample whereas Cronbach`s alpha displays the variance in a sample in relation to the variance of the scale items (142).

4.4.1.3.2 How valid is the person-measurement?

Similar to the examination of item responses, it is important to assess whether the measurement of individual persons is in line with the Rasch model expectations (142, 517). Person fit residuals are used to examine whether the person-trait interaction is in line with the Rasch model. Person fit residuals represent the difference between the observed and expected total scores on a scale for each person in the study sample.

Person fit residuals are analogous to the item fit residuals. The residuals (i.e. observed-expected=residual) for each person in the sample are squared, summed and transformed in order to produce the fit residual for each person in the sample. Fit residuals are then transformed to approximate a normal distribution and are therefore expected to have a mean of zero. Person fit residuals were examined with reference to the "rule of thumb," expecting 99% of the sample to produce a fit residual between -2.5 to 2.5. Fit residuals outside this range indicate problematic measurements for those persons (142, 517).

4.4.1.3.3 To what extent are raw scores linear?

It is important to assess the extent to which the ordinal raw scores approach linear (interval) measurement and their subsequent transformation on an interval scale. This is important as one point on a scale is not necessarily the same across the breadth of the scale (517, 527). It is important to consider the extent to which the data fit the Rasch model as the greater the misfit the lower the precision of the linear estimates (517). Considering the stringent mathematical criteria of the RMT minor deviations of raw scores from interval/linear measurement is expected. These analyses will only be performed on the final version of the PCQ scales (Figure 4.1), and they will be presented in Chapter 5.

Table 4.1 Rasch Measurement Theory Analysis

Property:		**Psychometric Criteria:**
Targeting	Sample to scale	person & item locations and thresholds distributions
Measurement ruler	Response categories	response threshold ordering
	Continuum	item range, spread and proximity
	Goodness of fit	fit residuals (-2.50 to 2.50) chi square statistic item characteristic curves (ICCs)
	Response bias	residual correlations r>0.4
	Scale stability	differential item functioning (DIF)
Sample measurement	Sample separation	person separation index (PSI)
	Validity	person fit residual 99% within (-2.50 to 2.50)
	Implications	linear transformation of raw scores*

4.5 Results

4.5.1 Response Rate

A total number of 637 participants were invited and a resulting sample of 388 participants completed this study, bringing the overall response rate to 61% (Table 4.2). Response rate varied between sites and condition groups, ranging from 52.7% to 70.5% between the five sites and from 55.0% to 80.0% within the SLE in comparison to 45.1% to 70.1% in the RA sample. To address this sub-optimal response rate, reasons for non-response were investigated further by contacting non-respondents at two of the five sites (UCH & KCH). The following reasons for non-response were recovered in this procedure:

- Patients never received packs through the post, although the study obtained correct contact details.
- Study documents never reached intended participant due to incorrect contact details on hospital records.
- Limited ability of reading in English. Fluency in English was judged on the basis of the need for a translator as recorded on the hospitals` electronic datasets. Some patients were reportedly fluent in spoken English, but they were subsequently not able to read in English and complete the study documents.
- Participants were not well enough to complete the study due to a recent adverse health event (e.g. hospitalisation, or injury).
- Participants were not wishing to participate as they had recently completed another research study involving questionnaire completion.
- Participants did not believe they could benefit from this study because they are elderly (> 75 years of age).
- Participants could not concentrate long enough to complete the questionnaire because of (i) older age and/or (ii) ill health.
- Participants did not wish to discuss their personal issues.

As this was a post-hoc investigation it is not possible to estimate what percentage of the overall non-response rate each of these reasons represents. Nevertheless, it does highlight some limitations of the screening procedure (i.e. judging eligibility on the basis of electronic hospital records) and the study`s methodology (i.e. lack of updated hospital records)

Table 4.2 1st Field Test: Response Rate

Site	Total N (invited)	Over all response rate	SLE N (invited)	SLE response rate	RA N (invited)	RA response rate
UCH	104(180)	57.8%	67 (98)	68.3%	37 (82)	45.1%
KCH	79(150)	52.7%	33(60)	55.0%	46(90)	51.1%
RBH*	77 (120)	64.2%	33 (51)	64.7%	44 (69)	63.7
RJAH*	72 (102)	70.5%	4(5)	80.0%	68(97)	70.1%
LRI	56 (85)	65.8%	41(60)	68.3%	15 (25)	60.0%
Total:	**388 (637)**	**60.9%**	**178(274)**	**65%**	**210(363)**	**57.9%**

** Clinic recruitment – no reminder letters sent out*

4.5.2 Sample Characteristics

A total sample of 383[3] participants with mean age of 52.3 years (SD=16.3) and the mean disease duration of 12.3 years (SD=10.8) was used in this analysis. The sample consisted of 173 patients with SLE, 157 female and 16 male, with a mean age of 43.83 years (SD=15.2) and the mean disease duration of 11.1 years (SD=9.6). The remaining sample of 210 participants were patients with RA, 163 female and 47 male, with a mean age of 59.4 years (SD=13.3) and the mean disease duration of 13.30 years (SD=11.7). The gender difference and younger mean age of SLE patients were expected as SLE is far more common in women than men and is usually diagnosed earlier in life than RA (36, 101, 315). Additional information on the sample demographics is shown in Table 4.3.

[3] Although 388 participants completed the study, questionnaire packs for 5 of these participants reached the research team months after the completion of the data analysis as the packs were misplaced by internal mail.

Table 4.3 1st Field Test: Sample Characteristics

	Total (n=383)	SLE (n=173)	RA (n=210)
Age (years)			
Mean (SD)	52.3 (16.28)	43.8 (15.2)	59.4 (13.3)
Range	18-86	18-80	23-86
Disease Duration (years)			
Mean (SD)	12.3(10.8)	11.1 (9.7)	13.3 (11.7)
Range	0.08 - 54	0.08 - 39	0.25 – 54
Gender n (%)			
Female	320 (83.6)	157 (90.7)	163 (77.6)
Male	63 (16.4)	16 (9.3)	47 (22.4)
Ethnicity n (%)			
White	283 (73.9)	101 (58.4)	182 (86.7)
Black	45 (11.7)	33 (19.1)	12 (5.7)
Indian/Pakistani/Bangladeshi	27 (7.0)	21 (12.1)	6 (2.9)
Mixed race	11 (2.9)	7 (4.0)	4 (1.9)
Other	11 (2.9)	9 (5.2)	2 (1.0)
Missing	6 (1.6)	2 (1.2)	4 (1.9)
Employment Status n (%)			
Employed (full-time)	84 (21.9)	49 (28.3)	35 (16.7)
Employed (part-time)	43 (11.2)	23 (13.3)	20 (9.5)
Student	21 (5.5)	19 (11.0)	2 (1.0)
Retired	125 (32.6)	28 (16.2)	97 (46.2)
Unemployed	18 (4.7)	10 (5.8)	8 (3.8)
Homemaker	20 (5.2)	10 (5.8)	10 (4.8)
Disability retirement	59 (15.4)	29 (16.8)	30 (14.3)
Other	8 (2.1)	4 (2.3)	2 (1.0)
Missing	5 (1.3)	1 (0.6)	6 (2.9)
Living situation n (%)			
Alone	72 (18.8)	25 (14.5)	47 (22.4)
Spouse/partner	166 (43.3)	57 (32.9)	109 (51.9)
Children	31 (8.1)	19 (11.0)	12 (5.7)
Partner & children	47 (12.3)	29 (16.8)	18 (8.6)
Family (parents/siblings)	44 (11.5)	30 (17.3)	14 (6.7)
Student accommodation	7 (1.8)	5 (2.9)	2 (1.0)
Shared housing/friends	4 (1.0)	2 (1.2)	2 (1.0)
Missing	12 (3.1)	6 (3.5)	6 (2.9)
Education n (%)			
No formal education	68 (17.9)	25 (14.5)	43 (20.5)
GCSEs / O-Levels	103 (26.9)	48 (27.7)	55 (26.2)
A Levels / HNC	56 (14.6)	30 (17.3)	26 (12.4)
University	43 (11.2)	20 (11.6)	22 (10.5)
Graduate / Professional	88 (23.0)	42 (24.3)	46 (21.9)
Missing	25 (6.5)	8 (4.6)	18 (8.6)

4.5.3 Missing Data

No missing data were reported on participant condition and gender. Data on age and disease duration were missing out of 0.8% and 6.8% of the total sample respectively. Missing data on other demographic characteristics are shown in Table 4.3. Missing data of the PCQ were calculated on scale and item level. Scale-level missing data were calculated by examining the total number of missing responses per scale in comparison to the total responses for each scale. Scale-level missing data were low, ranging from 0.07% to 1.7% (Table 4.4) suggesting sufficient data quality for this sample (196, 203). Item-level missing data (Appendix 4.5) were also low, ranging from 0.0% to 2.9%.

The RUMM2030 software used for the RMT analysis accounts for item-level missing data by the computation of class intervals on an item and not a person basis in order to control for any bias brought by missing data.

Table 4.4 1st Field Test: Scale-level Missing Data

PCQ 1st Draft Scales	Total Items	Total Responses*	Missing responses	%
Symptom & Prognosis	27	10,341	39	0.88
Medical Management	26	9958	98	098
Self-management	5	1945	6	0.31
Impact	18	6894	116	1.68
Social Functioning	7	2681	44	1.64

**** The product of the total number of items per scale and the total sample, n=383***

4.5.4 PCQ 1st Draft Rasch Analysis Results

RMT psychometric evaluation was undertaken for the first draft of the five PCQ scales independently. Results are presented in detail for the symptoms and prognosis scale, whereas for the remaining scales, results and modifications are presented in summary. Results are presented in the analysis format described in the methods section.

4.5.4.1 PCQ 1st Draft: *Symptoms & Prognosis* Scale Results

4.5.4.1.1 How adequate is the sample to scale targeting?

Figure 4.2 displays the sample-to-scale targeting based on item locations (Figure 4.2A) and threshold[4] (Figure 4.2B) estimates and plotted on a histogram axis ranging from -6 to 6 logits for symmetry. The upper parts of the histograms display the person location continuum and the lower part the item location continuum. Higher logits reflect persons with higher ability (i.e. higher levels of the trait/certainty), and similarly higher logits reflect items with an increased level of difficulty in relation to the trait.

The range of certainty measured in the sample (-2.917 to 5.076 logits, mean -0.056 logits) numerically appears poorly matched with the range of certainty measured by the item locations (1.995 to 1.549 logits mean 0.0 logits) and by item thresholds (-2.674 to 2.667 logits). However reviewing the targeting histograms (Figure 4.2) indicates the relative sufficiency of the scale to sample targeting that can be deducted from the person mean which is very close to zero, despite some outliers within the sample distribution located at the higher end of the measurement continuum. Sample to scale targeting was therefore relatively good.

The green curve represents the measurement of standard error inversely and hence showing the locations on the continuum that the scale performs best at, indicating the scale works optimally for the majority of the sample (within the logit range -3 to +3 logits) apart from the minority located above +3 logits (i.e. persons with the highest certainty) for whom the precision in measurement compromised. Some item bunching is displayed as several item locations are clustered on the same logit location, suggesting some of these items may be redundant. Only one item gap is displayed on the item location continuum around the -2 logit location, and two item gaps on both ends of the item-threshold continuum. The items also appear to be marginally positively skewed as the item fit skewness statistic (Table 4.9) that is reported is 1.149

[4] Thresholds reflect the difficulty of each of the multiple response options to each item for polytomous scales. The mean location of all the thresholds to each item is used to indicate the item location.

(acceptable range -1 to 1). This indicates that more items are located on lower logits, i.e. lower item difficulty in measuring certainty.

Figure 4.2: PCQ 1st Draft *Symptoms & Prognosis* Scale: Targeting of Sample to Scale

Figure 4.2A

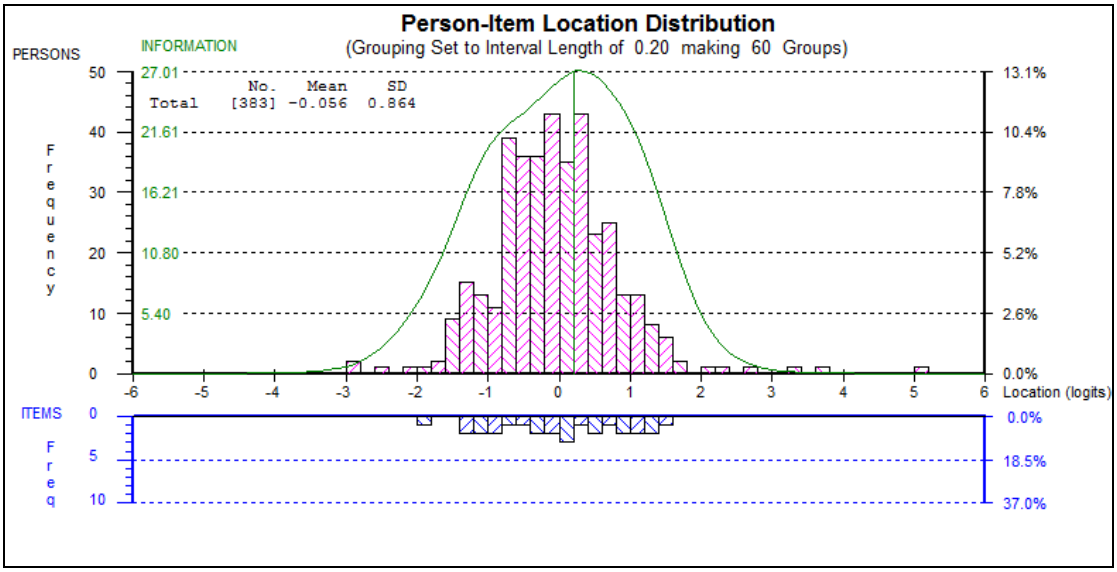


Figure 4.2B

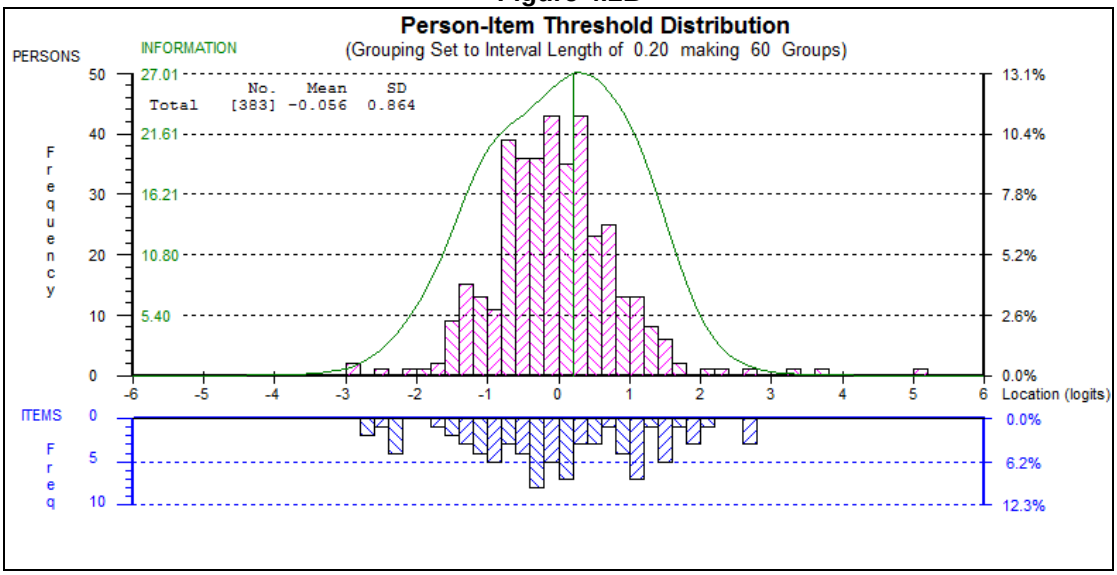


Figure 4.2: *The pink blocks represent the sample distribution for the symptoms and prognosis scale and the blue blocks represent the scale distribution of the 27 items on the same measurement continuum indicating that the location of item thresholds and persons is well matched. The green curve shows the location on the continuum the scale performs at its best.*

4.5.4.1.2 To what extent has a measurement continuum been constructed successfully?

4.5.4.1.2.1 Did the response categories work as intended?

Figure 4.3 indicates that responses for two items (1f, 18c) were not ordered sequentially as intended. Item 20b also appears problematic, as the response “2, somewhat certain” occupies a very narrow span of the logit continuum. The remaining

24 items displayed response categories ordered in sequence from 0 to 3 on the logit continuum. This information can also be deduced from Table 4.5 displaying logit locations for each of the items response thresholds. Thresholds denoted by the Greek symbol 'τ' (tau) are used to represent:

τ1 – logit location where the probability of scoring either 0 (very uncertain) and 1 (somewhat uncertain) is the same

τ2 – logit location where the probability of scoring either 1 (somewhat uncertain) and 2 (somewhat certain) is the same

τ3 – logit location where the probability of scoring either 2 (somewhat certain) and 3 (very certain) is the same

As respondents with higher levels of the trait (i.e. more certainty) are expected to endorse higher response categories, we expect threshold location logits to increase sequentially; for example it would be expected that a person at τ3 would be located on the right hand side of the logit continuum in comparison with a person at τ1. Similar to Figure 4.3, Table 4.6 also marks the two items (1f & 18c) to have reversed thresholds, as τ3 is located at lower levels of certainty than τ2. In terms of item "20b", τ2 and τ3 are located within less than 0.1 logit of each other but ordered sequentially.

These relationships are also displayed graphically (Figures 4.4 & 4.5) by plotting the probability of choosing each of the four response categories (different coloured curve lines) on the y-axis against person locations (i.e. different levels of certainty) on the x-axis. Thresholds (τ1, τ2, τ3) represent the points where each pair of probability curves meet. As the level of certainty increases on the x-axis, the RMT expects the probability of endorsing a higher response category to increase and thresholds to be ordered in sequence. In line with this expectation, 24 items (Figure 4.4) display ordered category probability curves with sequentially ordered thresholds.

In line with the evidence above, category probability curves "1f" and "18c" display disordering, as τ3 appears before τ2 on the measurement continuum (Figure 4.5). Item "20c" appears to approach disordering, but the location logits prove that the thresholds are actually sequentially ordered (Table 4.5). These findings suggest that response categories for items "1f" and "18c" do not work as intended, as higher scores do not reflect higher levels of certainty.

Figure 4.3 PCQ 1st Draft *Symptoms & Prognosis* Scale: Item Threshold Map

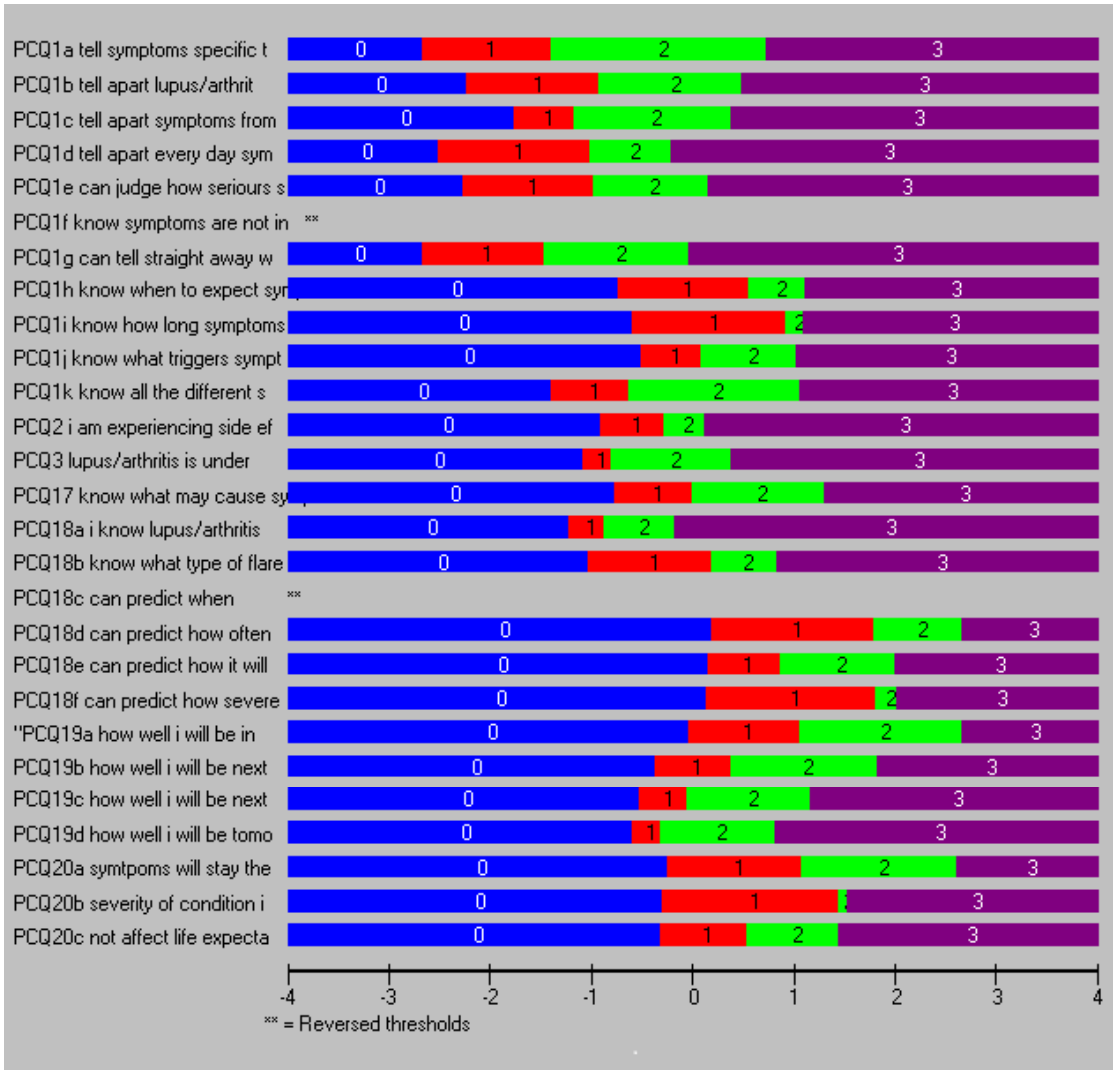


Figure 4.3: *Threshold maps for all items in the Symptoms & Prognosis scale. The x-axis represents the measurement continuum of the trait (certainty), with increasing ability from left to right. The y-axis shows each of the items response categories 'Very Uncertain' labeled as 0; 'Somewhat Uncertain" labeled as 1; 'Somewhat Certain' labeled as 2 and "Very Certain" labeled as 3. Thresholds for items 1f and 18c are missing as they are reversed, i.e. response categories do not appear in a consecutive increasing order in relation to the construct (x-axis).*

Table 4.5 PCQ 1st Draft *Symptoms & Prognosis* Scale: Item Threshold Location

	Item	τ1	τ2	τ3
1a	I can tell which symptoms are specific to lupus/arthritis.	-2.67	-1.40	0.73
1b	I can tell apart lupus/arthritis symptoms from the natural symptoms of getting older.	-2.23	-0.92	0.49
1c	I can tell lupus/arthritis symptoms apart from side-effects caused by the medication I am taking.	-1.77	-1.17	0.38
1d	I can tell apart everyday lupus/arthritis symptoms from flares.	-2.51	-1.02	-0.21
1e	I can judge how serious my lupus/arthritis symptoms are.	-2.28	-0.99	0.14
1f	I know that my lupus/arthritis symptoms are not in my head (i.e. not imaginary).	-2.28	-1.49	-2.22
1g	I can tell straight away when I am experiencing a lupus/arthritis symptom.	-2.68	-1.47	-0.05
1h	I know when to expect a lupus/arthritis symptom.	-0.74	0.56	1.12
1i	I know how long my lupus/arthritis symptoms last.	-0.60	0.93	1.09
1j	I know what triggers my lupus/arthritis symptoms.	-0.50	0.08	1.02
1k	I know all the different symptoms related to my lupus/arthritis.	-1.40	-0.63	1.06
2	I am experiencing side effects because of the medication I am taking.	-0.91	-0.28	0.11
3	My lupus/arthritis is under control at the moment.	-1.09	-0.81	0.38
17	I know what may cause my symptoms to get worse.	-0.77	-0.01	1.30
18a	I know that my lupus/arthritis will flare-up at some time in the future.	-1.22	-0.87	-0.18
18b	I know what type of flare-ups I will experience.	-1.03	0.18	0.83
18c	I can predict when I will experience a flare-up.	-0.23	1.45	1.44
18d	I can predict how often I will experience a flare-up.	0.19	1.79	2.66
18e	I can predict how lupus/arthritis will affect me in the future.	0.15	0.86	2.00
18f	I can predict how severe my flare-ups will be.	0.13	1.81	2.02
19a	I can predict how well I will be in six months.	-0.04	1.05	2.67
19b	I can predict how well I will be next month.	-0.37	0.37	1.82
19c	I can predict how well I will be next week.	-0.53	-0.05	1.16
19d	I can predict how well I will be tomorrow.	-0.59	-0.32	0.82
20a	The symptoms of my lupus/arthritis will stay the same in the future.	-0.26	1.07	2.61
20b	The severity of my lupus/arthritis will stay the same in the future.	-0.30	1.44	1.53
20c	Lupus/arthritis will NOT affect my life expectancy.	-0.33	0.54	1.44

τ; *threshold logit location*

Figure 4.4 PCQ 1st Draft *Symptoms & Prognosis* Scale: Category Probability Curves

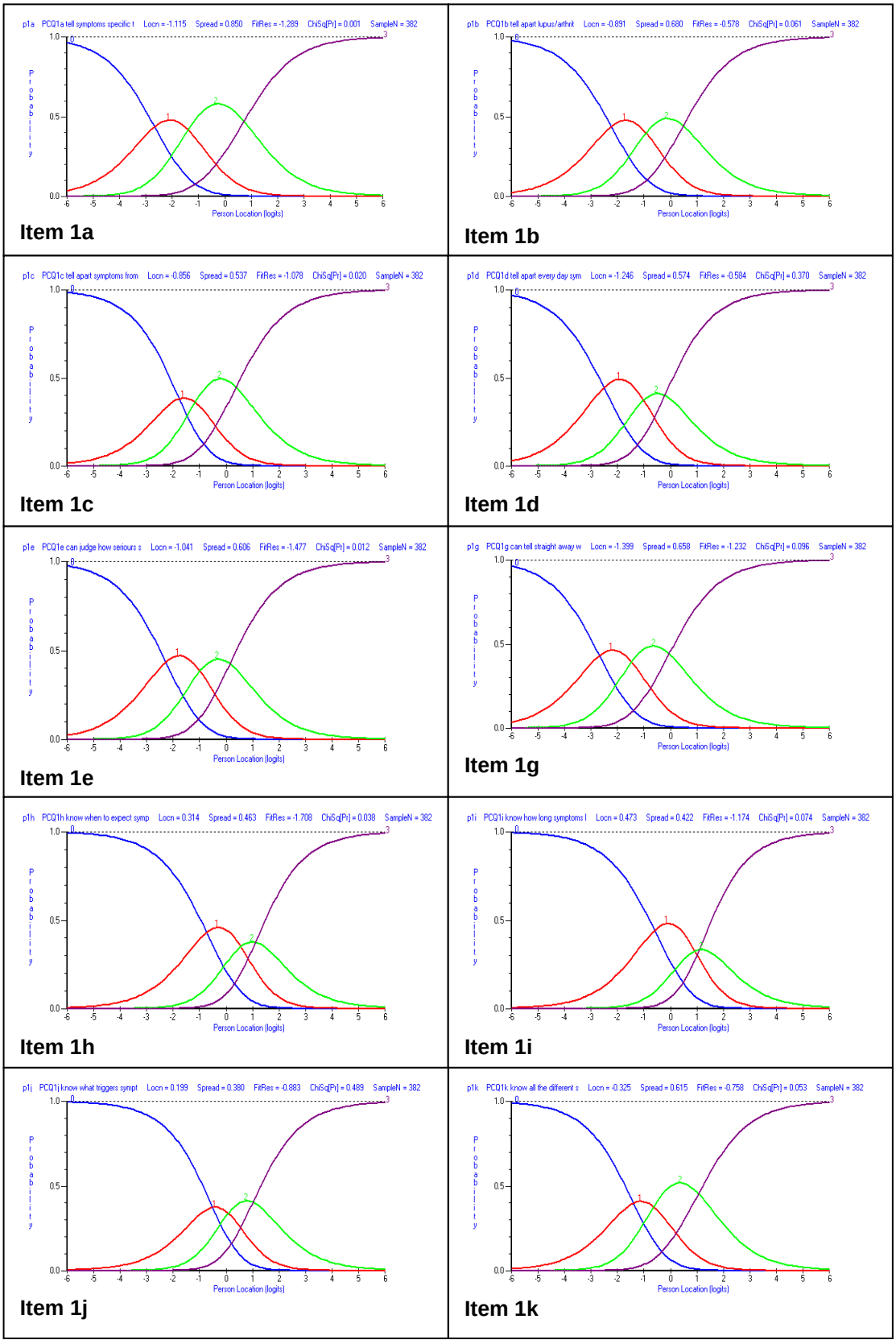


Figure 4.4 (cont`d)

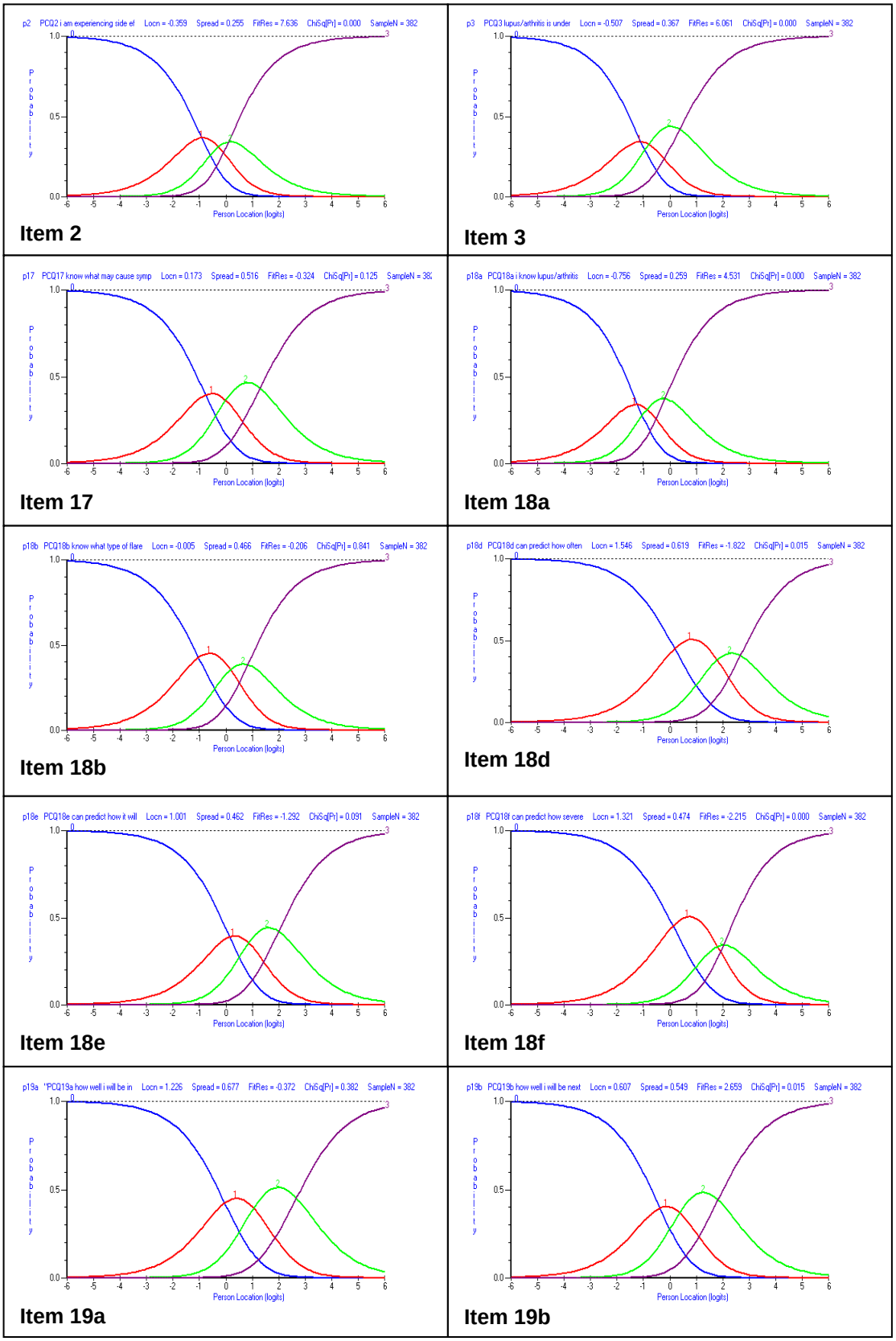


Figure 4.4 (cont`d)

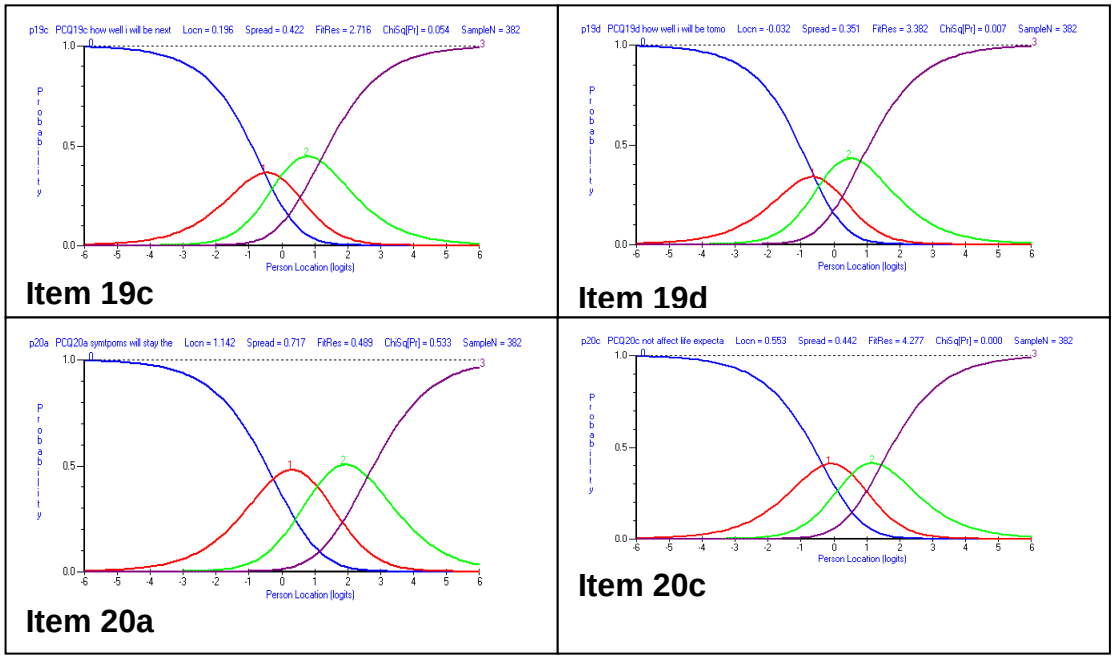
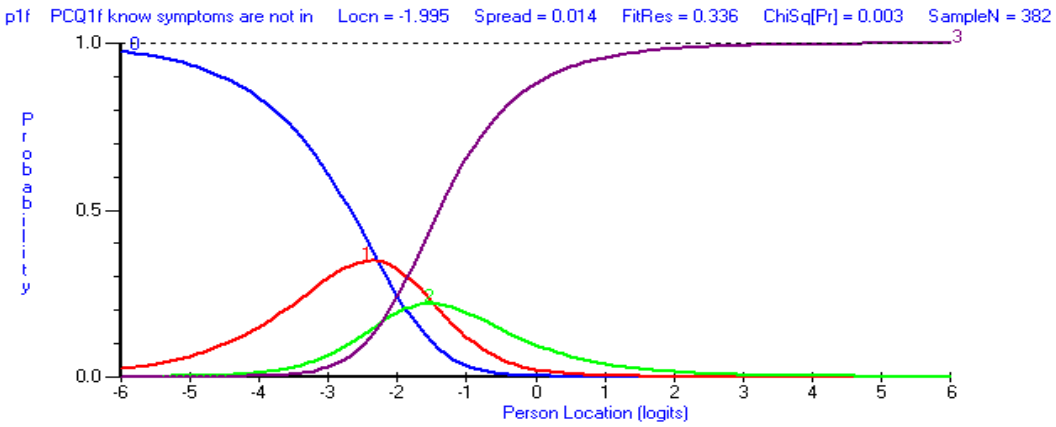
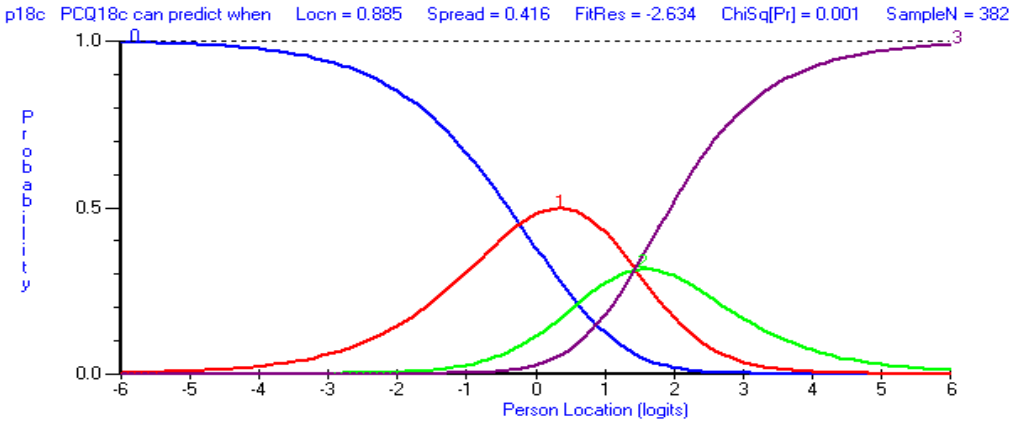


Figure 4.4: *a different way of representing the threshold map presented in Figure 4.3. The x-axis represents the measurement continuum of the trait (certainty), with increasing ability from left to right and the y-axis represents the probability of choosing each of the four response categories. The blue line represents 'Very Uncertain'; the red 'Somewhat Uncertain"; the green 'Somewhat Certain' and the purple "Very Certain". Thresholds (τ1, τ2, τ3) represent the points where each pair of probability curves meet. In line with the Rasch model category probability curves and thresholds are ordered consecutively on the measurement continuum.*

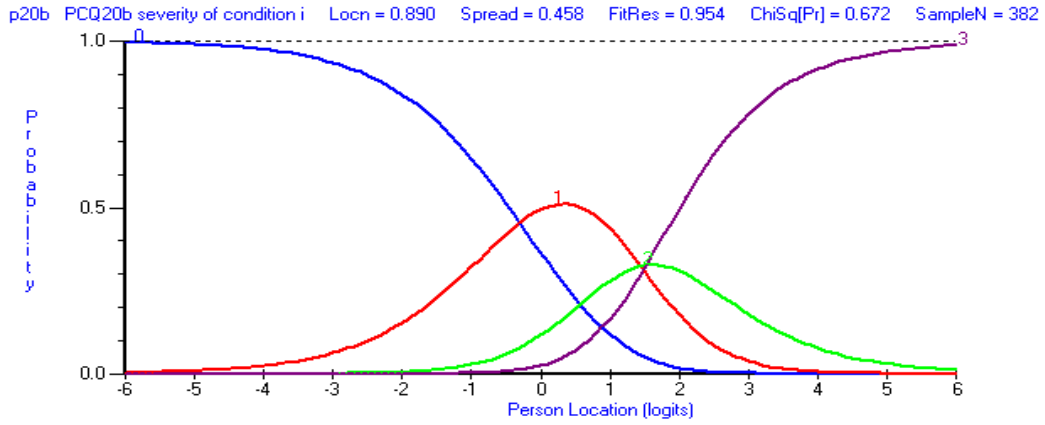
Figure 4.5 PCQ 1st Draft & Prognosis Scale: Category Probability Curves (disordered thresholds)



Item1f: I know my symptoms are not in my head



Item18c: I can predict when I will experience a flare-up



Item20b: The severity of my condition will stay the same in the future

Figure 4.5: *In line with Figure 4.4 Category Probability Curves are plotted on a graph against the measurement continuum. These items show some disordering as the curves and thresholds are not ordered consecutively on the measurement continuum.*

4.5.4.1.2.2 Did the "*symptoms & prognosis*" items map out a continuum?

The item location histogram (Figure 4.2A) indicated a gap on the left hand side of the measurement continuum. This information can also be deduced from Table 4.6 displaying the exact item location logits, indicating that the largest item gap is located between items "1f" and "1g" at 0.6 logits which is more than twice the size of the second largest item gap between items "18f" and "18d" at 0.23 logits. Standard error measurements are consistently below 0.1 across all scale items. Two pairs of items (highlighted on Table 4.6) are located on the same logit location, indicating some degree of item redundancy.

Table 4.6: PCQ 1st Draft *Symptom & Prognosis* Scale: Item Fit Statistics Ordered by Location

Item	Location	SE	Fit-residual	DF	ChiSq	Prob
1 f	-2.00	0.09	0.34	363.62	18.33	0.00
1 g	-1.40	0.08	-1.23	360.76	9.36	0.10
1 d	-1.25	0.07	-0.58	364.58	5.39	0.37
1 a	-1.12	0.08	-1.29	363.62	19.73	**0.00***
1 e	-1.04	0.07	-1.48	361.71	14.63	0.01
1 b	-0.89	0.07	-0.58	361.71	10.53	0.06
1 c	-0.86	0.07	-1.08	355.99	13.43	0.02
18 a	-0.76	0.06	**4.53**	360.76	39.86	**0.00***
3	-0.51	0.06	**6.06**	362.67	39.98	**0.00***
2	-0.36	0.07	**7.64**	270.09	34.24	**0.00***
1 k	-0.33	0.07	-0.76	364.58	10.90	0.05
19 d	-0.03	0.06	**3.38**	360.76	15.99	0.01
18 b	-0.01	0.06	-0.21	359.80	2.06	0.84
17	0.17	0.06	-0.32	358.85	8.63	0.12
19 c	0.20	0.06	**2.72**	360.76	10.89	0.05
1 j	0.20	0.06	-0.88	362.67	4.44	0.49
1 h	0.31	0.06	-1.71	360.76	11.75	0.04
1 i	0.47	0.06	-1.17	362.67	10.03	0.07
20 c	0.55	0.06	**4.28**	362.67	27.88	**0.00***
19 b	0.61	0.07	**2.66**	360.76	14.03	0.02
18 c	0.89	0.07	-2.63	356.94	19.68	**0.00***
20 b	0.89	0.07	0.95	361.71	3.18	0.67
18 e	1.00	0.07	-1.29	361.71	9.50	0.09
20 a	1.14	0.07	0.49	362.67	4.12	0.53
19 a	1.23	0.07	-0.37	362.67	5.28	0.38
18 f	1.32	0.08	-2.22	360.76	23.57	**0.00***
18 d	1.55	0.08	-1.82	360.76	14.16	0.01

significant with Bonferroni adjustment at p<0.05

4.5.4.1.2.3 Did the *symptoms & prognosis* scale items define a single variable? Two statistical and one graphical indicator were assessed in order to evaluate the items` goodness of fit as a single variable. Highlighted values on Table 4.6 signify items misfitting the predicted scores. Six items (2,3,18a,19c,19d,20c) lay well above the “rule of thumb” fit residual range of -2.5 to 2.5, indicating that the observed scores were significantly higher than the ones expected by the RMT. Another item (19b) lay just outside the expected range, whereas the remaining seven items lay within the acceptable range of -2.5 to 2.5, thus satisfying the fit residual statistic.

Chi square probabilities were also computed across six class intervals of the trait (i.e. six levels of certainty). Four of the items (2,3,18a,20c) with high fit residuals (>4.00) also displayed significant chi square probabilities (Table 4.6), and another three items did not fall outside the fit residual range (1a,18c,18f), thus indicating that the observed scores were significantly different from expected across the six class intervals of certainty. The remaining items satisfied the chi square statistic, as non-significant probabilities indicate that the observed scores are not significantly different from the expected ones in the six class intervals.

This relationship is also displayed graphically with item characteristic curves (ICCs). ICCs plot expected scores against the trait value (line curve) and observed scores in the six class intervals as black dots. The ICCs of the seven items misfitting the chi square statistic are displayed in Figure 4.6. The four items (2, 3, 18a, 20c) are failing both fit statistics display rather than misfitting ICCs, with more than three of the six black dots (i.e. observed scores in class intervals) lying well away from the expected curve. The remaining three items (1a, 18c, 18f) do not imply a significant misfit as the black dots are plotted closer to the line.

The dots for four of these items (2, 3, 18a, 20c) signify a line that is flatter than the expected curve, indicating that these items were underestimating the trait. In other words the observed scores were higher than expected at lower levels of the trait, and they were lower than expected at higher levels of the trait, as signified by the relative location of the dots on the ICC. The remaining three items (1a, 18c, 18f) display the reverse association, dots steeper than the ICC indicating overestimation. Figure 4.7 displays ICCs for items satisfying the chi square statistic, showing that the observed black dots lay close to the expected curve.

Figure 4.6 PCQ 1st Draft Symptom & Prognosis Scale: Item Characteristic Curves (items displaying misfit)

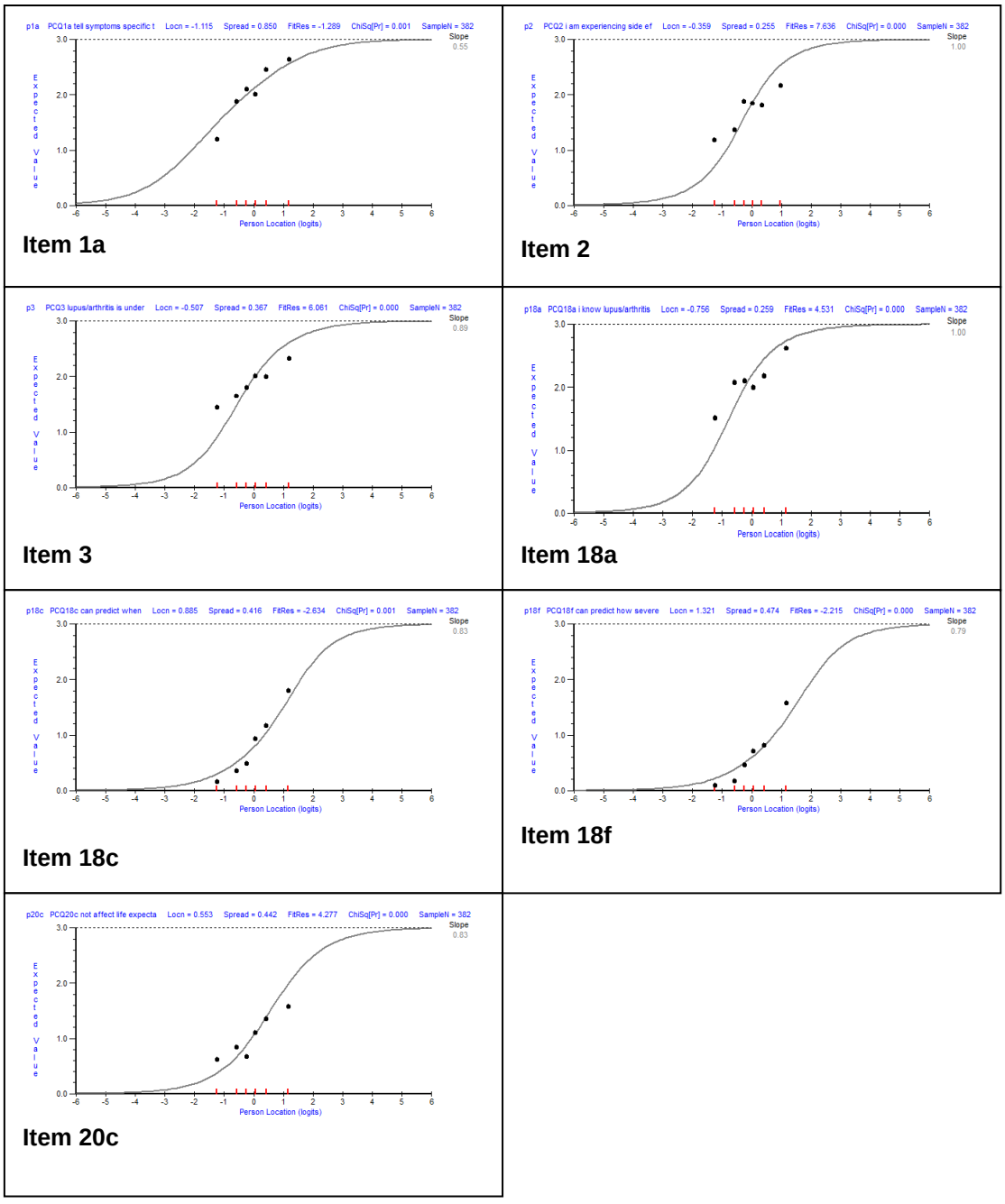


Figure 4.6: *The y-axis represents the person scores and the x-axis represents the person location logits. The curve denotes the expected score across the range of person locations. The black dots represent the observed scores in each of the six class intervals (class intervals of person location).Graphs for items 2, 3, 18a and 20c denote under discrimination of the trait as the line indicated by the dots is flatter than the expected curve. Graphs for items 1a, 18c and 18f denote over discrimination of the traits as the line indicated by the black dots is steeper than the expected curve.*

Figure 4.7 PCQ 1st Draft: *Symptoms & Prognosis* Scale: Item Characteristic Curves

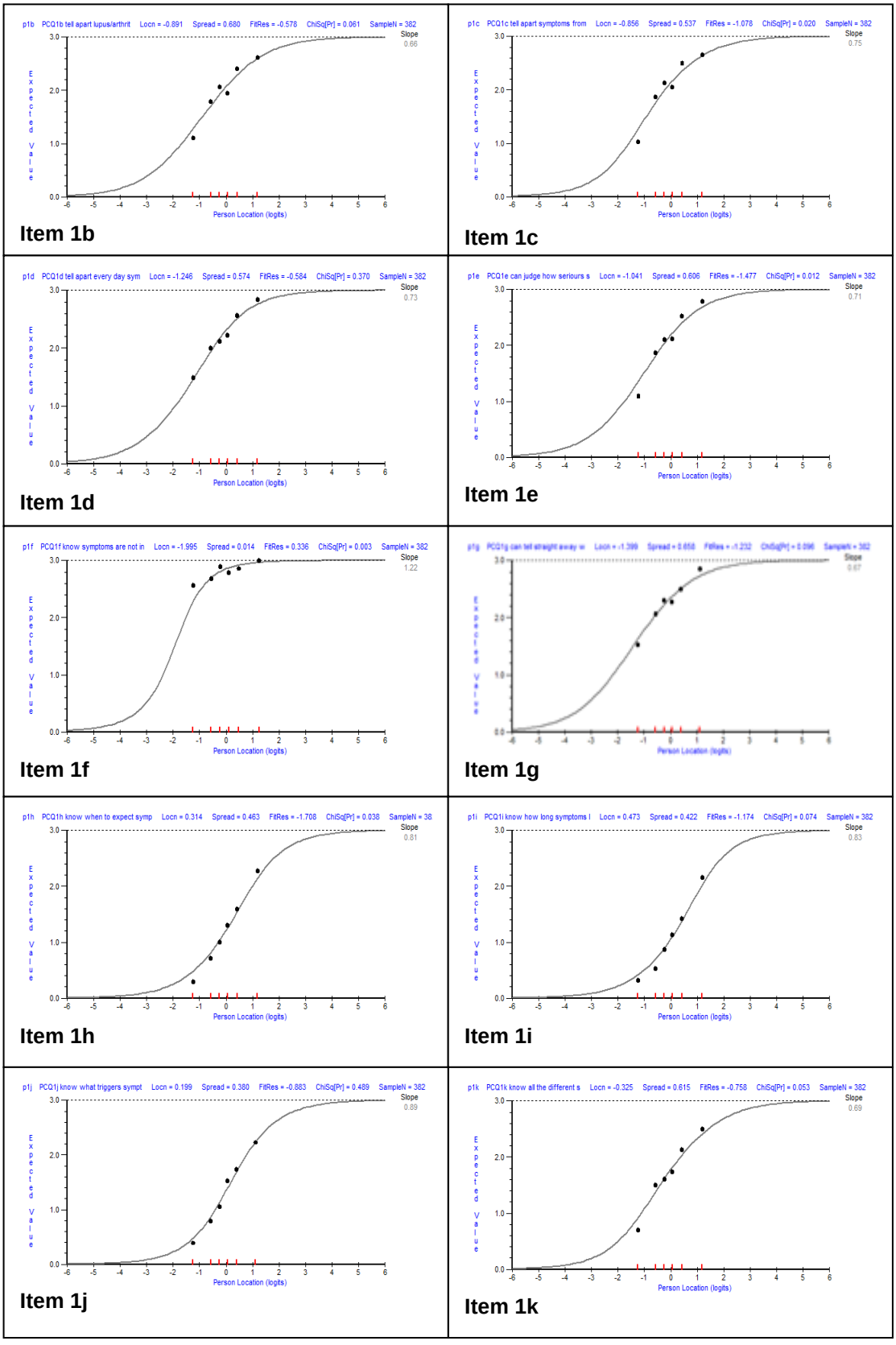


Figure 4.7 (cont`d)

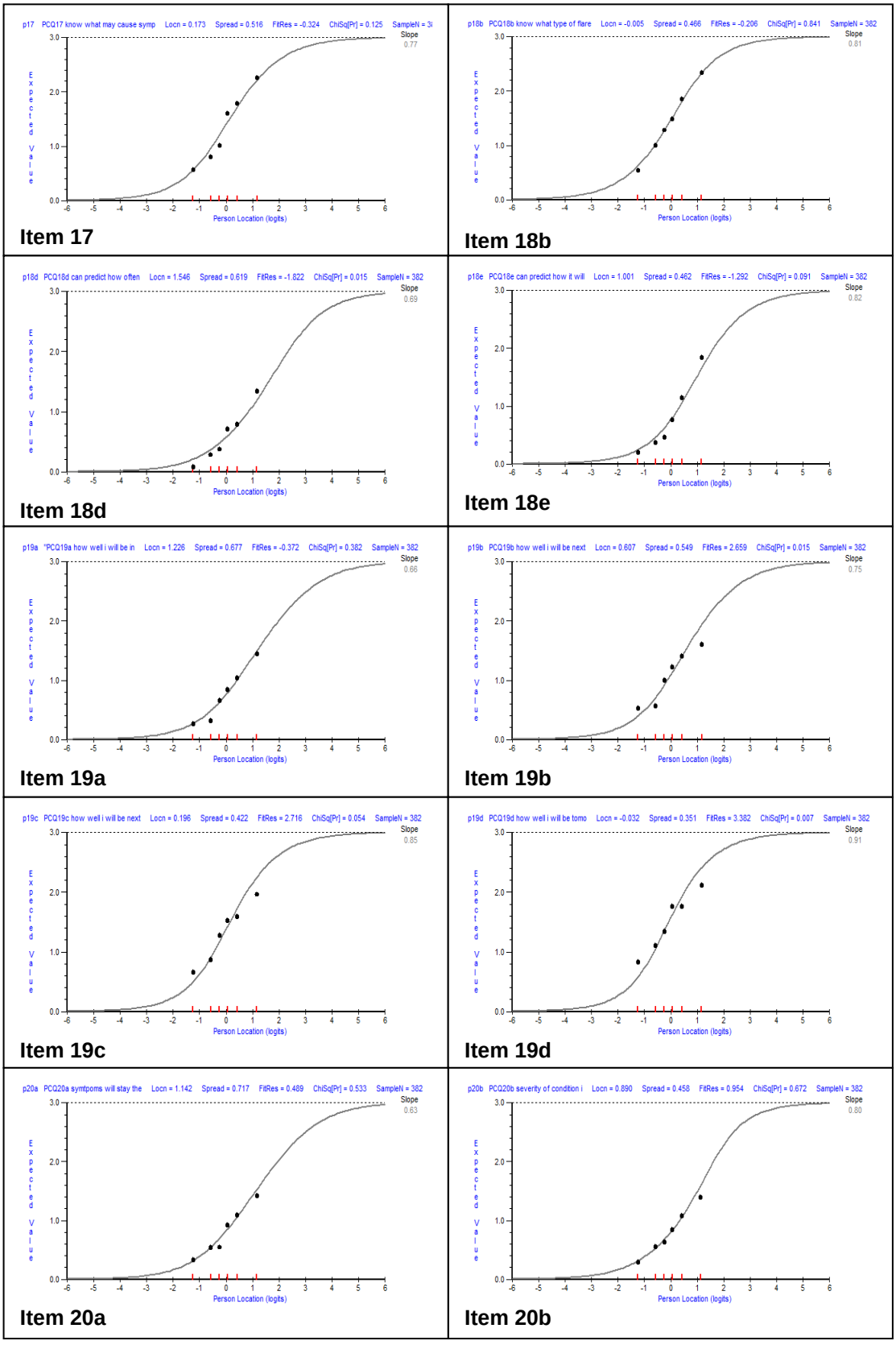


Figure 4.7: *In line with Figure 4.6 the observed scores in the six class intervals (black dots) are plotted against the curve representing the expected values across the range of person locations. None of the items displays misfit as the black dots lye very closely on the expected curve.*

4.5.4.1.2.4 Do responses to one item bias responses to others?

Response bias was assessed via the calculation of residual correlations between all potential pairs of the 27 items. Only 12 out of the 351 calculated residual correlations exceeded the 0.4 coefficient criterion set by this study, and another 6 fell between 0.30 and 0.40 (Table 4.7). Response bias was reported amongst four different sub-domains covered in this scale. Firstly, a pair of items related to symptom specificity to condition (1a) and older age (1b) reported a residual correlation of 0.52. Secondly, items related to future flares (18a, 18c, 18d, 18e) reported residual correlations between 0.43 and 0.52. Thirdly, all four of the items related to illness predictability (19a-19d) produced residual correlations between 0.44 and 0.89. Finally, items related to the severity of future symptoms and illness in general (20a & 20b) reported a residual correlation of 0.68. The high residual correlations amongst these items indicates a higher percentage of shared variance of error between them, thereby suggesting response bias and item redundancy.

4.5.4.1.2.5 Is the performance of the scale stable across relevant groups?

Three items displayed differential item functioning (DIF) by condition group (Table 4.8). DIF in these items is also displayed graphically (Figure 4.8) by plotting expected scores against the different levels of the trait and adding that to the observed scores for the two conditions. The graphs for items “1a” and “1g” display evidence that participants in the RA group (red line) are plotted higher on the graph than participants in the SLE group (blue line) (Figure 4.8). In other words, these two items performed differently in the two condition groups, thereby resulting in the RA group scoring higher than the SLE group, a difference that was statistically significant (Table 4.8). The opposite was reported for item “1j,” where the SLE group scored significantly higher than the RA group. Figure 4.8 also presents example graphs for three items that were stable and displaying no significant difference between the two lines of the SLE and RA groups.

The scale performance was stable across the seven different age groups (18-25; 26-35; 36-45; 46-55; 56-65; 66-75; >76 years) as no significant DIF was displayed in any of the items across these groups (Table 4.8). Stability was also displayed in the seven groups of disease duration years (<18months; 1.5-3; 4-5; 6-10; 11-20; 21-30; >30 years) (Table 4.8). The relevant graphical indicators are presented in Appendix 4.6.

Table 4.7 PCQ 1st Draft: Symptom & Prognosis Scale Residual Correlations

	1a	1b	1c	1d	1e	1f	1g	1h	1i	1j	1k	2	3	17	18a	18b	18c	18d	18e	18f	19a	19b	19c	19d	20a	20b	20c
1a	1.00																										
1b	0.52	1.00																									
1c	0.34	0.35	1.00																								
1d	0.21	0.25	0.25	1.00																							
1e	0.26	0.19	0.11	0.26	1.00																						
1f	0.12	0.16	0.20	0.06	0.18	1.00																					
1g	0.27	0.23	0.21	0.26	0.31	0.23	1.00																				
1h	0.05	-0.01	0.03	0.00	0.12	-0.02	0.12	1.00																			
1i	0.04	-0.01	-0.03	0.03	0.10	0.00	0.06	0.32	1.00																		
1j	-0.09	-0.11	-0.13	-0.05	-0.03	-0.20	-0.03	0.26	0.19	1.00																	
1k	0.30	0.18	0.10	0.16	0.28	-0.07	0.14	0.13	0.11	0.20	1.00																
2	-0.03	0.04	0.04	-0.03	-0.03	0.10	0.03	-0.06	-0.05	0.05	-0.03	1.00															
3	-0.11	-0.13	-0.08	-0.06	-0.09	-0.05	-0.16	-0.24	-0.19	-0.13	-0.09	0.04	1.00														
17	-0.03	-0.07	-0.05	-0.06	0.00	-0.13	-0.19	0.03	0.03	0.23	0.06	0.02	-0.08	1.00													
18a	-0.14	-0.03	-0.07	0.06	-0.01	0.17	0.13	-0.06	-0.09	-0.07	-0.06	0.06	-0.14	-0.04	1.00												
18b	-0.02	-0.04	-0.06	0.07	0.04	0.02	0.06	-0.03	-0.04	0.01	-0.03	-0.04	-0.20	-0.01	0.45	1.00											
18c	-0.08	-0.14	-0.22	-0.10	-0.04	-0.13	-0.11	0.19	0.12	0.26	0.03	-0.13	-0.27	0.15	0.05	0.19	1.00										
18d	-0.24	-0.19	-0.28	-0.25	-0.09	-0.15	-0.06	0.17	0.04	0.09	-0.03	-0.17	-0.24	0.03	0.05	0.15	0.52	1.00									
18e	-0.14	-0.17	-0.19	-0.18	-0.14	-0.08	-0.18	-0.01	-0.01	-0.05	-0.07	-0.14	-0.21	0.08	0.13	0.11	0.15	0.26	1.00								
18f	-0.08	-0.12	-0.28	-0.14	0.01	-0.05	-0.14	0.05	0.05	-0.03	-0.01	-0.11	-0.27	0.02	0.01	0.11	0.33	0.43	0.48	1.00							
19a	-0.28	-0.25	-0.17	-0.24	-0.32	-0.19	-0.34	-0.22	-0.18	-0.14	-0.30	-0.23	0.15	-0.11	-0.32	-0.25	-0.15	-0.08	0.00	0.01	1.00						
19b	-0.26	-0.27	-0.12	-0.26	-0.40	-0.19	-0.35	-0.28	-0.22	-0.17	-0.36	-0.19	0.23	-0.18	-0.30	-0.32	-0.21	-0.13	-0.08	-0.15	0.68	1.00					
19c	-0.23	-0.22	-0.06	-0.26	-0.39	-0.17	-0.30	-0.32	-0.25	-0.20	-0.34	-0.16	0.22	-0.17	-0.26	-0.31	-0.24	-0.19	-0.10	-0.18	0.50	0.82	1.00				
19d	-0.25	-0.26	-0.08	-0.23	-0.36	-0.15	-0.29	-0.29	-0.28	-0.19	-0.33	-0.14	0.27	-0.14	-0.26	-0.30	-0.22	-0.16	-0.12	-0.19	0.44	0.73	0.89	1.00			
20a	-0.27	-0.22	-0.19	-0.22	-0.21	-0.23	-0.22	-0.13	-0.06	-0.16	-0.24	-0.19	0.00	-0.05	-0.23	-0.16	-0.07	0.08	0.04	0.05	0.29	0.18	0.10	0.07	1.00		
20b	-0.22	-0.17	-0.29	-0.26	-0.13	-0.19	-0.21	-0.13	-0.11	-0.18	-0.23	-0.16	0.05	-0.09	-0.16	-0.11	-0.08	0.07	0.04	0.04	0.24	0.13	0.07	0.04	0.68	1.00	
20c	-0.20	-0.14	-0.17	-0.20	-0.20	0.00	-0.17	-0.15	-0.19	-0.21	-0.16	0.05	0.13	-0.12	-0.07	-0.14	-0.21	-0.07	-0.02	-0.13	0.14	0.11	0.10	0.14	0.29	0.35	1

Table 4.8 PCQ 1st Draft Symptom & Prognosis Scale: Differential Item Functioning

Item	Condition				Age				Disease Duration			
	MS	F	DF	Prob*	MS	F	DF	Prob*	MS	F	DF	Prob*
1a	12.38	15.18	1.00	0.00*	1.90	2.31	6.00	0.03	0.89	1.10	6.00	0.36
1b	7.99	9.10	1.00	0.00	1.10	1.21	6.00	0.30	0.57	0.65	6.00	0.69
1c	3.73	4.41	1.00	0.04	1.44	1.67	6.00	0.13	1.35	1.55	6.00	0.16
1d	1.24	1.36	1.00	0.24	2.18	2.45	6.00	0.02	1.88	2.07	6.00	0.06
1e	4.57	5.51	1.00	0.02	0.39	0.49	6.00	0.82	1.54	1.97	6.00	0.07
1f	12.15	12.65	1.00	0.00	4.05	4.26	6.00	0.00	1.75	1.71	6.00	0.12
1g	24.55	31.08	1.00	0.00*	3.05	3.80	6.00	0.00	0.20	0.22	6.00	0.97
1h	4.72	5.80	1.00	0.02	0.39	0.47	6.00	0.83	1.00	1.21	6.00	0.30
1i	7.59	8.92	1.00	0.00	2.02	2.37	6.00	0.03	0.36	0.41	6.00	0.87
1j	22.48	26.80	1.00	0.00*	3.98	4.69	6.00	0.00	0.53	0.57	6.00	0.75
1k	0.11	0.12	1.00	0.73	1.28	1.47	6.00	0.19	1.04	1.22	6.00	0.30
2	2.64	1.54	1.00	0.22	2.11	1.26	6.00	0.28	2.25	1.30	6.00	0.26
3	15.09	10.79	1.00	0.00	2.34	1.71	6.00	0.12	2.51	1.83	6.00	0.09
17	10.63	11.75	1.00	0.00	2.04	2.25	6.00	0.04	0.46	0.48	6.00	0.82
18a	1.15	0.88	1.00	0.35	1.87	1.40	6.00	0.21	0.53	0.39	6.00	0.89
18b	0.47	0.49	1.00	0.48	1.20	1.27	6.00	0.27	1.90	2.03	6.00	0.06
18c	4.98	7.11	1.00	0.01	1.96	2.79	6.00	0.01	0.98	1.43	6.00	0.20
18d	0.62	0.79	1.00	0.37	0.50	0.64	6.00	0.70	0.21	0.26	6.00	0.95
18e	0.63	0.74	1.00	0.39	1.10	1.36	6.00	0.23	0.35	0.45	6.00	0.84
18f	0.00	0.00	1.00	0.98	0.87	1.21	6.00	0.30	0.80	1.15	6.00	0.34
19a	0.99	1.06	1.00	0.30	1.56	1.77	6.00	0.10	1.41	1.56	6.00	0.16
19b	4.74	4.21	1.00	0.04	3.63	3.45	6.00	0.00	3.12	2.72	6.00	0.01
19c	3.56	3.15	1.00	0.08	3.61	3.35	6.00	0.00	3.48	3.08	6.00	0.01
19d	5.87	4.99	1.00	0.03	3.41	3.00	6.00	0.01	3.03	2.59	6.00	0.02
20a	0.01	0.01	1.00	0.92	3.52	3.80	6.00	0.00	0.33	0.32	6.00	0.92
20b	0.03	0.03	1.00	0.86	1.82	1.77	6.00	0.10	0.46	0.43	6.00	0.86
20c	0.79	0.65	1.00	0.42	2.17	1.74	6.00	0.11	1.53	1.18	6.00	0.31

probability significant with Bonferroni adjustment; MS mean square; DF degrees of freedom

Figure 4.8 PCQ 1st Draft *Symptoms & Prognosis* Scale: Differential Item Functioning by Condition (Graphical Indicator)

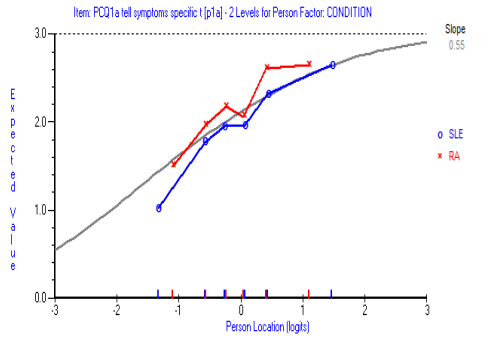
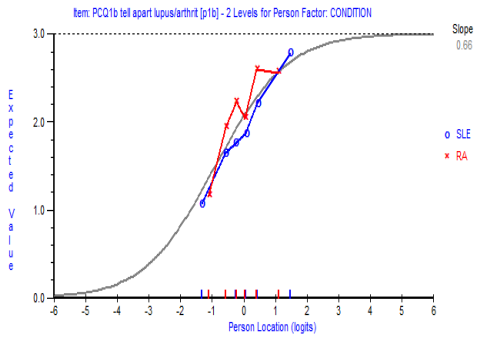
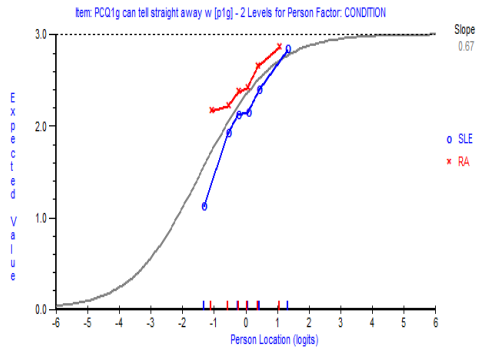
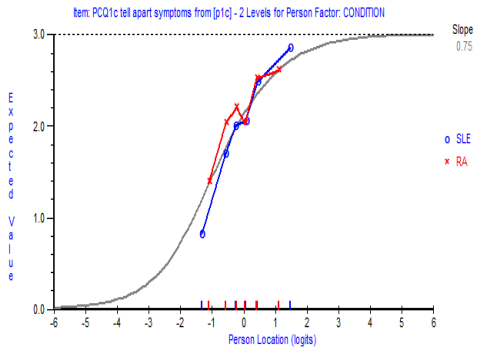
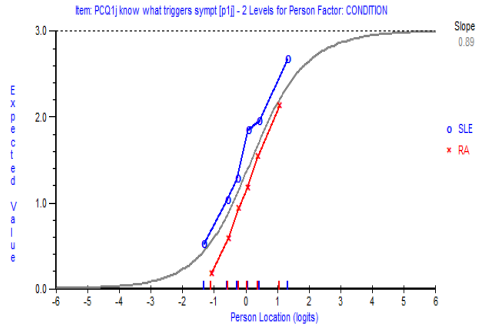
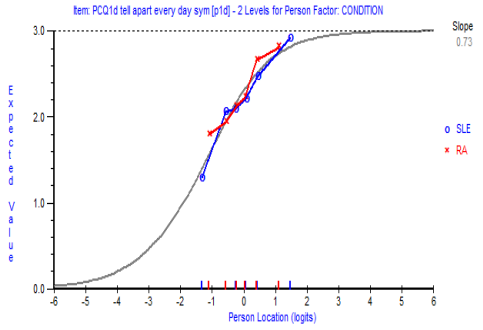
Items displaying DIF SLE Vs RA	Items without DIF SLE Vs RA
 **Item 1a**	 **Item 1b**
 **Item 1g**	 **Item 1c**
 **Item 1j**	 **Item 1d**

Figure 4.8: The x-axis represents the person location logits and the y-axis the expected value of scores. The blue line represented the observed scores of the SLE sample and the red line the observed scores of the RA sample, plotted against the curve of expected scores for the combined sample. Graphs for items 1a, 1g and 1j that displayed the greatest DIF statistically (Table 4.8) indicate that the observed scores for each condition lye on opposite sides of the curve, whilst DIF for the remaining items (1b, 1c & 1d) is less apparent as there is cross-over between the two lines of observed scores. Graphs indicated that the SLE sample scored consistently higher than expected and the RA sample lower than expected on items 1a and 1g and vice versa on item 1j.

4.5.4.1.3 How has the sample been measured?

4.5.4.1.3.1 Is the sample separated by the “symptom & prognosis” scale?
The person separation index (PSI) was 0.90, indicating that the separation of the sample by this scale was excellent (Table 4.13) and the random error was low. As indicated on the distribution histograms (Figure 4.2), measurement in the sample spread over a wide range of certainty levels (>7 logits). A high PSI also indicates the power of the scales to produce reliable evaluations of scale item.

4.5.4.1.3.2 How valid are the person-measurements?
Person fit residuals for 32 participants (8.4% of sample) fell outside the “rule of thumb” range of -2.5 to + 2.5. Twenty-one of these (5.5% of sample) were negative fit residuals (<-2.5), indicating observed scores were significantly lower than expected for these participants, and the remaining eleven (2.9% of sample) were positive residuals (>+2.5), indicating observed scores were significantly higher than expected. This finding indicates that the scale performed sub-optimally for 8% of the sample as the measurement produced was not in line with the RMT.

4.5.4.2 PCQ 1st Draft: *Medical Management* Scale Summary Results

The sample to scale targeting was satisfactory (Table 4.13). Person location range (from -2.189 to 3.664 logits, mean=0.588) indicated the sample`s sufficiency for the scale evaluation. Item location range (from -1.336 to 1.768 logits, mean=0.00) and item threshold range (from -2.252 to 2.637 logits) were satisfactory, indicating the range of certainty covered by the scale item matched the range of certainty in the sample well. However, the item skewness statistic fell above the +1 criterion (1.404), suggesting more items than expected fell on the negative side of the measurement continuum (> 0 logits), i.e. items with lower difficulty with regards to the trait. A relatively consistent spread of items with the largest item gap (0.54 logits) displayed between items 22 and 23b and some item bunching can be observed as some pairs of items are located on the same logit or within 0.01 logits (Table 4.9). Item 4b had the largest standard error (0.1) whereas the remaining items had a standard error of < 0.1.

Response categories for four of the items did not work as expected (Table 4.9). The second response category (somewhat uncertain) did not work as expected for two of the items (4a & 4b), and the third category (somewhat certain) for the other two items (5a & 24b) (Appendix 4.9). Several items failed to satisfy the goodness of fit statistics (Table 4.9). Four items (22, 24a-24c) produced positive fit residuals above the +2.5 acceptable boundary and subsequently displayed a significant chi square probability. Reviewing the ICCs for these items indicated that they all displayed observed scores in

the six class intervals (black dots) which produced lines that were flatter than the expected curve, thus indicating that the items were underestimating. In other words, observed scores for these items were higher than expected at lower levels of the trait and lower than expected at higher levels of the trait. Another four items (9b-9d, 9g) reported significant chi square probabilities, and their subsequent ICCs indicated overestimation as the observed scores (black dots) created lines steeper than the expected curve. Relative to the magnitude of fit residuals, items 9c, 22 and 24b produced the most misfitting black dots on the ICCs.

Response bias was displayed in seven item pairs reporting residual correlations above the 0.4 criterion. These five pairs of items related to the treatment (medication) sub-domain (4a & 4b; 5a & 5b 5d & 5e; 5d & 5f; 5e & 5f), one pair of the *trust in doctor* sub-domain (9c & 9d); and two items (23 & 23b) related to side-effects (Table 4.10). Significant DIF by condition (Table 4.10) was displayed in item 22, as the SLE participants scored higher than expected and RA participants lower than expected, which is contrary to item 5c that displayed DIF in the opposite direction between the two groups. Another item (23b) displayed DIF by different age groups.

A high PSI (0.89) was reported, indicating excellent ability to separate the sample (Table 4.13).The validity of sample measurement was not adequate as 8.9% of the sample reported fit residuals outside the “rule of thumb range”; 5% below -2.5 and 3.9% above +2.5. The complete RMT results for this scale are presented in Appendix 4.8.

Table 4.9 PCQ 1st Draft: *Medical Management* Scale Item Fit Statistics by Ordered Location

Index			Thresh.	Loc.	SE	FitRes	ChiSq prob	Res. r	DIF prob.		
									C	A	D
4	b	I understand why I am being treated.	Disord.	-1.34	0.10	-2.47	0.02	0.498	0.00	0.04	0.42
8		I understand my doctor's/nurse's questions, recommendations…	Order.	-1.13	0.09	-0.91	0.03	<0.30	0.01	0.02	0.38
9	c	My doctor(s) know which medication(s) and dose(s) are the best…	Order.	-1.06	0.08	-2.56	0.00*	0.647	0.86	0.41	0.01
5	c	I need the medication I am currently taking for my lupus/arthritis.	Order.	-1.03	0.08	-1.03	0.66	<0.40	0.00*	0.26	0.38
4	a	I understand how my lupus/arthritis is treated.	Disord.	-0.86	0.08	-2.30	0.01	0.498	0.01	0.69	0.06
5	a	The medications I am taking are helping my lupus/arthritis symptoms.	Order.	-0.81	0.08	-1.84	0.01	0.583	0.38	0.06	0.07
9	d	My doctor(s) know which medication will work best for me.	Order.	-0.81	0.08	-2.47	0.00*	0.647	0.65	0.17	0.01
9	g	My doctor(s) know how to help me control the physical aspects.	Order.	-0.54	0.07	-2.21	0.00*	<0.30	0.07	0.28	0.59
5	b	The medication I am taking is controlling my lupus/arthritis.	Order.	-0.48	0.07	-2.04	0.00	0.583	0.91	0.12	0.18
9	f	My doctor(s) know exactly what's wrong with me.	Order.	-0.45	0.07	-0.65	0.89	<0.30	0.06	0.08	0.08
6		I have the continuous support of the hospital team	Order.	-0.44	0.06	0.34	0.78	<0.30	0.00	0.37	0.74
7		I understand what my medical test results mean.	Order.	-0.43	0.07	1.23	0.12	<0.30	0.01	0.10	0.35
5	d	I do NOT need a stronger dose of medication for my lupus/arthritis.	Order.	-0.17	0.07	-0.04	0.67	0.705	0.00	0.66	0.37
5	e	I do NOT need additional medication for my lupus/arthritis.	Disord.	-0.02	0.06	-0.84	0.25	0.705	0.00	0.12	0.03
9	b	My doctor(s) know exactly how physically active I should be.	Order.	0.01	0.07	-0.49	0.00*	<0.40	0.00	0.06	0.35
5	f	I do NOT need alternative medication for my lupus/arthritis.	Order.	0.08	0.06	-1.08	0.15	0.672	0.05	0.08	0.11
24	a	It would not be a problem if a doctor other than my personal…	Order.	0.25	0.06	**4.53**	**0.00***	<0.40	0.37	0.51	0.86
9	h	My doctor(s) know how to help me with the non-physical aspects…	Order.	0.33	0.07	-0.46	0.08	<0.40	0.06	0.01	0.55
21		The medication I am taking will continue to control my symptoms…	Order.	0.68	0.08	-0.58	0.00	<0.30	0.04	0.02	0.22
9	a	My doctor(s) know exactly what caused my lupus/arthritis.	Order.	0.73	0.06	2.10	0.06	<0.40	0.47	0.51	0.16
9	e	My doctor(s) know exactly how my lupus/arthritis will progress…	Order.	0.74	0.06	1.25	0.87	<0.40	0.00	0.06	0.86
24	c	It would not be a problem if I had to receive healthcare whilst abroad	Order.	1.01	0.06	**4.41**	**0.00***	<0.30	0.27	0.32	0.03
24	b	It would not be a problem if my care was moved to a different hospital.	Disord.	1.12	0.06	**9.24**	**0.00***	<0.40	0.00	0.01	0.00
22		I will NOT need to have surgery related to my lupus/arthritis in the future.	Order.	1.15	0.06	**5.44**	**0.00***	<0.40	0.00*	0.05	0.07
23	b	The medication I am taking will NOT cause any severe side effects…	Order.	1.69	0.07	0.93	0.63	0.741	0.00	0.00	0.15

4.5.4.3 PCQ 1st Draft: *Self-management* Scale Summary Results

The sample to scale targeting was not adequate. The sample targeting was satisfactory as the person location range spanned over 7 logits (range -2.326 to 4.235 logits, mean=0.404), but the scale targeting was sub-optimal. The range of item locations (range -0.836 to 1.001 logits, mean=0.00) and the thresholds (range -1.826 to 2.186 logits) did not match the level of certainty in the sample adequately (Table 4.13). The person-item threshold distribution histogram indicated the presence of gaps in the measurement continuum (Appendix 4.11.1), which were also displayed by item locations as 0.47 logit gap was displayed between items 12 and 13 and a 0.79 logit gap between items 10 and 25 (Table 4.10).

All response categories worked as expected as all thresholds were ordered in sequence. Two items failed the goodness of fit statistics (Table 4.10). Item 11 produced a negative fit residual below the expected level of -2.5 and a significant chi square probability. The ICC revealed the observed scores (black dots) produced a line steeper than the expected scores, indicating the item was overestimating the trait. In other words, lower scores than expected were observed at lower levels of the trait and higher than expected on higher levels of the trait. On the other hand, item 25 produced a positive fit residual above +2.5, failed the chi square statistic and revealed a flatter observed curve on the ICC, thereby indicating underestimation.

No response bias was revealed as all residual correlations fell under the 0.30 criterion (Table 4.10). Three items displayed DIF by condition, as the SLE participant observed scores were higher and the RA participant observed scores lower than expected for items 10 and 25 (Table 4.10), and the reverse for item 13.

The PSI (0.72) was satisfactory, and a good scale ability to separate the sample into different levels of certainty was reported (Table 4.13). This scale produced the lowest percentage of person fit residuals falling outside the “rule of thumb” range (1.8%, 7 participants), all of which were below the -2.5 level, thus indicating observed scores which were lower than expected. The complete RMT results for this scale are presented in Appendix 4.11.

Table 4.10 PCQ 1st Draft: *Self-management* Scale Item Fit Statistics Ordered by Location

Index		Thresh.	Loc.	SE	FitRes	ChiSq prob	Res. r	DIF prob.		
								C	A	D
12	I know which symptoms I need to report to my doctor.	ordered	-0.84	0.08	- 0.37	0.47	<0.30	0.02	0.02	0.27
13	I know which types of physical activity I should avoid.	ordered	-0.37	0.07	1.20	0.33	<0.30	0.00*	0.00	0.06
11	I know exactly how to manage my lupus/arthritis.	ordered	-0.01	0.08	- 3.09	0.00*	<0.30	0.73	0.68	0.08
10	There are things I can do to help control my lupus/arthritis	ordered	0.21	0.07	- 1.18	0.19	<0.30	0.00*	0.11	0.33
25	I will be able to manage my lupus/arthritis in the future.	ordered	1.00	0.08	**4.89**	**0.00***	<0.30	0.00*	0.02	0.00

Chi square probabilities significant at 0.05; DIF by condition, age and disease duration group significant at 0.01 with Bonferroni adjustment

4.5.4.4 PCQ 1st Draft: *Impact* Scale Summary Results

The person location range (Table 4.13) was rather wide, ranging over 9 logits (range -4.598 to 4.556 logits, mean=-0.011). Scale targeting was sub-optimal as item locations (range -0.745to 0.803 logits, mean=0.00) and thresholds (range -1.974 to 1.795 logits) were not as wide as the sample range, thus suggesting that the range of certainty measured by the scale items did not match the level of certainty in the sample. No significant item gaps were displayed (Table 4.11); however some item bunching was evident.

Two items (26n & 26o) displayed a misfit on three levels; disordered response thresholds, fit residuals outside the expected level of +2.5 and positive chi square probabilities (Table 4.11). Reviewing the ICC for these items confirmed they were underestimating the trait as the observed scores (black dots) produced a line flatter than the expected curve. Another two items (26e & 26i) produced fit residuals narrowly outside the expected boundaries but satisfied the chi square statistic.

Significant response bias was reported as 14 item pairs produced high residual correlations (0.46 – 0.76), thus suggesting significant item redundancy (Table 4.11). Significant DIF by condition was reported by two items (26a & 26b) as SLE participants scored significantly higher and RA participants significantly lower than expected. Item 26o also displayed DIF by condition (Table 4.11), however this was expected as the item related to pregnancy, and uneven results were expected related to participants` demographics.

The PSI (0.89) was equally high, confirming the scale`s excellent ability to separate the sample into different levels of certainty (Table 4.13). A high percentage of person fit residuals (14.6%, 56 participants) fell outside the “rule of thumb range,” thus indicating the validity of the sample measurement was poor. Of these 11% were below the -2.5 level, indicating that the observed scores were lower than expected, and the remaining 3.6% were above the +2.5, thus indicating that the observed scores were higher than expected. The complete RMT results for this scale are presented in Appendix 4.13.

Table 4.11 PCQ 1st Draft: *Impact* Scale Item Fit Statistics Ordered by Location

Index		Threshold	Loc.	SE	Fit Res	ChiSq prob.	Res. r	DIF prob.		
								C	A	D
14b	I can plan social events in advance	ordered	-0.75	0.07	0.33	0.92	0.63	0.00	0.89	0.13
14a	I can plan everyday things e.g. grocery shopping	ordered	-0.71	0.07	1.38	0.48	0.63	0.13	0.93	0.28
26f	will NOT affect my ability to complete my education	ordered	-0.70	0.12	0.73	0.17	<0.30	0.71	0.31	0.87
14c	I can plan holidays in advance	ordered	-0.39	0.07	0.78	0.39	0.61	0.00	0.67	0.02
26k	will NOT affect my ability to maintain a relationship	ordered	-0.37	0.07	1.03	0.31	0.76	0.03	0.01	0.02
26j	will NOT affect my relationship with my partner	ordered	-0.32	0.07	1.24	0.27	0.76	0.03	0.00	0.00
26m	will NOT affect my ability to care for my children	ordered	-0.28	0.10	0.23	0.73	0.49	0.26	0.03	0.16
26a	will NOT affect my ability to cook.	ordered	-0.13	0.08	-1.07	0.38	0.61	0.00*	0.00	0.82
26b	will NOT affect my ability to dress myself	ordered	-0.11	0.08	-1.68	0.17	0.61	0.00*	0.00	0.33
26c	will NOT affect my ability to travel abroad	ordered	0.09	0.08	-1.19	0.07	0.46	0.04	0.02	0.24
26l	will NOT affect my ability to find a partner	ordered	0.10	0.11	-0.62	0.92	0.36	0.88	0.91	0.04
26i	will NOT affect my finances	ordered	0.19	0.08	2.70	0.77	<0.30	0.09	0.00	0.38
26o	will NOT affect my ability to get pregnant	disordered	0.43	0.12	**3.77***	**0.00***	0.40	0.03	0.00*	0.23
26d	will NOT affect my ability to exercise	ordered	0.30	0.08	-1.36	0.01	<0.40	0.00	0.08	0.93
26g	will NOT affect my ability to find a job	ordered	0.33	0.10	-1.30	0.03	0.62	0.39	0.11	0.31
26h	will NOT affect my ability to keep a job	ordered	0.37	0.10	-2.09	0.01	0.62	0.73	0.00	0.24
26e	will NOT affect my mobility	ordered	0.72	0.08	-2.64	0.02	<0.31	0.00	0.11	0.61
26n	will NOT cause problems during my pregnancy	disordered	0.80	0.14	**3.31***	**0.00***	0.40	0.13	0.00	0.28

chi square probabilities significant at 0.05; DIF by condition, age and disease duration group probabilities significant at 0.01 both with Bonferroni adjustment

4.5.4.4 PCQ 1st Draft: *Social Functioning* Scale Summary Results

The sample to scale targeting was rather poor. The person location range was satisfactory, ranging over 6 logits (Table 4.13, but the person location mean was more than 1 logit away from the item mean (range -3.566 to 3.334 logits, mean=1.359). Scale targeting was sub-optimal as item locations (range -0.687 to 0.724 logits, mean=0.00) and thresholds (range -1.432 to 1.359 logits) were rather narrow, suggesting that the range of certainty measured by the scale items did not match the level of certainty in the sample. The sample was sufficient for evaluating this scale but was located to the higher end of the measurement logits (i.e. displayed higher trait levels than the items). Apart from being narrow, the measurement continuum also displayed a large item gap of >0.7 logits (Table 4.12).

Response categories for all seven items worked as expected as thresholds were ordered in sequence. Two items (16a, 16b) reported fit residuals well above the +2.5 criterion level and also failed to satisfy the chi square statistic (Table 4.12). IICs for these items indicated that observed scores in the six class intervals (black dots) were flatter than the expected line curve, suggesting the items were underestimating the trait. In other words, the observed scores were higher than expected at lower levels of the trait and lower than expected at higher levels of the trait. Overestimating was observed in the ICCs for another three items misfitting the chi square probability (27a-27c) which lay marginally below the lower fit residual criterion level -2.5 (Table 4.12).

Significant response bias was reported between three items (27a-27c) related to future levels of social support, thereby producing residual correlation coefficients higher than the accepted criterion >0.4 (Table 4.12). Significant DIF was displayed by item 27c "family will care for me if necessary" by condition, as the observed SLE scores were higher and the observed RA scores lower than expected, and by age as younger participants scored higher than expected (Table 4.12). Another item 16b "disclosing diagnosis to others" displayed DIF by age, as older participants scored higher than expected and younger participants lower than expected.

The PSI (0.70) was satisfactory, and a good scale ability to separate the sample into different levels of certainty was reported (Table 4.13). This scale produced a relatively low percentage of person fit residuals falling outside the "rule of thumb" range (2.8%, 11 participants). Of these, 2.6% were below the -2.5 level, indicating that the observed scores were lower than expected, and the remaining 0.2% above the +2.5 level, thus indicating that the observed scores were higher than expected. The complete RMT results for this scale are presented in Appendix 4.14.

Table 4.12 PCQ 1st Draft: *Social Functioning* Scale Item Fit Statistics Ordered by Location

Index		Thresh.	Loc.	SE	FitRes	ChiSq prob	Res. r	DIF prob.		
								C	A	D
27a	My family and loved ones will be supportive of me in relation to my lupus/arthritis.	ordered	-0.69	0.09	**-3.37**	**0.00***	0.33	0.11	0.69	0.73
15a	My family and loved ones are supportive in helping me to manage my lupus/arthritis.	ordered	-0.36	0.08	-1.67	0.03	<0.40	0.67	0.81	0.38
27c	My family and loved ones will care for me if necessary	ordered	-0.12	0.08	-2.61	**0.00***	0.39	0.00*	0.00*	0.47
27b	My family and loved ones will help me manage the day-to-day issues which happen because of my lupus/arthritis.	ordered	-0.11	0.08	-2.67	**0.00***	0.39	0.07	0.09	0.22
16b	I can confidently reveal my diagnosis to others	ordered	-0.07	0.08	**4.28**	**0.00***	<0.30	0.02	0.00*	0.69
13b	My family and loved ones understand the variety and severity of lupus/arthritis symptoms I am experiencing.	ordered	0.62	0.08	0.63	0.63	<0.40	0.91	0.73	0.10
16a	I can confidently reveal my lupus/arthritis diagnosis to a potential employer or at my workplace.	ordered	0.72	0.08	**3.79**	**0.00***	<0.30	0.01	0.39	0.84

chi square probabilities significant at 0.05; DIF by condition, age and disease duration group probabilities significant at 0.01 both with Bonferroni adjustmen

Table 4.13 Rasch Analysis Scale-Level Summary Statistics

	PSI		Person-Item Distribution (targeting)			Item fit				Person fit			
PCQ Scale revisions	With extremes	No extremes	Person location range	Item location range	Item threshold range	Mean (SD)	Fit Res. Mean (SD)	Skewn.	Fit Res. range	Mean (SD)	Fit Res. Mean (SD)	Skewn.	Fit Res. range
Symptom & Prognosis													
1st Draft (27 items)	0.903	0.899	-2.917 – 5.076	-1.995 – 1.549	-2.674 – 2.667	0.000 (0.941)	0.497 (2.662)	1.149	-2.634 -7.636	-0.056 (0.864)	-0.267 (1.539)	0.231	-4.587 -5.962
2nd Draft (16 items)	0.906	0.896	-5.216 – 5.073	-1.579 – 1.997	-3.213 – 3.566	0.000 (1.149)	0.208 (1.689)	1.485	-1.775 -5.073	0.050 (1.299)	-0.298 (1.325)	0.092	-4.306 -4.547
Medical Management													
1st Draft (26 items)	0.886	0.886	-2.189 – 3.664	-1.336 – 1.768	-2.252 – 2.637	0.00 (0.888)	0.339 (2.854)	1.404	-2.555 -9.244	0.588 (0.824)	-0.244 (1.505)	0.345	-4.445 –5.608
2nd Draft Medication* (6 items)	0.761	0.721	-4.008 – 4.038	-1.107 – 0.906	-2.601 – 2.329	0.000 (0.759)	0.087 (1.552)	-0.002	-1.878 -1.938	1.643 (1.745)	-0.425 (1.180)	-0.180	-3.726 -2.767
2nd Draft Trust in Dr. (9 items)	0.836	0.818	-3.514 – 3.541	-1.169 – 1.216	-2.724 – 2.612	0.000 (0.917)	0.015 (1.227)	-0.082	-1.878 -1.938	0.970 (1.594)	-0.366 (1.194)	-0.345	-4.099 -2.914
Self-management													
1st Draft (5 items)	0.717	0.671	-3.326 – 4.235	-0.836 – 1.001	-1.833 – 3.142	0.000 (0.685)	0.290 (2.997)	0.415	-3.087 -4.887	0.404 (1.311)	-0.345 (1.090)	-0.403	-3.014 -2.365
2nd Draft (6 items)	0.746	0.691	-2.177 – 4.242	-0.967 – 0.797	-1.760 – 2.895	0.000 (0.656)	0.150 (1.330)	-0.337	-1.676 -1.449	1.023 (1.416)	-0.374 (1.131)	-0.368	-3.668 -2.188
Impact***													
1st Draft (18 items)	0.893	0.883	-4.598 – 4.556	-0.745 – 0.803	-1.935 – 2.353	0.000 (0.516)	0.298 (2.137)	0.810	-2.636 -5.771	-0.011 (1.490)	-0.538 (1.855)	-0.369	-6.634 –3.993
Social Functioning***													
1st Draft (7 items)	0.700	0.693	-3.566 – 3.334	-0.687 – 0.724	-2.120 – 1.814	0.000 (0.507)	-0.231 (3.182)	0.424	-3.370 -4.280	1.359 (1.439)	-0.283 (1.151)	-0.664	-5.541 -2.650

**** The draft medication scale is incomplete, an additional 5 items were added to the scale, the complete scale will only be tested in the 2nd field test***

*****No results available for second draft of the scales; the second draft of impact scale comprised 10 items resulting from the integration of the initial 18 items; the social functioning scale was eliminated***

4.5.5 PCQ 1st Draft Scale Modifications

Findings of the RMT analysis were reviewed and interpreted within the study research group and items failing to fit the expectation of the Rasch model were re-evaluated. Where necessary, the original qualitative patient data which formed the basis of item generation (Chapter 3) were revisited for clarification or additional information. Modifications to scale items were decided in line with deviation of findings from the Rasch model expectations and criteria, and in association with qualitative data, as interpreted within the multidisciplinary research team. Interpretation and modifications are presented in detail for the s*ymptoms and prognosis* scale, whereas for the remaining scales results and modifications are presented in summary.

4.5.5.1 PCQ 1st Draft: *Symptoms & Prognosis* Scale Modifications

Evaluation tests for items of the first draft of the *symptoms and prognosis* scale were reviewed and assessed within the research group, and several amendments were made in consultation with the qualitative patient data (Chapter 3).

Item 1f “my symptoms are not in my head (i.e. not imaginary)” displaying disordered thresholds was eliminated taking into consideration remarks made by participants on the completed questionnaires suggesting that the implication that symptoms could potentially be imaginary was somewhat offensive to patients and was a condescending statement. Item elimination was therefore based on the extent of the item` s misfit to the Rasch model and the original qualitative findings.

Out of the three items displaying DIF by condition 1j, “what triggers symptoms,” was the most significant one. Reviewing the qualitative data and discussing the results with the clinician collaborators it was decided to split this item by DIF when analysing data, as the significantly higher scores observed in the SLE scores were reflective of more certainty in the qualitative data and different characteristics of the condition.
Items 2 “experiencing side-effects” and 3 “condition is under control” displayed the highest misfit on the fit residuals and chi square statistics. It was decided to eliminate item 2 as the *symptoms and prognosis* scale comprised a conceptually similar item “1c, I can tell symptoms apart from side-effects” which performed in line with the RMT model expectations. Item 3 was the only one reflecting the “health status interpretation” sub-domain (Table 4.18), and a revision of the qualitative data confirmed that no other statements could be deducted for this sub-domain. It was therefore decided to leave this item in the second draft of the PCQ, but as an independent single item.

It was decided to eliminate item 17 “I know what may cause my symptoms to deteriorate” as it was judged to be conceptually unfitting with the scale as it comprised causal attributions. Review of the qualitative data led to the conclusion that statements in the qualitative data related to this item were covered by item 20a “symptoms will stay the same in the future”.

Items 18a “I know that my condition will flare-up in the future” and 18c “I can predict when I will experience a flare-up” were not revised despite displaying misfit and disordered thresholds respectively. It was decided to re-evaluate their performance in the second draft of the scale, as conceptually it matched the other five items relating to future flares (18b-18f) well, and it also displayed moderately high residual correlations.

Items related with the illness predictability sub-domain (19a-19d) displayed very high residual correlations (0.44 - 0.89). Revising the qualitative data, it was decided that the breadth of patient statements could be reflected with a single item related to illness predictability instead of the four-item temporal structure (Appendix 4.4) that was developed during the item generation phase. Therefore these four items were replaced by the single item “I can predict how well I will be in the future” (Table 4.18).

Items 20a “symptoms will stay the same” and 20b “severity will stay the same” displayed significantly high residual correlation. However, as the sub-domain of future illness severity was strong in the qualitative data it was decided to retain them, but independently as single items (Table 4.18). Item 20c “condition will not affect life expectancy” displayed a misfit on fit residual and the chi square statistic and was therefore eliminated as the potential insensitivity and inappropriateness of its content (i.e. the issue of life-expectancy) was judged to be unnecessary within the research team.

In summary, the scale was reduced to 16 items across two sub-domains; symptom interpretation (10 items) and future flares (6 items). Items related with the other sub-domains were reduced to single items (Table 4.18) in order to better reflect the breadth of content presented in the qualitative data. To reflect these modifications the scale was renamed *symptoms & flares*.

4.5.5.2 PCQ 1st Draft: *Medical Management* Scale Modifications Summary

Reviewing the misfitting items, it was decided to eliminate item 22 from the scale but retain it as a single item, and in the same way eliminate items 23a and 23b relating to side-effects. However, as these two items displayed very high residual correlations it was decided to integrate them into a single item. Revisiting the qualitative data, it was

also agreed that the quotations leading to items 24a to 24c could be better reflected in a single item rather than a scale representing a measurement continuum.

Conversely, revisiting the qualitative data showed that item 21 “medication will continue to control symptoms” could potentially be extended into a scale in order to reflect the breadth of data. It was therefore agreed to mirror items “5b-5f” in the future tense to better reflect the qualitative data. Review of these findings led to the decision to divide the *medical management* scale into two distinct scales; *medication* and *trust in doctor*. This choice was made as revisiting the qualitative data led us to conclude that the themes in these two sub-domains differed conceptually, and we therefore decided to attempt to measure them independently (Table 4.18).

Re-evaluation of the items within the multidisciplinary team resulted in the elimination of items 4a and 4b that displayed misfitting and item 6 that was judged to be conceptually ill-fitting the trait which was measured by the scale. Experts on the team indicated that items 7 and 8 were conceptually associated to self-management and were misplaced in this first draft of scale. It was therefore decided to move these items into the *self-management* scale. Modification of the *medical management* scale resulted in two distinct scales reflecting the *medication* (treatment) and *trust in doctor* sub-domains and three single items (Table 4.18).

4.5.5.3 PCQ 1st Draft: *Self-management* Scale Modifications Summary

Reviewing findings of the *self-management* scale within the research team it was agreed that including additional items to address sub-optimal targeting and item gaps on the continuum could benefit scale performance. Review of the first draft of the *medical management* scale concluded that two of its items “understanding doctors` recommendations and questions” and “understanding the meaning of medical test results” were not conceptually analogous to the rest of the scale items. In consultation with the original qualitative data the research team decided to move these two items (7 & 8) to the *self-management* scale in order to better reflect the issues they are addressing (Table 4.18). It was further decided to eliminate item 25 as it was found to be overly misfitting the scale, however, as this item was directly inducted from qualitative statements the item was retained in but as a single item (Table 4.18).

4.5.5.4 PCQ 1st Draft: *Impact* Scale Modifications Summary

Reviewing the Rasch analysis findings for the *impact* scale within the research team it was decided to revise the first draft of the scale by integrating some of the items. Item 26o “not affect ability to get pregnant” displayed significant misfit and was removed.

Item 26n “not cause problems to pregnancy” displaying a similar but not as overt misfit (i.e. fit residual closer to expected level, ICC less deviant from expected) was retained at this level of the analysis, as this issue (i.e. pregnancy) was highlighted greatly in the qualitative data (Chapter 3).

As the most dominant misfit issue displayed by these items was response bias suggesting item dependency it was decided to integrate and reduce items using the guidance of residual correlations (Table 4.11). Three items related to the planning sub-domain (14a-14c) which produced residual correlations in the range of 0.61-0.63 were integrated into one general forward planning item. Another three items (26a – 26c) related to the functionality sub-domain produced residual correlation in the range of 0.46 - 0.61 and were integrated into one general functionality item. Two items (26g, 26h) related to the occupational sub-domain reported a residual correlation coefficient of 0.62 and were integrated into one general item about job prospects. Two items related to the pregnancy sub-domain (26n- 26o) were further integrated into one item about pregnancy. Finally, three items related to the relationships sub-domain (26j-26l) produced residual correlations in the range of 0.56 - 0.76 and were integrated into one general item about relationships.

Items 26d – 26f, 26i, 26m were retained as they did not produce any significantly high residual correlations with other items that they could potentially be integrated with. The second draft of the *impact* scale therefore comprised 10 items derived from the original 18 items of the first draft of the scale (Table 4.18). Where necessary the wording of these items was slightly changed to better match the remainder of the scale items. It was not possible to re-evaluate the second draft of the scale as no data were available in the first field test for the revised integrated items. Evaluation of the second draft of the *impact* scale will be performed in the second field test.

4.5.5.5 PCQ 1st Draft: *Social Functioning* Scale Modifications Summary

Reviewing findings within the research team it was decided to eliminate this scale and replace it with two single items. The breadth of the revisited qualitative data did not offer the potential of adding further items to improve the scale targeting. Items related to current social support (15a, 15b) were eliminated, as revising the qualitative data revealed that this theme was only reported in the future sense and was covered by items (27a-27c). Considering the item misfitting and the response bias of individual items (Table 4.12), in the second draft of PCQ (Table 4.18) they were replaced with two single items related to disclosing diagnosis to others and future social support through the integration of the three items related to future support (27a-27c).

4.5.6 PCQ 2nd Draft Rasch Analysis Results

The above modifications led to the revised second draft of the PCQ scales, which were further evaluated in a second round of RMT analysis (Figure 4.1). A summary of results is presented in the analysis format described in the methods section for all available data. The integration and addition of new items prohibited the re-evaluation of the *medication* and *impact* scales which will be completed in the second field test.

4.5.6.1 PCQ 2nd Draft: *Symptoms & Flares* Scale Summary Results

The second draft *symptoms and flares* scale performed better than the first draft on both the scale (Table 4.13) and item level (Table 4.14).The person location range was wider (>10 logits) and more symmetrical (range -5.216 to 5.073 logits, mean=0.050) than the first draft of the scale (-2.917 to 5.076 logits, mean -0.056 logits). Item location range maintained a range of approximately 3.5 logits (Table 4.13) and the item threshold location range increased from a range of 5.341 logits in the first draft to a range of 6.779 in the second draft (range-3.213 to 3.566). This indicates that the range of certainty measured by the *symptoms and flares* items was improved (Figure 4.9), but; that precision of measurement has been reduced to some extent as more person measurements fell outside the information function curve suggesting that their measurement was associated with greater standard error. The items maintained positive (1.485) skewness, signifying that the items were skewed on lower logits, i.e. lower levels of item difficulty

The measurement continuum appears to be somewhat improved as the largest item gap was 0.53 logits wide between items 18a and 1k (Table 4.14) compared to the largest item gap in the first draft of the scale which was 0.6 logits (Table 4.6). Compared with the first draft, no items appear to be located on exactly the same location logits. On item-level examination (Table 4.14) none of the items displayed response threshold disordering, signifying that all response categories worked as expected. Item 18a was still misfitting (fit residual > +2.5, chi square <0.05), as the ICC curve suggested higher scores than expected were observed on lower levels of the trait and lower scores than expected on higher levels of the trait. Another item (18e) lay marginally above the +2.5 fit residual level but met the chi square statistic criterion.

The same pairs of items displayed item dependency, but residual correlations were reduced (<0.5) (Table 4.14). Two items were still unstable between the two condition groups as the RA group scored significantly higher than expected as compared to the SLE on 1g “can tell straight away when experiencing symptom” and lower than expected as compared to the SLE on 18c “can predict when I will experience a flare”

The PSI (0.90) was equally as high as the first draft scale (Table 4.13), confirming the scale`s excellent ability to separate the sample into different levels of certainty. The validity of sample measurement improved but was still sub-optimal, as 5.5% of the person item fit residuals fell outside the “rule of thumb range” compared to 9% of the first draft of the scale. Of these, 3.1% were below the -2.5 level, indicating observed scores which were lower than expected and the remaining 2.4% were above the +2.5 level, indicating observed scores which were higher than expected.

Figure 4.9 PCQ 2nd Draft *Symptoms & Flares* Scale: Targeting of Sample to Scale

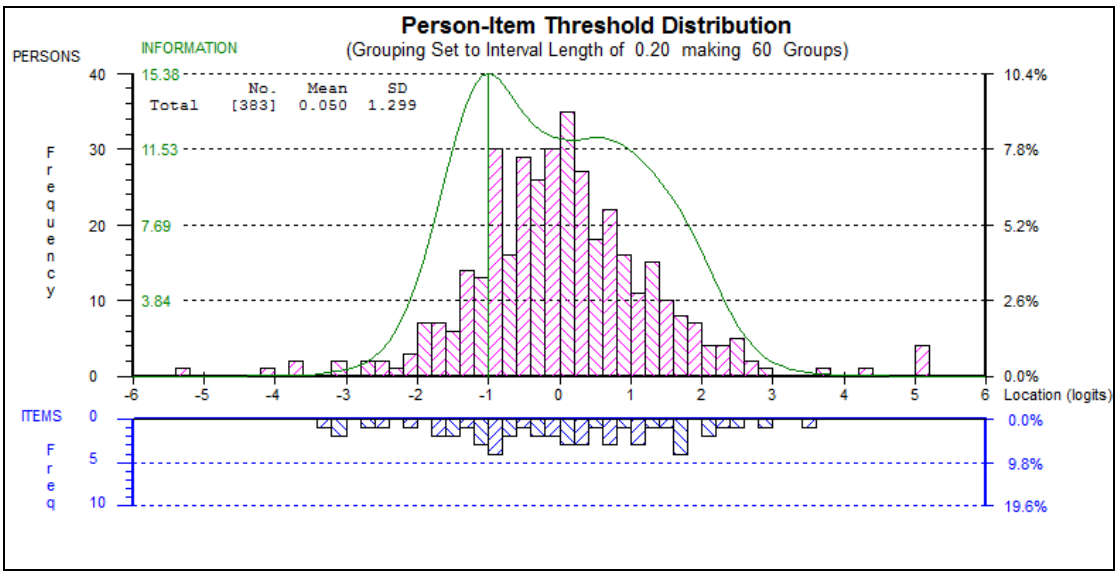


Figure 4.9: *The pink blocks represent the sample distribution for the symptoms and flares scale and the blue blocks represent the scale distribution of the 16 items on the same measurement continuum indicating that the location of item thresholds and persons is well matched. The green curve shows the location on the continuum the scale performs at its best.*

Table 4.14 PCQ 2nd Draft: *Symptom & Flares* Scale Item Fit Statistics Ordered by Location

1st Index	2nd Index	Response Thresholds	Loc.	SE	FitRes	ChiSq prob	Res. r	DIF prob.		
								C	A	D
1g	1a	Ordered	-1.58	0.08	-1.31	0.10	<0.30	0.00*	0.01	0.87
1d	1b	Ordered	-1.40	0.08	0.33	0.54	<0.30	0.62	0.03	0.13
1a	1c	Ordered	-1.19	0.08	-0.62	0.12	0.454	0.02	0.24	0.29
1e	1d	Ordered	-1.14	0.08	-1.23	0.08	<0.30	0.39	0.64	0.34
1b	1e	Ordered	-0.93	0.08	0.39	0.96	0.454	0.16	0.70	0.39
1c	1f	Ordered	-0.90	0.08	2.06	0.58	<0.30	0.78	0.73	0.40
18a	7a	Ordered	-0.81	0.07	**5.07**	**0.00**	0.364	0.67	0.67	0.72
1k	1g	Ordered	-0.28	0.07	-0.61	0.18	<0.30	0.06	0.21	0.70
1jSLE	1hSLE	Ordered	-0.12	0.10	0.13	0.47	<0.30	1.00	0.29	0.75
18b	7b	Ordered	0.13	0.07	0.28	0.74	0.364	0.49	0.77	0.05
1h	1i	Ordered	0.51	0.07	-0.50	0.19	<0.30	0.29	0.46	0.51
1i	1j	Ordered	0.71	0.07	0.06	0.60	<0.30	0.13	0.19	0.95
1jRA	1hRA	Ordered	0.74	0.09	-0.65	0.24	<0.30	1.00	0.46	0.19
18c	7c	Ordered	1.24	0.08	-1.78	0.38	0.485	0.00*	0.00	0.11
18e	7d	Ordered	1.29	0.08	2.79	0.68	0.472	0.41	0.41	0.74
18f	7e	Ordered	1.74	0.09	-0.25	0.27	0.472	0.13	0.05	0.33
18d	7f	Ordered	2.00	0.09	-0.61	0.51	0.485	0.04	0.45	0.95

1hSLE/1hRA data for item split and presented separately for the SLE and RA sample; Loc location; SE standard error; FitRes fit residual; ChiSq prob chi square probability; Res. r residual correlations; DIF prob differential item functioning probability; C condition; A age; D disease duration*significant with Bonferroni adjustment

4.5.6.2 PCQ 2nd Draft: *Trust in Doctor* Scale Summary Results

The *trust in doctor* scale included 8 items resulting from the first draft of the *medical management* scale (Table 4.18).

Sample to scale targeting was improved (Table 4.13). The person location range was widened (from -3.514 to 3.541, mean: 0.970), as was the item threshold range (from -1.951 to 2.087), whereas the item location range was similar (from -1.169 to 1.216, mean=0.000). The range of certainty measured in the sample was relatively well matched to the range of certainty measured by the items that were no longer positively skewed. Item bunching was improved compared to the first draft of the scale (Table 4.9) where 3 items pairs were located in less than 0.01 logits. In the second draft no items were located on the same logits and the largest item gap between items was 0.56 logits (items 4f and 4g) (Table 4.15). Scale performance on an item level improved

greatly as all response categories worked as expected and all items satisfied the fit residuals, chi squares, residual correlations and DIF statistics (Table 4.15).

A satisfactory PSI (0.84) was reported, thus indicating the draft scale`s good level of ability to separate the sample into certainty levels (Table 4.13). The validity of sample measurement improved as 3.6% of the person item fit residuals (14 participants) fell outside the "rule of thumb range," compared to 8.9% of the first draft of scale. Of these, 3.4% were below the -2.5 level, indicating observed scores which were lower than expected and the remaining 0.2% were above the +2.5 level, indicating observed scores which were higher than expected. Sample-measurement was still sub-optimal as the "rule of thumb" for person fit residuals outside the recommended range was only 1%.

Table 4.15 PCQ 2nd Draft: *Trust in Doctor* Scale Item Fit Statistics Ordered by Location

1st Index	2nd Index	Thresh	Loc.	SE	FitRes	ChiSq prob	Res. r	DIF prob.		
								C	A	D
9c	4a	ordered	-1.17	0.09	-1.88	0.17	0.33	0.09	0.23	0.14
9d	4b	ordered	-0.86	0.09	-1.01	0.04	0.33	0.02	0.28	0.14
9g	4c	ordered	-0.38	0.09	-1.02	0.33	<0.30	0.87	0.87	0.43
9f	4d	ordered	-0.31	0.08	0.70	0.72	<0.30	0.66	0.62	0.16
9b	4e	ordered	0.14	0.08	0.33	0.28	<0.30	0.01	0.86	0.73
9h	4f	ordered	0.60	0.08	0.29	0.41	<0.30	0.76	0.71	0.89
9a	4g	ordered	1.16	0.07	1.94	0.30	<0.30	0.39	0.74	0.06
9e	4h	ordered	1.22	0.08	0.36	0.79	<0.30	0.07	0.66	0.69

Chi square probabilities significant at 0.05; DIF by condition, age and disease duration group significant at 0.01 with Bonferroni adjustment

4.5.6.3 PCQ 2nd Draft: *Medication* Scale Summary Results

The *medication* scale comprised 11 items, 6 items from the first draft of the *medical management* scale and an additional 5 new items added to reflect future medication effectiveness and needs (Table 4.18). Re-evaluation using Rasch analysis was performed on the 6 items that were available from the first draft of the scale.
Sample to scale targeting was somewhat improved (Table 4.13). The person location range was widened (from -4.008 to 4.038, mean: 1.643), as was the item threshold range (from -2.187 to 1.857), whereas the item location range was similar (from -1.107 to 0.906, mean=0.000). Items were no longer positively skewed, but the person location mean was located further away from the item mean. Item bunching was improved, compared to the first draft of the scale (Table 4.9) where 3 items pairs were located in less than 0.01 logits In the second draft no items were located on the same

logits and the largest item gap between items was 0.52 logits (items 3cRA and 3a) and no significant item gaps were displayed (Table 4.16).

All response categories worked as expected, even for item 5e which displayed disordered thresholds in the first draft scale, and no misfit was displayed on the item level (Table 4.16). Contrary to the four item pairs showing response bias in the first draft, all of the residual correlations fell under the 0.4 criterion and none of the items displayed significant DIF (Table 4.16).

The ability of the second draft of the scale to separate the sample into certainty levels was good, with a 0.76 PSI (Table 4.13). The validity of the sample measurement improved as 3.1% of the person item fit residuals (12 participants) fell outside the "rule of thumb range" compared to 8.9% of the first draft scale. Of these, 2.8% were below the -2.5 level, indicating observed scores which were lower than expected and the remaining 0.3% were above the +2.5 level, thus indicating that observed scores were higher than expected. Although improved, this percentage is still sub-optimal compared to the 1% "rule of thumb".

The *medication* scale displayed improved measurement properties compared to the first draft of the overarching *medical management* scale however re-evaluation of the scale was conducted on incomplete data as 5 more items were added. Evaluation of the complete scale was be performed in the second field test (Chapter 5).

Table 4.16 PCQ 2nd Draft *Medication* Scale Item Fit Statistics Ordered by Location

1st Index	2nd Index	Thresh.	Loc.	SE	FitRes	ChiSq prob	Res. r	DIF prob.		
								C	A	D
5a	3cRA	ordered	-1.11	0.14	1.09	0.03	<0.30	1.00	0.48	0.33
5b	3a	ordered	-0.63	0.10	-0.38	0.06	0.39	0.00	0.23	0.26
5a	3cSLE	ordered	-0.41	0.14	2.39	0.08	<0.30	1.00	0.39	0.02
5c	3b	ordered	0.01	0.09	0.91	0.03	0.39	0.14	0.11	0.28
5d	3d	ordered	0.49	0.09	0.22	0.17	0.36	0.04	0.41	0.99
5e	3e	ordered	0.76	0.09	-1.83	0.24	0.36	0.04	0.06	0.13
5f	3f	ordered	0.91	0.09	-1.77	0.31	<0.30	0.36	0.03	0.29

Chi square probabilities significant at 0.05; DIF by condition, age and disease duration group significant at 0.01 with Bonferroni adjustment

4.5.6.4 PCQ 2nd Draft: *Self-management* Scale Summary Results

The second draft of the *self-management* scale comprised six items, four from the first draft of the scale and an additional two items which initially belonged to the *medical management* scale (Table 4.18). Higher scores reflected higher levels of certainty, as in all the PCQ scales.

Sample to scale targeting was not altered greatly (Table 4.13). The sample was still sufficient for using this scale, but it was located at the higher end of the measurement logits (i.e. displayed higher trait levels than the items) as person locations ranged from 2.117 to 4.242 logits, but the person mean (1.023) was further away from the item mean. Item location range (-0.967 to 0.797 logits, mean=0.000) and item threshold range (-1.867 to 2.296 logits) were still sub-optimal, suggesting that the range of certainty measured by the scale items did not match the extent of certainty in the sample. Gaps (Table 4.17) on the measurement continuum displayed a slight improvement with the largest gap being 0.64 logits between items 5a and 5b in comparison to 0.79 in the first draft of the scale (Table 4.10).

Unlike the first draft of the scale one item (8) displayed reversed thresholds. On closer examination, disordering was marginal as threshold 1 was located on -0.792 and threshold 2 on -0.817 (Appendix 4.12.1). The item goodness of fit improved (Table 4.17) as no items produced fit residuals outside the "rule of thumb" range of -2.5 to 2.5 and significant chi square probabilities. Response bias remained insignificant as all residual correlations fell below the 0.30 criterion. Item 10 displayed significant DIF by condition and age as SLE and younger participant observed scores were significantly higher than expected, while RA and older participant observed scores were lower than expected. The PSI was slightly improved (0.75) and the scale maintained a good ability to separate the sample into different levels of certainty (Table 4.13). The validity of the second draft scale measurement was reduced as 4.2 % (16 participants) produced a person fit residual lower than the -2.5 "rule of thumb" boundary.

Table 4.17 PCQ 2nd Draft: *Self-management* Scale Item Fit Statistics Ordered by Location

1st Index	2nd Index	Thresh.	Loc.	SE	FitRes	ChiSq prob	Res. r	DIF prob.		
								C	A	D
8	5a	disorder.	-0.97	0.09	1.43	0.04	<0.30	0.04	0.08	0.61
7	5b	ordered	-0.33	0.08	0.80	0.68	<0.30	0.04	0.20	0.34
12	5c	ordered	-0.28	0.08	-1.68	0.06	<0.30	0.42	0.31	0.30
13	5d	ordered	0.18	0.07	0.23	0.31	<0.30	0.00	0.07	0.09
11	5e	ordered	0.60	0.08	-1.26	0.08	<0.30	0.04	0.33	0.30
10	5f	ordered	0.80	0.07	1.33	0.29	<0.30	0.00*	0.00	0.37

Chi square probabilities significant at 0.05; DIF by condition, age and disease duration group significant

Table 4.18: Patient Certainty Questionnaire (PCQ) Item Revisions

1st Draft	2nd Draft	1st Draft Item Index	2nd Draft Item Index	2nd Draft Item N:
Scales				
Sym. & Prognosis	Symptoms - Flares	1a-1e, 1g-1k,	1a-1j, 7a-	16
Med. Management.	Medication	3a-3f, 21	3a-3f, 9a–	11
Med. Management.	Trust in Doctor	9a-9h	4a-4h	8
Self-management.	Self-management	7,8,10-13	3a-3f	6
Impact	Impact	14a-14c, 26a-*	13a-13j	10
Single Items				
Sym. & Prognosis	Health status	3	2	1
Sym. & Prognosis	Future severity	20a-20b	8a-8b	2
Sym. & Prognosis	Predictability	19a-19d*	8c	1
Med. Management	Surgery	22	10	1
Med. Management	Treatment side-effects	23b	11	1
Med. Management	Continuity of care	24a-24c*	12	1
Self-management	Future self-man.	23	13	1
Soc. Functioning	Diagnosis disclosure	16a-16b*	6	1
Soc. Functioning	Future social support	27a-27c*	14	1
			Total:	**61**

** Item integration, ** New items - not present in the first draft of the PCQ*

4.6 Psychometric Evaluation Conclusions

Analyses and interpretation of the RMT psychometric tests resulted in modification and the second draft PCQ containing 61 items in total in comparison to the 83 items of the first draft. The revised PCQ consisted of five scales and 10 single items. RMT analysis retained the conceptual domains of *symptoms and flares*, *self-management* and *impact* as measurement scales whilst dividing the overarching conceptual domain and scale of *medical management* into two scales; *medication* and *trust in doctor*. To match the breadth of the qualitative data better 5 items were added to the *medication* scale. Finally, the *social functioning* scale was reduced to single items as findings indicated that although social functioning was one of the domains of the conceptual framework, items of this scale did not perform sufficiently as a scale.

Items in the second draft of the PCQ scales were ordered in the location generated by the RMT analysis. The performance of the revised *symptoms and flares*, *trust in doctor*, *self-management* and an incomplete version of the *medication* scale improved when re-evaluated. The integration and addition of new items prohibited the re-evaluation of the complete *medication* and *impact* scales which will be completed in the second field test.

4.7 Chapter 4 Summary

The first draft PCQ was field tested across five hospital sites and completed by 383 participants. Psychometric evaluation of the five scales was initially conducted using RMT, whose results were reviewed within the research group and evaluated in consultation with the qualitative data to guide scale development and item reduction. One of the scales (*social functioning*) was eliminated and another scale (*medical management*) was split into two distinct scales (*medication* and *trust in doctor*). The second draft PCQ comprised 51 items across five scales and 10 single-items, whilst new items were added on the *medication* and *impact* scales. Psychometric properties were re-evaluated for the four scales, data for which were available in the first field test. The performance of the second draft PCQ improved both on a scale and an item level in the second round of RMT tests indicating the adequacy of the measurement properties of four of the second draft PCQ scales. Chapter 5 presents a second field test which provided data for all of the five scales and ten single-items used for the final psychometric evaluation in this thesis.

Chapter 5: Psychometric Evaluation of the second draft of the Patient Certainty Questionnaire (PCQ): 2nd Field Test

5.1 Chapter 5 Overview

Chapter 5 presents the methods and results of the second of the two quantitative field tests conducted in order to evaluate the psychometric properties of the PCQ scales. Consistent with Chapter 4, Rasch Measurement Theory (RMT) analysis was performed on the PCQ scales. Additional revisions were made where necessary following a review and interpretation of the RMT analysis findings, thereby resulting in the final version of the PCQ. Additional tests of external validity not included in the RMT analysis were further performed on the final version of the PCQ scales using traditional psychometric tests. This chapter describes the methodology and results of these tests.

5.2 Introduction

Psychometric evaluation conducted in the first field test resulted in the scale formation and item reduction of the second draft PCQ scales. The *social functioning* scale was eliminated and replaced by two single items, while the *medical management* scale was divided into two distinct scales; *medication* and *trust in doctor*. PCQ scale items were reduced to 51 from 83 and an additional set of 10 items resulting from item reduction were added to the second draft PCQ (Table 4.18).

Evaluation of measurement properties for three of the five revised scales (*symptoms & flares*; *trust in doctor*; *self-management*) was presented in Chapter 4, but modifications made to the *medication* and *impact* scales including additional and integrated items prohibited their evaluation in the first field test. Therefore the second field test was utilised to evaluate the measurement properties of the second draft of all five scales and confirm the performance of three of the scales which were evaluated previously and presented in the first field test.

As discussed in Chapter 1, different psychometric paradigms exist in relation to the theory, models and techniques used to guide the psychometric evaluation of instruments and their rating scales. Rasch Measurement Theory (RMT) was the chosen technique for the psychometric evaluation in this thesis (141, 142) as it addresses several limitations of traditional psychometric techniques and adds greatly to the scientific rigour of evaluation. Therefore, similar to the first field test, an initial

evaluation and any further revisions required to the scales to improve performance was conducted using the modern psychometric techniques within the RMT.

Subsequently, traditional psychometrics were utilised to complement the evaluation of the final version of the PCQ scales. Traditional psychometric tests evaluating the external validity of the scales were performed to complement RMT analysis, which is restricted to the evaluation of a scale` s internal validity (142). These tests examine a scale` s convergent and discriminant validity, in other words assess whether the scales display the expected relationships with other scales and/or demographic and disease variables based on pre-existing hypotheses (139, 528). Such tests allow the collection of information of how a scale can be used or interpreted, and have previously been used to provide additional validation to RMT-developed and evaluated scales (529).

Health care professionals (HCPs) in the qualitative interviews presented in Chapter 3, suggested that younger age and shorter disease duration is linked with higher levels of patient uncertainty but suggested no gender differences in the levels of patient uncertainty. In addition, HCPs indicated positive links between the different domains of patient uncertainty and particularly between the *symptoms and flares* and *trust in doctor* domains as well as the *medication* and *impact* domains. These relationships related to the association of the PCQ scales with either demographic variables, and/or other PCQ scales were explored using traditional tests of validity following the RMT analysis of the scales. Traditional psychometric tests were further performed to assess the utility and potential of the resulting single-items, as RMT analysis used for the evaluation of the remaining scales is not intended for use for the evaluation of single items.

5.2.1 Aims

Similar to the first field test the polytomous Rasch model (213) was utilised to evaluate the measurement properties of the five scales, with the objective to examine the following:

- How adequate is the scale to sample targeting?
- To what extent has a measurement continuum been constructed successfully?
- How has the sample been measured?

Additionally to the first field tests aims, the evaluation of the scales between the two field tests will be compared in order to assess the consistency of the scales` performance and evaluation. Traditional tests of convergent and discriminant validity

were further performed to assess the external validity of the final version of the PCQ scales.

5.3 Method

The methodology used was identical to the one used in the first field test presented in Chapter 4.

5.3.1 Study Design

A cross-sectional observational field-test study was set up across four of the five hospitals taking part in the first field test: University College Hospital (UCH), Royal Blackburn Hospital (RBH), Robert Jones and Agnes Hunt Orthopaedic Hospital (RJAH) and Leicester Royal Infirmary (LRI). National Research Ethics Committee (REC) approval was obtained for this study as well as local approvals issued by the Research & Development (R&D) offices at the four hospital sites. The study was also registered on the National Institute for Health Research (NIHR) portfolio database as the second phase of the first field test.

5.3.2 Participants – Sample Size

As no explicit guidelines exist for sample size calculation in psychometrics, “the rule of thumb” recommendation for the sample to comprise five to ten subjects per scale items (168, 514) was used. To this effect, a minimum sample of 160 participants would be required to allow for 10 subjects for each of the 16 items of the longest scale.

5.3.3 Participants – Eligibility

The eligibility criteria were consistent with the criteria of the first field test for participant eligibility, including a clinical diagnosis of SLE or RA, fluency in English and a minimum 18 years of age (see section 4.3.2). Additional to this, in order to ensure independence of the two field tests, participant completion of the first field test was set as an exclusion criterion for the second field test.

5.3.4 Participants - Sampling and Recruitment

Participants were recruited between June and December 2012 using the two different methods of convenience sampling utilised in the first field test and detailed in section 4.3.4. Clinic recruitment was utilised at the RBH site, whereas the rest of the sites (UCH, RJAH & RLI) invited and recruited participants through invitations via post. The study documents utilised in the field test are presented in Appendices 5.1 to 5.3.

5.3.5 Materials

The second draft of the PCQ was the instrument which was administered and evaluated in the second field test. This consisted of five scales, including *symptoms & flares* (16 items), *medication* (11 items), *trust in doctor* (8 items), *self-management* (6 items) and *impact* (10 items), and 10 single items (Appendix 5.4). Items were scored on a 4-point Likert scale ranging from "very uncertain" to "very certain". A "not applicable" response option was included in all scales apart from the symptoms and flares. Responses were analysed on scale basis (though summed totals), with higher scores (in all scales and items) reflecting more certainty. "Not applicable" responses were coded as missing data.

A brief demographics questionnaire was also administered to participants (Appendix 4.4.1). Details of the participant age, year of diagnosis, gender, ethnic group, employment status, living status and highest level of education were recorded. In addition to the draft PCQ, nine more instruments were administered, assessing beliefs, mood, quality of life and adherence and will be presented in detail in Chapter 6. They were administered to serve an extended validity analysis which was intended to take place after the final psychometric evaluation and revision of the PCQ presented in this chapter.

5.3.6 Data collection and monitoring

Participant consent was carried out by the candidate (SC) for all sites apart from RJAH and some of the RLI, where local researchers led participant recruitment. Data collection, study co-ordination and monitoring were solely controlled by SC at the UCL Centre for Rheumatology Research, who also saw to the update of accrual data on the NIHR portfolio. Data were entered onto an SPSS dataset and transferred onto RUMM2030 software (516) in order to perform the RMT data analysis.

5.4 Psychometric analysis

Modern psychometric techniques (RMT) were utilised to evaluate the measurement properties of all five PCQ scales and any additional revisions made if necessary. Traditional psychometric techniques were then used to assess the measurement properties of the final version of the PCQ scales. The psychometric criteria and tests utilised were consistent with those used in Chapter 4 (Table 4.2).

5.4.1 Modern Psychometrics: Rasch Measurement Theory Analysis

A series of tests were performed to evaluate the extent to which the observed scores fit the expectations of the Rasch model and whether the performance of the scales was consistent with the first field test. Similar to the first field test, the tests included person-

to-item distribution histograms, response threshold locations, item locations, item fit residuals, chi square probabilities, item characteristic curves (ICCs), residual correlations, differential item functioning (DIF), person separation index (PSI) and person fit residuals. These tests were described in detail in Chapter 4 (see section 4.4.1.1 to 4.4.1.3.2).

Moreover, the extent to which raw (ordinal) scores of the final PCQ scales approached linear (interval) measurement was examined (See section 4.4.1.3.3). This is important as one point on a scale is not necessarily the same across the breadth of the scale (517, 527). It is important to consider the extent to which the data fit the Rasch model as the greater the misfit the lower the precision of the linear estimates (517). Considering the stringent mathematical criteria of the RMT minor deviations of raw scores from interval/linear measurement is expected.

This was examined through both a graphical and a numerical indicator. Firstly, the raw scores were plotted against interval logit measurements to assess the graphical linearity of this relationship, and secondly the raw total scores of each scale were transformed to logit measurements and linear 0 to 100 scores. As higher scores reflect lower levels of uncertainty, and consequently higher levels of certainty, for simplification purposes certainty will be referred to as the trait in these analyses (i.e. instead of lower uncertainty). Finally, the datasets of the two field tests were combined to assess the stability of the items and the consistency of scale evaluation between the two field tests. This was only possible for three of the scales (*symptoms & flares*, *trust in doctor* and *self-management*), data for which were available in the first field test.

5.4.2 Traditional Psychometric Analysis

All five PCQ scales and single items were submitted to tests of convergent and discriminant validity (139, 528, 530). Convergent validity relates to the association of the scale under evaluation with other scales that measure theoretically the same or similar conceptual variables. Discriminant validity refers to the extent to which a scale is not associated with other measures designed to assess theoretically unrelated conceptual variables. Convergent validity i.e. the association between the final version of the PCQ scales was assessed through examining the association between the different PCQ scales using Pearson correlations with an expected range criterion of 0.30 to 0.70. The association of the final PCQ scales with demographic variables were further conducted using simple t-tests, one way ANOVAs and Pearson correlations for binary, nominal and continuous demographic variables respectively. Single items were further

evaluated for their convergent and discriminant validity in association with the scales, as descriptive parameters.

5.5 Results

5.5.1 Response Rate

A total number of 440 participants were invited to take part in this study, of which 279 participants completed the study materials across the four hospital sites. The overall response rate was 63.4%, 70.4% in SLE and 57% in RA (Table 5.1). The response rate was evidently higher at the main site (UCH), where recruitment was co-ordinated by the research team and reminder letters were sent out as per the study protocol. The reasons for non-response recovered in the first field test ad hoc investigation (see section 4.5.1), were still applicable and relative to the sub-optimal response rate in the second field test. In addition to those reasons, the increased required completion time for the second field test materials (estimated 60 minutes) was another reason suggested by invited participants for non-participation.

Table 5.1 2nd Field Test Response Rate

Site	Total N (invited)	Over all response rate	SLE N (invited)	SLE response rate	RA N (invited)	RA response rate
UCH	182 (270)	67.4%	139 (200)	69.5%	43 (70)	61.4%
RBH*	14 (20)	70%	14 (20)	70%	-	-
RJAH*	42 (80)	52.5%	-	-	42 (80)	52.5%
LRI*	41 (70)	58.6%	12 (20)	60%	29 (50)	58%
Total:	**279 (440)**	**63.4%**	**165 (240)**	**70.4%**	**114 (200)**	**57%**

** no reminder letters sent out*

5.5.2 Sample Characteristics

A total sample of 279 participants with a mean age of 49.93 years (SD= 14.8) and the mean disease duration of 15.9 years (SD=11.1) was used in this analysis. The study protocol was not followed strictly at the external sites (RBH, RJAH, LRI) with regards to the exclusion criteria of participation in the first field test. This resulted in an overlap of a small ration of the external site`s sample between the two field tests. The sample of this field test cannot therefore be assumed to be 100% independent from the first field test. Regretfully the external sites were not able to provide specific details on the sample overlap.

The resulting sample comprised 165 patients with SLE (Table 5.2), 158 female and 7 male, with a mean age of 45.31 years (SD=14.34) and the mean disease duration of 16.04 years (SD=10.08). The remaining sample of 114 participants were patients with

RA, 87 female and 27 male, with a mean age of 56.95years (SD=12.5) and the mean disease duration of 15.60 years (SD=12.5). The gender difference and younger mean age of SLE patients were expected as SLE is far more common in women than men and is usually diagnosed earlier in life than RA (36, 101, 315).

Table 5.2 2nd Field Test: Sample Characteristics

	Total (N=279)	SLE (N=165)	RA (N=114)
Age (years)			
Mean (SD)	49.93 (14.8)	45.31 (14.3)	56.95 (12.5)
Range	18 – 84	18 - 76	20 - 84
Disease Duration (years)			
Mean (SD)	15.87 (11.2)	16.04 (10.1)	15.60 (12.5)
Range	0.50 – 52	1 - 40	0.50 – 52
Gender N (%)			
Female	245 (87.8)	158 (95.8)	87 (76.3)
Male	34 (12.2)	7 (4.2)	27 (23.7)
Ethnicity N (%)			
White	191 (68.5)	97 (58.8)	94 (82.5)
Black	43 (15.4)	40 (24.2)	3 (2.6)
Indian/Pakistani/Bangladeshi	21 (7.6)	15 (9)	6 (5.3)
Mixed race	6 (2.2)	5 (3.0)	1 (0.9)
Other	11 (3.9)	8 (4.8)	3 (2.6)
Missing	7 (2.5)	-	7 (6.1)
Employment Status N (%)			
Employed (full-time)	83 (29.7)	57 (34.5)	26 (22.8)
Employed (part-time)	48 (17.2)	24 (14.5)	24 (21.1)
Student	12 (4.3)	11 (6.7)	1 (0.9)
Retired	63 (21.6)	26 (15.8)	37 (32.5)
Unemployed	11 (3.9)	7 (4.2)	4 (3.5)
Homemaker	16 (3.7)	12 (7.3)	4 (3.5)
Disability retirement	34 (12.2)	23 (13.9)	11 (9.6)
Other	3 (1.1)	3 (1.8)	-
Missing	7 (2.5)	-	7 (6.1)
Living situation N (%)			
Alone	54 (19.4)	36 (21.8)	18 (15.8)
Spouse/partner	127 (45.5)	70 (42.4)	57 (50.0)
Children	18 (6.5)	13 (7.9)	5 (4.4)
Partner & children	41 (14.7)	18 (10.9)	23 (20.2)
Family (parents/siblings)	20 (7.4)	18 (10.9)	2 (1.8)
Shared housing/friends	14 (5.1)	10 (6.0)	4 (3.5)
Missing	5 (1.8)	-	5 (4.4)
Education N (%)			
No formal education	30 (10.8)	13 (7.9)	17 (14.9)
GCSEs / O-Levels	63 (22.6)	38 (23.0)	25 (21.9)
A Levels / HNC	37 (13.3)	21 (12.7)	16 (14.0)
University	39 (14.0)	29 (17.6)	10 (8.8)
Graduate / Professional	91 (32.6)	56 (33.9)	35 (30.7)
Missing	19 (6.8)	8 (4.8)	11 (9.6)

5.5.3 Missing Data

No missing data were reported on participant condition and gender. Data on age and disease duration were missing out of 3.2% and 7.2% of the total sample respectively. Missing data on other demographic characteristics are displayed in Table 5.2. PCQ missing data were calculated on scale and item level. Scale-level missing data were calculated by examining the total number of missing responses per scale in comparison to the total responses for each scale. Scale-level missing data were low, ranging from 0.57% to 1.43% (Table 5.3), suggesting sufficient data quality for this sample (196, 203). Item-level missing data (Appendix 5.5) were also low, ranging from 0.4% to 2.9%.

Missing data are excluded from RMT analysis using the RUMM2030 software. However, missing data are accounted for by the computation of class intervals on an item and not on a person basis in order to control for any bias brought by missing data. Missing data for the traditional psychometric analyses were not input, but they were instead excluded pairwise (516) on a scale level. In other words, no total scores were computed for scales containing missing data on an item-level.

Table 5.3 2nd Field Test: Scale-level Missing Data

PCQ scales	Total Items	Total Responses*	Missing responses	%
Symptom & Flares	16	4464	64	1.43
Trust in Doctor	8	2232	21	0.94
Treatment	11	3069	32	1.04
Self-management	6	1674	16	0.96
Impact	10	2790	16	0.57

**** The product of the total number of items per scale and the total sample, n=279***

5.5.4 Rasch Analysis Results

RMT psychometric evaluation was undertaken for each of the five PCQ scales independently. Interpretation and review of results led to a further revision in the *symptoms and flares* scale only (this was the third set of revisions, resulting in the final version of the scale). No further revisions were made to the second draft of the remaining four scales. The results are presented in relation to the tests and criteria described in the methods section (4.4.1) for each of the five scales.

5.5.4.1 PCQ 2nd Draft: *Symptoms & Flares* Scale Summary Results

The second draft *symptoms and flares* scale comprised 16 items addressing two sub-domains of the conceptual framework; symptom interpretation and illness progression. Targeting was satisfactory (Figure 5.1) but measurement precision as denoted from the information function curve, was sub-optimal and scale-level results were comparable to the first field test (Table 4.13). On an item-level two items displayed an evident misfit to the RMT expectations. Item 7a “I know my condition will flare-up” and 1j “I know how long my symptoms will last” displayed a fit residual above the +2.5 expected level and a significant chi square probability (Table 5.4). Examination of the ICC curves for both items (Figure 5.2) indicated item underestimation as the observed scores in the three class intervals (black dots) created a line which was flatter than the expected curve. The ICC curve for item 1a, of which the chi square probability was also significant, was not as misfitting. The review of these results within the research team led to the decision to eliminate both items 1j and 7a. Item 1j displayed a great misfit whereas item 7a was consistently misfitting in both field tests (Table 4.14).

Figure 5.1 PCQ 2nd Draft *Symptoms & Flares* Scale: Targeting of Sample to Scale

Figure 5.1A

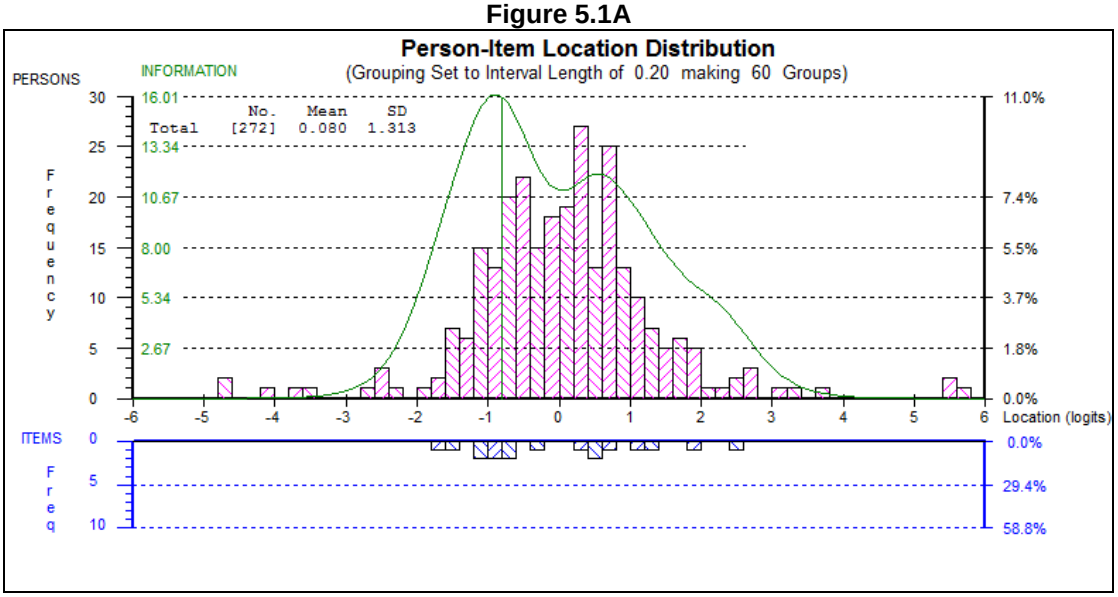


Figure 5.1B

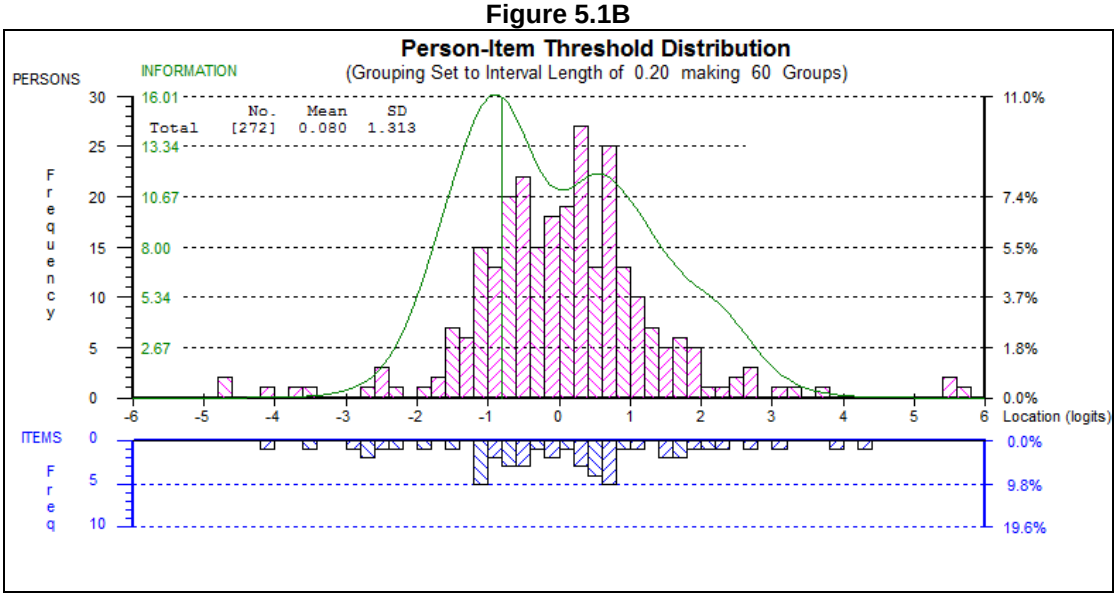


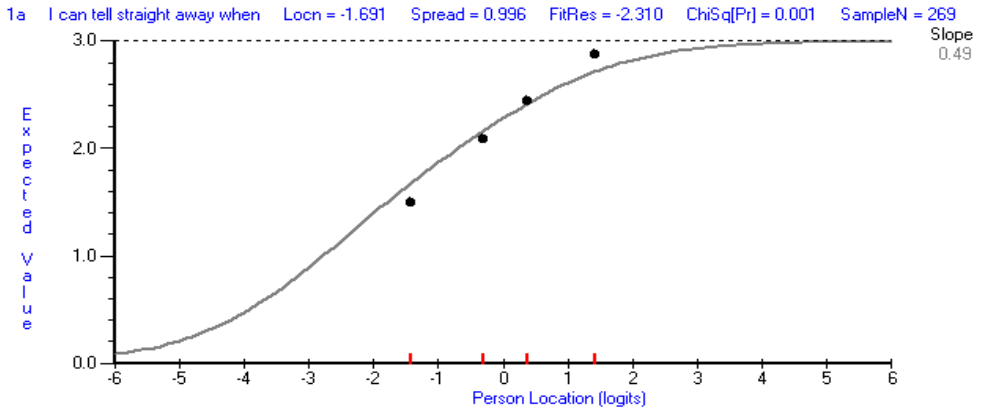
Figure 5.1: *the pink blocks represent the sample distribution for the symptoms & flares scale and the blue blocks represent the scale distribution of the 16 items on the same measurement continuum. The green curve shows the location on the continuum the scale performs at its best, indicating that the location of item thresholds and persons is well matched.*

Table 5.4 PCQ 2nd Draft: *Symptoms & Flares* Scale: Item Fit Statistics Ordered by Location

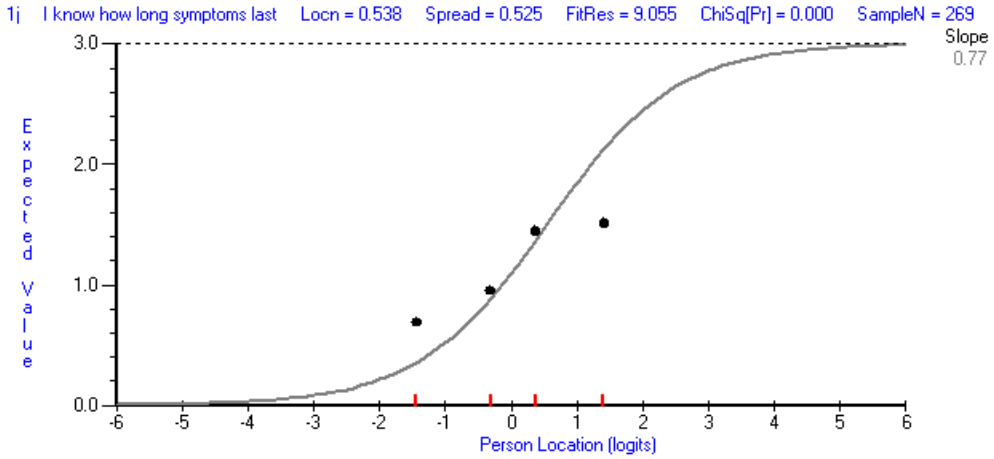
Item Index	Threshold	Loc.	SE	FitRes	ChiSq prob	Res. r	DIF prob.		
							C	A	D
1a	Ordered	-1.69	0.10	-2.31	0.00*	0.365	0.01	0.62	0.37
1c	Ordered	-1.54	0.10	-1.37	0.17	0.331	0.27	0.53	0.89
1b	Ordered	-1.13	0.09	-0.85	0.08	0.365	0.12	0.46	0.08
1d	Ordered	-1.06	0.09	-0.17	0.37	<0.30	0.36	0.56	0.33
1e	Ordered	-0.98	0.09	0.43	0.95	<0.30	0.19	0.91	0.28
1f	Ordered	-0.81	0.09	2.27	0.16	<0.30	0.66	0.06	0.08
1g	Ordered	-0.74	0.09	-1.31	0.01	<0.30	0.81	0.21	0.39
7a	Ordered	-0.64	0.08	**3.12**	**0.00***	<0.30	0.93	0.68	0.63
1hSLE	Ordered	-0.36	0.10	1.72	0.03	0.367	1.00	0.52	0.99
7b	Ordered	0.37	0.08	-1.62	0.01	<0.30	0.10	0.39	0.72
1i	Ordered	0.44	0.09	-0.06	0.64	0.367	0.15	0.69	0.60
1j	Ordered	0.54	0.08	**9.06**	**0.00***	<0.30	0.64	0.22	0.00
1hRA	Ordered	0.76	0.13	0.75	0.39	<0.30	1.00	0.39	0.89
7d	Ordered	1.14	0.09	0.90	0.48	0.447	0.64	0.57	0.87
7c	Ordered	1.33	0.09	-0.58	0.15	0.344	0.00	0.37	0.90
7e	Ordered	1.96	0.10	-0.61	0.13	0.529	0.13	0.13	0.50
7f	Ordered	2.43	0.11	-1.32	0.04	0.529	0.44	0.17	0.68

Loc location; SE standard error; FitRes fit residual; ChiSq prob chi square probability; Res. r residual correlations; DIF prob differential item functioning probability; C condition; A age; D disease duration *significant with Bonferroni adjustment

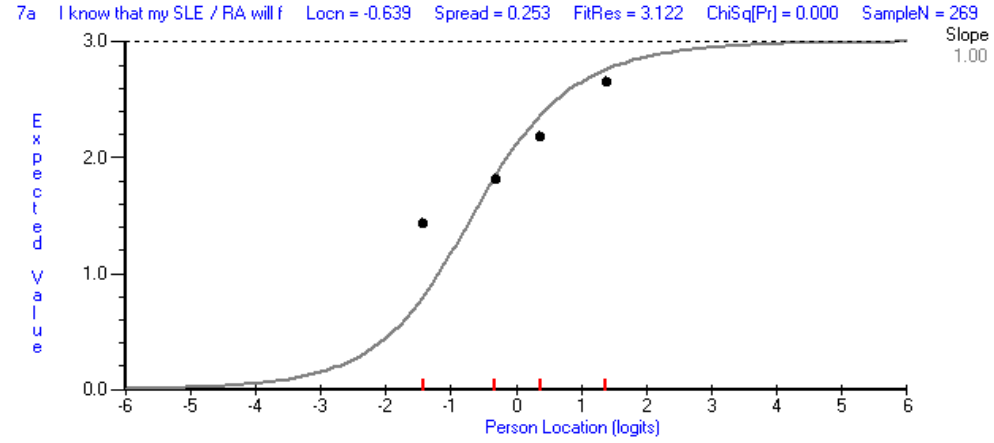
Figure 5.2 PCQ 2nd Draft Symptom & Flares Scale: Item Characteristic Curves (items displaying misfit)



Item1a: I can tell straight away when I am experiencing a symptom



Item 1j: I know how long my symptoms will last



Item 7a: I know my condition will flare-up

Figure 5.2: *The y-axis represents the person scores and the x-axis represents the person location logits. The curve denotes the expected score across the range of person locations. The black dots represent the observed scores in each of the four class intervals (class intervals of person location).Graphs for items 1j and 7a denote under discrimination of the trait as the line indicated by the dots is flatter than the expected curve. Graphs for item 1a, denote slight over discrimination as although the black dots indicate a line steeper than the expected curve the dots lye close to the curve.*

5.5.4.1.1 PCQ 3rd Draft: *Symptoms & Flares* Scale Results

Following the elimination of items 1j and 7a the final *symptoms and flares* scale comprised 14 items; 9 related to symptom interpretation and 5 related to future flares. Following modifications in the first field test (See section 4.5.4.2) the scale was analysed by splitting item 1h "what triggers symptoms" by condition.

5.5.4.1.1.1 How adequate was the sample to scale targeting?

Sample to scale targeting of the 14-item *symptoms and flares* scale was satisfactory and improved from the 16-item version of the scale (Table 5.21). The person location spanned over more than 11 logits (range -5.797 to 5.892 logits) and was relatively well matched by the item threshold locations (range: -4.337 to 4.490 logits, mean=0.00) and item locations (range: -1.815 to 2.569 logits). Reviewing the person-to-item distribution histograms (Figure 5.3) also indicates the sufficiency of the sample for evaluating this scale as the range of certainty in the sample (Figure 5.3A) covers the range of certainty measured by the scale items (Figure 5.3B), and similarly the relative sufficiency of the scale items to cover the range of certainty in the sample. Precision of measurement as denoted by the information function curve was sub-optimal as many person measurements estimates fell outside the information function curve suggesting that their measurement was associated with greater standard error.

Figure 5.3 PCQ 3rd Draft *Symptoms & Flares* Scale: Targeting of Sample to Scale

Figure 5.3A Item Locations

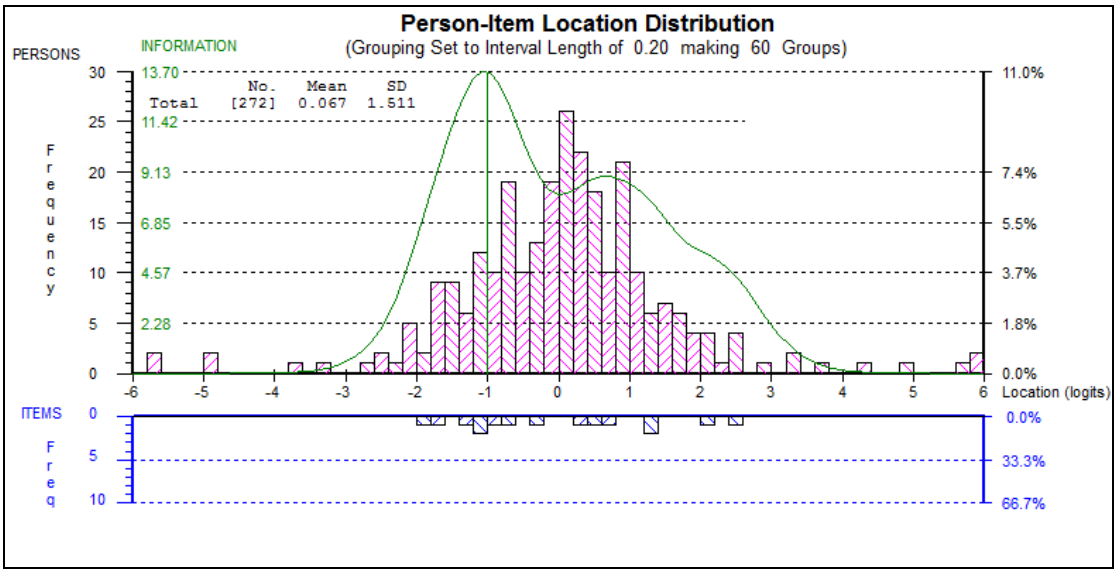


Figure 5.3 (cont`d)

Figure 5.3B

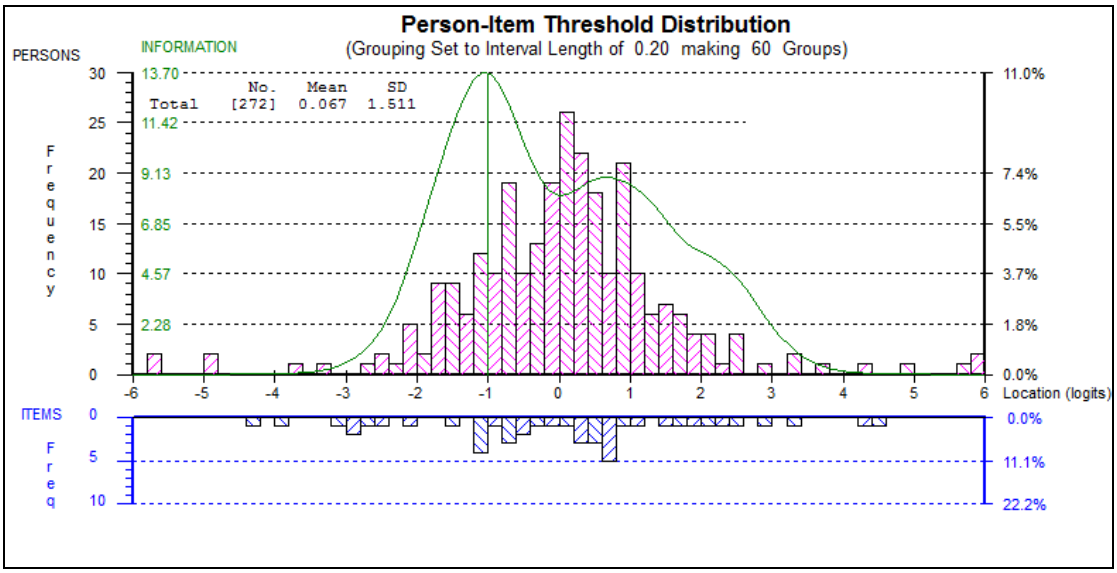


Figure 5.3 Legend: *the pink blocks represent the sample distribution for the symptoms and prognosis scale and the blue blocks represent the scale distribution of the 14 items on the same measurement continuum. The green curve shows the location on the continuum the scale performs at its best, indicating that the location of item thresholds and persons is well matched.*

5.5.4.1.1.2 To what extent has a measurement continuum been constructed successfully?

Consistent with the first field test (Table 4.14), response categories worked as expected as the thresholds of all 14 items were ordered in sequence on the measurement continuum (Table 5.5). The item location histogram (Figure 5.3A) indicated two minor item gaps and no significant item bunching of the measurement continuum. Reviewing the item location logits (Table 5.6) reveals the largest item gap spans across 0.75 logits. Item locations also reveal that the item difficulty was to a large extent maintained at the same level as in the first field test, as all of the items appear in the pre-set sequence apart from 1c-1b and 7d-7c which were reversed. Item goodness of fit improved from the previous draft of the scale. The item skewness statistic (Table 5.21) no longer fell outside the expected range of -1 to 1 (0.118) and all fit residuals fell within the -2.5 to 2.5 expected range (Table 5.6). The item-trait interaction for item 1a displayed a misfit as the chi square probability was significant, however the graphical representation of this association (Figure 5.4) did not reveal any significant misfit similar to the remaining item ICCs (Figure 5.5). The observed scores in the four class intervals (black dots) did not lie considerably away from the expected curve. Response bias was consistent with that revealed in the first field test, as the

same three items revealed residual correlations above the expected criterion (>0.4). Items 7d and 7e produced a residual correlation coefficient which was marginally above the criterion (0.4190 and items 7e and 7f a coefficient of 0.512 (Table 5.7). The performance of the items was stable across both conditions and all age and disease duration groups as none of the items displayed significant differential item functioning (DIF).

Table 5.5: PCQ 3rd Draft *Symptom & Flares* Scale: Item Threshold Location

Index	Item	τ1	τ2	τ3
1a	I can tell straight away when experiencing a symptom	-3.84	-2.04	0.43
1b	I can tell apart everyday symptoms from flares	-2.84	-1.48	0.66
1c	I can tell which symptoms are specific to my condition	-4.34	-1.18	0.59
1d	I can judge how serious my symptoms are	-2.85	-1.09	0.57
1e	I can tell apart symptoms from getting older	-3.02	-0.76	0.67
1f	I can tell symptoms apart from side-effects	-2.74	-0.60	0.74
1g	I know all the different symptoms related to my condition	-2.54	-0.80	0.95
1i	I know when to expect a symptom	-1.13	0.63	1.87
7b	I know what type of flare-up I will experience	-0.99	0.30	1.77
7c	I can predict when I will experience flare-up	-0.26	1.18	3.25
7d	I can predict how my condition will affect me	-0.12	1.45	2.29
7e	I can predict how severe my flare-ups will be	0.04	2.01	4.29
7f	I can predict how often I will experience a flare-up	0.35	2.87	4.49
1hSLE	I know what triggers my symptoms	-1.18	-0.76	0.78
1hRA	I know what triggers my symptoms	-0.49	0.37	2.52

Table 5.6: PCQ 3rd Draft *Symptoms & Flares* Scale: Item Fit Statistics Ordered by Location

Item	Threshold	Loc.	SE	Fit Resid.	Chi Sq. prob.	Res. r	DIF prob		
							Condition	Age	Diagn.
1a	ordered	-1.82	0.11	-2.00	0.00	0.333	0.00	0.68	0.53
1c	ordered	-1.64	0.10	-0.98	0.34	<0.30	0.21	0.63	0.92
1b	ordered	-1.22	0.10	-0.40	0.14	0.333	0.09	0.43	0.16
1d	ordered	-1.12	0.09	0.40	0.83	<0.30	0.34	0.58	0.55
1e	ordered	-1.04	0.09	0.80	0.43	<0.30	0.17	0.91	0.21
1f	ordered	-0.87	0.09	2.35	0.21	<0.30	0.58	0.07	0.19
1g	ordered	-0.80	0.09	-0.89	0.02	<0.30	0.76	0.16	0.43
1hSLE	ordered	-0.39	0.10	2.09	0.01	0.371	1.00	0.51	1.00
7b	ordered	0.36	0.08	-0.24	0.39	<0.30	0.13	0.53	0.45
1i	ordered	0.46	0.09	0.84	0.62	0.371	0.14	0.62	0.55
1hRA	ordered	0.80	0.14	2.05	0.06	<0.30	1.00	0.28	0.88
7d	ordered	1.21	0.09	1.44	0.29	0.419	0.61	0.45	0.85
7c	ordered	1.39	0.10	0.11	0.07	0.318	0.00	0.37	0.85
7e	ordered	2.11	0.11	-0.38	0.64	0.512	0.10	0.12	0.39
7f	ordered	2.57	0.12	-1.12	0.16	0.512	0.35	0.16	0.66

Loc location; SE standard error; FitRes fit residual; ChiSq prob chi square probability; Res. r residual correlations; DIF prob differential item functioning probability; C condition; A age; D disease duration *significant with Bonferroni adjustment

Figure 5.4 PCQ 3rd Draft *Symptoms & Flares* Scale: Item Characteristic Curve (item 1a displaying misfit)

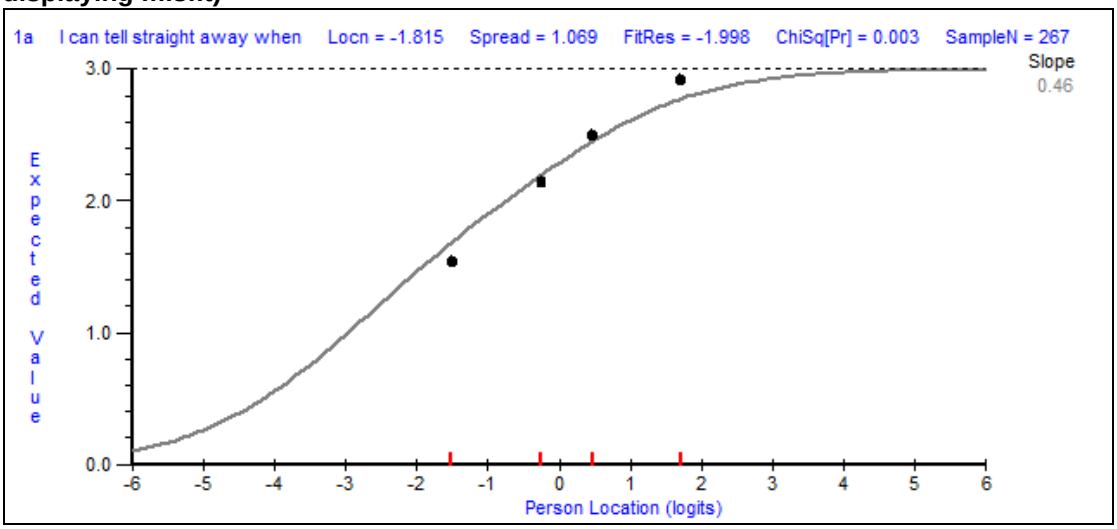


***Figure 5.4 Legend**: Final Symptoms & Flares scale – item characteristic curve for item 1a. The x-axis represents the person location logits, the y-axis the expected value and the dots represent the observed scores in the four class intervals.*

Figure 5.5 PCQ 3rd Draft *Symptom & Flares* Scale: Item Characteristic Curves

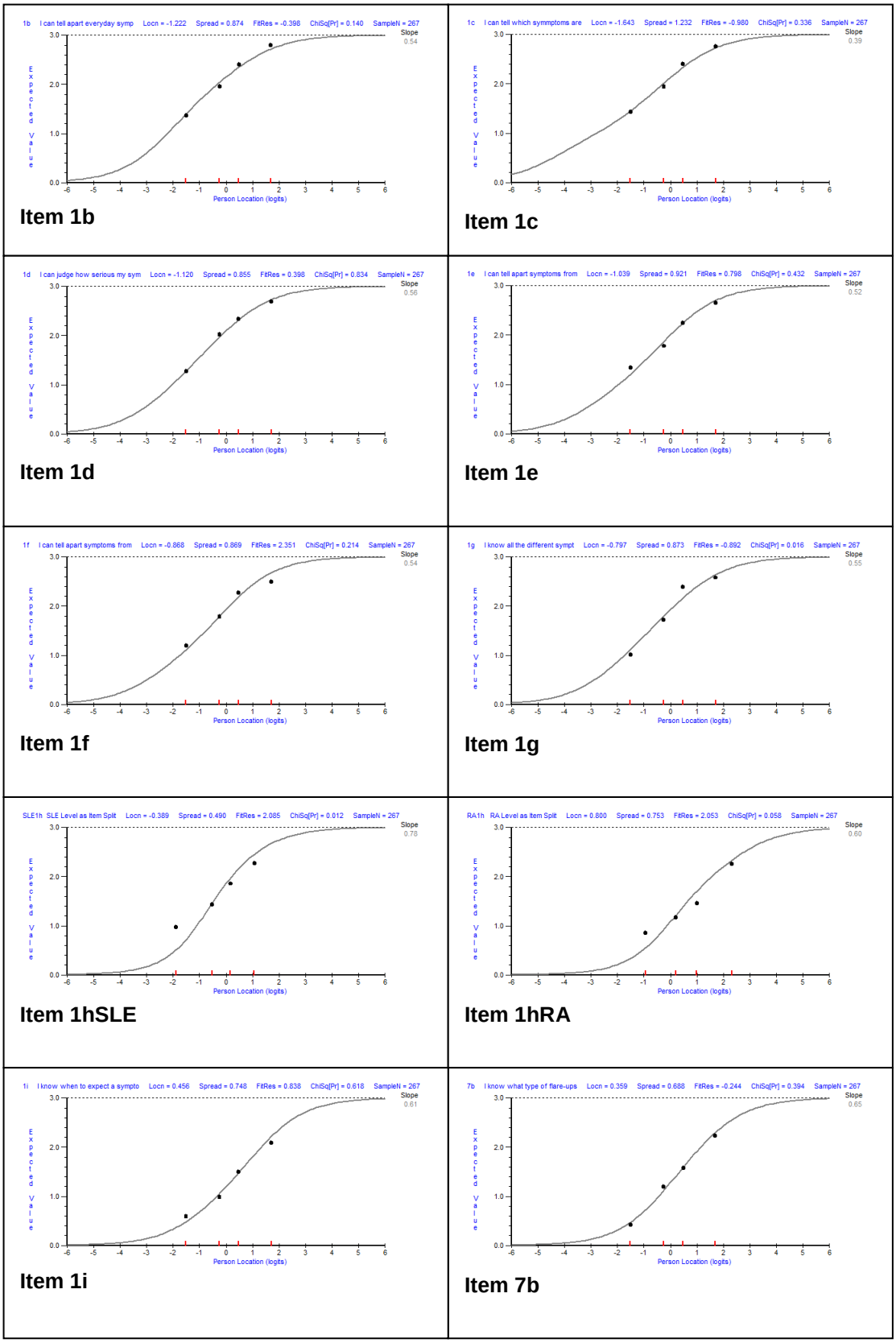


Figure 5.5 (Cont`d)

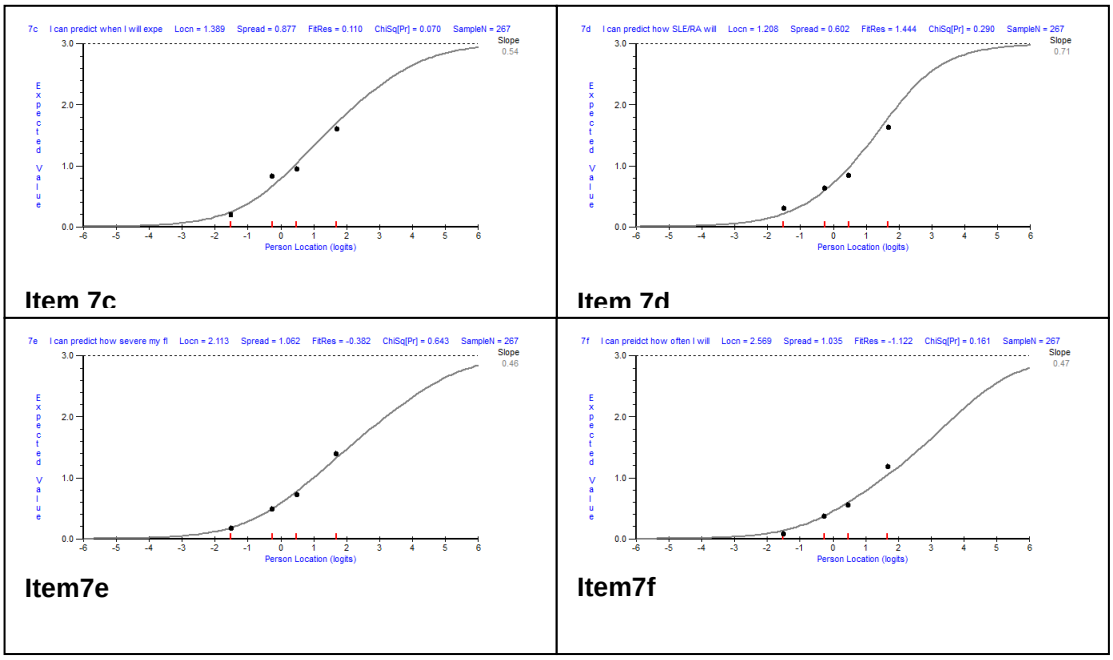


Figure 5.5 Legend: *In line with Figure 5.2 & 5.4 the observed scores in the four class intervals (black dots) are plotted against the curve representing the expected values across the range of person locations. None of the items displays misfit as the black dots lye very closely on the expected curve.*

5.5.4.1.1.3 How has the sample been measured?

The person separation index (PSI) was 0.91 (Table 5.21), indicating that the separation of the sample by the scale was excellent and therefore the random error low. A high PSI is also indicative of the power to produce reliable evaluations of scale items. Person fit residuals ranged from -4.096 to 4.061 logits, whilst residuals for 14 participants, 5.02% of the sample, fell outside the “rule of thumb” range of -2.5 to +2.5. Eleven of these participants (3.95%) produced a negative fit residual, thus indicating that observed scores were significantly lower than expected (residual = observed – expected) whilst three (1.08%) were positive residuals (>+2.5). This finding indicates that the scale measurement was sub-optimal as measurement was not valid for a higher percentage of the sample than expected. Figure 5.6 shows the relationship between the raw ordinals cores and the interval (logit) measurement they imply. They imply an S-shaped relationship instead of an absolute linear one is revealed by this graph, thereby indicating that measurement implied by 1 point in the *symptoms and flares* scores is not consistent across the range of the scale. This finding is also displayed numerically through observation of the transformed raw scores (Table 5.7). A change of ten points at the two ends of the total raw score between 0 and 10 and 35 and 45 related to approximately a change of 4 logits, whereas a change of ten points

between the total score of 10 and 20 related to a change of approximately 1.5 logits. This information indicates that interpretations made on the basis of raw total scores are sub-optimal, but it is an expected finding considering the stringent mathematical criteria of the RMT (517). Additional RMT result outputs are presented in Appendix 5.6.

Table 5.7 PCQ 3rd Draft *Symptoms & Flares* Scale: Transformed Raw Scores

Raw Score (ordinal)	Logit (interval)	0-100 Transformation	Raw Score (ordinal)	Logit (interval)	0-100 Transformation
0	-5.811	0*	23	0.068	51
1	-4.887	9	24	0.198	52
2	-4.222	14	25	0.329	53
3	-3.744	18	26	0.461	54
4	-3.361	22	27	0.595	55
5	-3.037	24	28	0.732	56
6	-2.752	27	29	0.872	57
7	-2.497	29	30	1.015	59
8	-2.264	31	31	1.164	60
9	-2.050	33	32	1.318	61
10	-1.851	34	33	1.480	63
11	-1.665	36	34	1.650	64
12	-1.490	37	35	1.830	66
13	-1.324	39	36	2.024	67
14	-1.166	40	37	2.234	69
15	-1.015	41	38	2.464	71
16	-0.870	43	39	2.721	73
17	-0.728	44	40	3.013	76
18	-0.591	45	41	3.353	78
19	-0.456	46	42	3.758	82
20	-0.323	47	43	4.263	86
21	-0.192	48	44	4.955	92
22	-0.062	49	45	5.900	100*

extrapolated values due to asymmetry of data

Figure 5.6 PCQ 3rd Draft *Symptoms & Flares* Scale: Total Raw Score to Logit Transformation

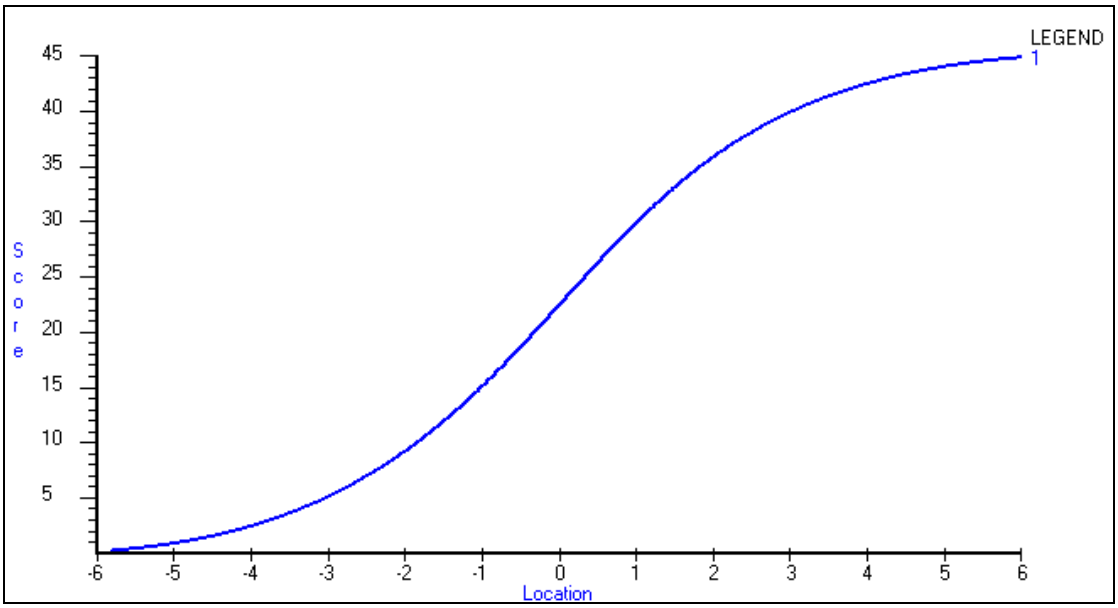


Figure 5.6: *The x-axis represents the construct as an interval logit score and the y-axis raw score on the Symptoms & Flares Scale*

5.5.4.2 PCQ 2nd Draft: *Medication* Scale Results

The second draft of *medication* scale comprised 11 items relating to current and future treatment necessity and effectiveness. Five of these items were added to the scale following the first draft scale evaluation, and as a result, evaluation of the second draft scale was not possible in the first field test, therefore this constituted the first psychometric evaluation of this version of the scale. Results are compared with the incomplete second draft which was evaluated in the first field test.

5.5.4.2.1 How adequate was the sample to scale targeting?

Sample to scale targeting was marginally better than the incomplete version (Table 5.21). The person location spanned over 8 logits (range 4.106 –to 4.620 logits) and was relatively well matched by the item threshold (range: -2.119 to 2.619 logits, mean=0.00), whereas the item location range was slightly wider (range: 1.536 to 1.368 logits). The person to item threshold distributions were sub-optimal but satisfactory, (Figure 5.7) as the range of certainty in the sample matched the range of certainty measured by the scale items well. The sample mean (0.675) was also much closer to the item mean than the mean in the first field (1.643), also indicating an improvement in the sample to scale targeting (Table 5.21). Precision of measurement as denoted by the information function curve was sub-optimal as many person measurement estimates (particularly at high ability levels) fell outside the information function curve suggesting that their measurement was associated with greater standard error. This denotes that measurement for people with higher level of certainty was less precise.

Figure 5.7 PCQ 2nd Draft *Medication* Scale: Targeting of Sample to Scale

Figure 5.7A

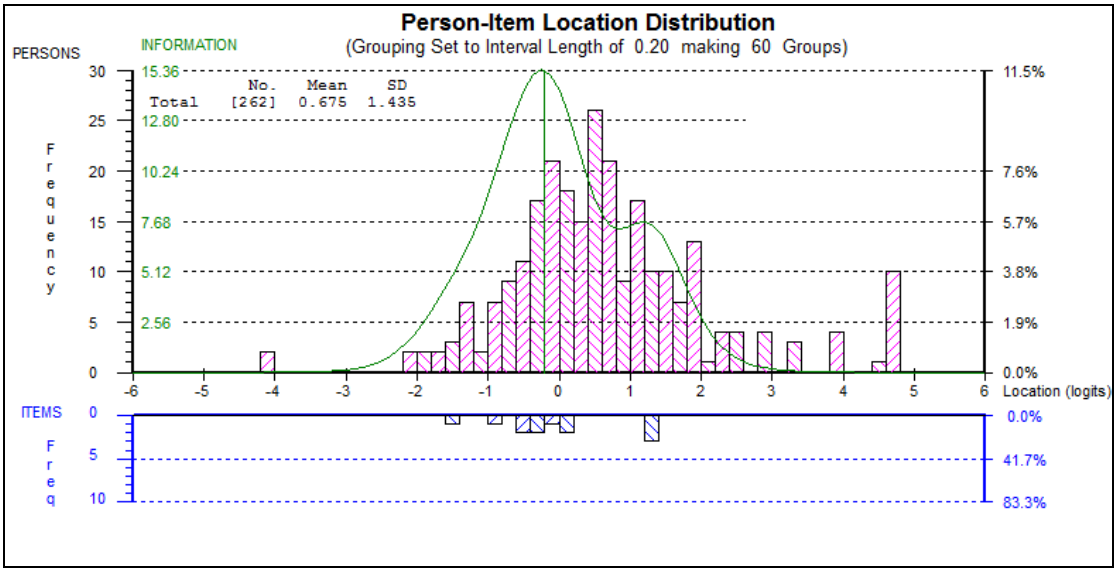


Figure 5.7B

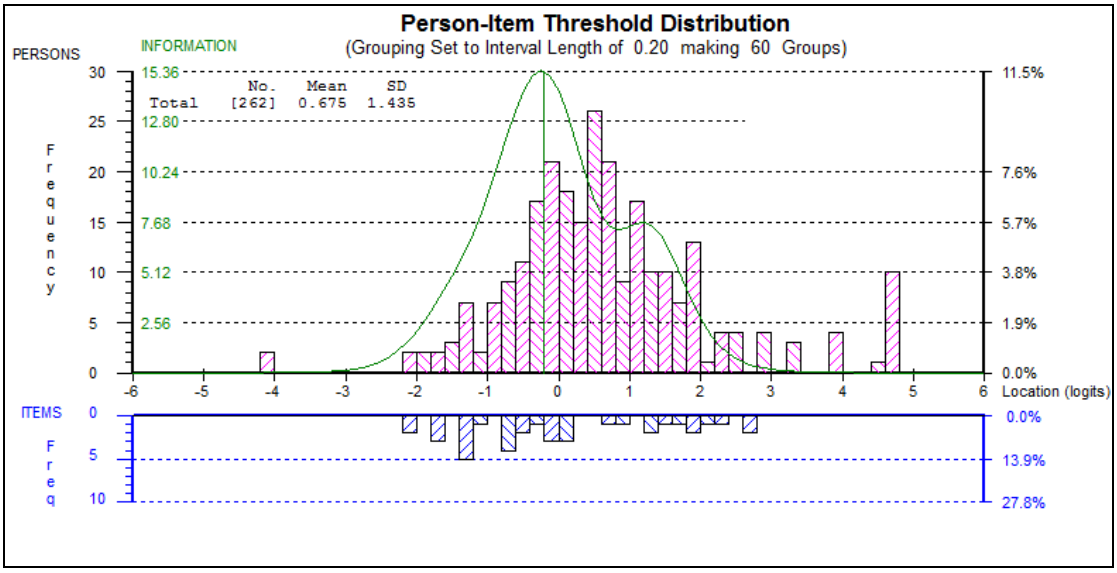


Figure 5.7: *the pink blocks represent the sample distribution for the medication scale and the blue blocks represent the scale distribution of the 11 items on the same measurement continuum. The green curve shows the location on the continuum the scale performs at its best, indicating that the location of item thresholds and persons is well matched.*

5.5.4.2.2 To what extent has a measurement continuum been constructed successfully?

Response categories were ordered in sequence as expected for all items apart from item 3b in the RA sample (Table 5.8). Threshold location logits were distorted as the first threshold was located at the higher measurement logits, indicating that participants with higher levels of the trait (i.e. more certainty) were the most likely to endorse “very uncertain” and “somewhat uncertain” for the *medication* necessity item (3b). Disordering of thresholds is also displayed in the category probability curve for this item (Figure 5.8).

The item location histogram (Figure 5.7A) indicated an evident item gap that was evident in the locations of items 9b and 9c that were located more than 1 logit apart (Table 5.9). Item goodness of fit was improved from the previous draft. The fit residual range was improved from the first draft (Table 5.21). No significant misfit was displayed between the expected and observed scores as all item fit residuals fell within the “rule of thumb” range of -2.5 to +2.5. Item 3b in the SLE group was marginally above the +2.5 level (Table 5.10) and was also the only item with a significant chi square probability. The ICC for item 3b (Figure 5.9) reveals that the observed scores (black dots) in the four class intervals for the SLE group create a flatter line than the expected curve whilst observed scores in the RA group lie closely by the expected curve. This finding indicates that item 3b is underestimating the trait in the SLE sample and producing higher scores than expected at lower levels of the trait and lower scores at higher levels of the trait. The remaining ten items produced optimal ICCs (Figure 5.10).

Significant misfit was suggested by residual correlation coefficients suggesting that most scale items were suffering from response bias. This was particularly true for the newly added items (9a-9e) which produced correlation coefficients >0.5 (Table 5.9). This finding indicates significant item dependency between these items. Scale items were stable between the different age and disease duration groups. One item (3a) displayed significant DIF between the two illness groups as the RA observed scores were higher than expected and the SLE ones lower than expected.

Table 5.8 PCQ 2nd Draft *Medication* Scale: Item Thresholds Location

Index	Item	τ1	τ2	τ3
3a	the medications are helping symptoms	-1.61	-1.26	0.151
3c	the medication is controlling condition	-1.61	-0.71	0.63
3d	I do not need stronger medication	-1.34	-0.22	0.85
3e	I do not need additional medication	-1.39	-0.05	1.211
3f	I do not need alternative medication	-1.35	0.17	1.333
9a	the medication will help symptoms	-1.64	-0.78	1.813
9b	The medication will control condition	-2.04	0.14	2.109
9c	I will not need stronger medication	-0.56	1.50	2.732
9d	I will not need additional medication	-0.47	1.68	2.744
9e	I will not need alternative medication	-0.16	1.88	2.391
3bLE	I need the medication I am currently taking	-0.80	-0.67	-0.092
3bRA	I need the medication I am currently taking	-1.138	-2.199	-1.27

Figure 5.8 PCQ 2nd Draft *Medication* Scale: Category Probability Curve (item 3bRA displaying disordered thresholds)

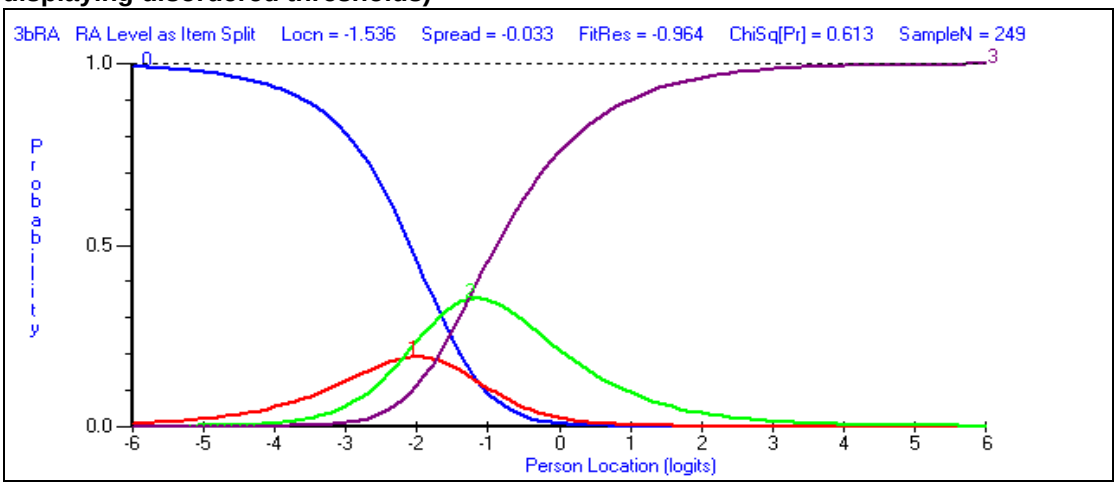


Figure 5.8: *The x-axis represents the measurement continuum of the trait (certainty), with increasing ability from left to right and the y-axis represents the probability of choosing each of the four response categories. The blue line represents 'Very Uncertain'; the red 'Somewhat Uncertain"; the green 'Somewhat Certain' and the purple "Very Certain". Thresholds (τ1, τ2, τ3) represent the points where each pair of probability curves meet. Item 3b shows disordering in the RA sample (3bRA) as the curves and thresholds are not ordered consecutively on the measurement continuum.*

Table 5.9 PCQ 2nd Draft *Medication* Scale: Item Fit Statistics Ordered by Location

Item	Thresh	Loc	SE	FitRes	ChiSq Prob	Res.r	DIF prob.		
							C	A	D
3bRA	Disorder	-1.54	0.17	-0.96	0.61	0.322	1.00	0.63	0.09
3a	Ordered	-0.91	0.10	-0.75	0.71	0.437	0.00	0.01	0.73
3c	Ordered	-0.56	0.09	-1.23	0.16	0.489	0.25	0.14	0.04
3bLE	Ordered	-0.52	0.11	2.56	0.00	0.489	1.00	0.25	0.58
3d	Ordered	-0.24	0.09	-0.68	0.34	0.479	0.12	0.69	0.61
9a	Ordered	-0.20	0.10	0.63	0.61	0.513	0.63	0.85	0.85
3e	Ordered	-0.08	0.09	-1.61	0.15	0.516	0.57	0.16	0.89
3f	Ordered	0.05	0.09	0.16	0.98	0.516	0.40	0.04	0.89
9b	Ordered	0.07	0.10	0.43	0.49	0.513	0.84	0.47	0.60
9c	Ordered	1.22	0.09	-0.30	0.54	0.753	0.02	0.24	0.11
9d	Ordered	1.32	0.10	0.66	0.24	0.753	0.07	0.28	0.19
9e	Ordered	1.37	0.09	1.05	0.52	0.618	0.60	0.14	0.07

Loc location; SE standard error; FitRes fit residual; ChiSq prob chi square probability; Res. r residual correlations; DIF prob differential item functioning probability; C condition; A age; D disease duration *significant with Bonferroni adjustment

Figure 5.9 PCQ 2nd Draft *Medication* Scale: Item Characteristic Curve (item 3bSLE displaying misfit)

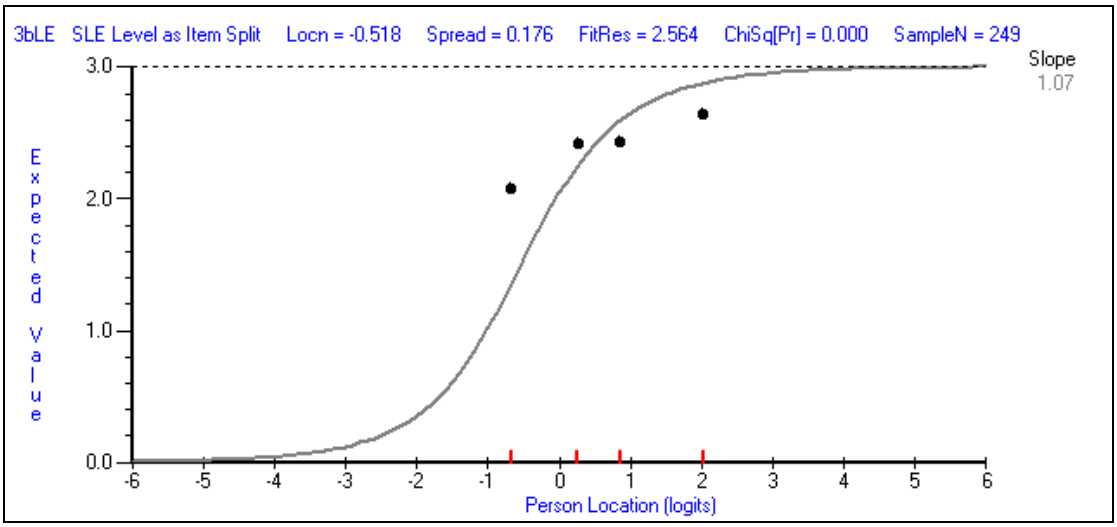
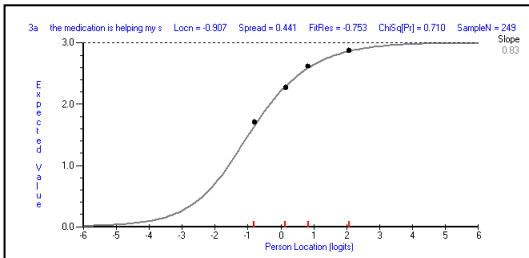
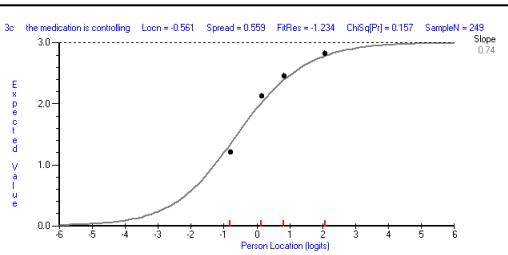


Figure 5.9: *The y-axis represents the person scores and the x-axis represents the person location logits. The curve denotes the expected score across the range of person locations. The black dots represent the observed scores in each of the four class intervals (class intervals of person location).The graph indicates that item 3b in the SLE sample (3bSLE) under discrimination of the trait as the line indicated by the dots is flatter than the expected curve.*

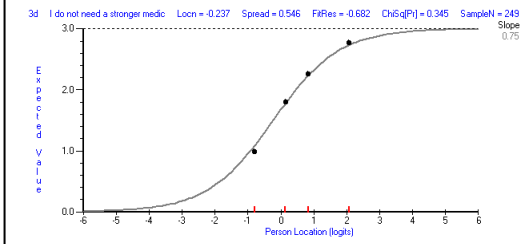
Figure 5.10 PCQ 2nd Draft *Medication* Scale: Item Characteristic Curves



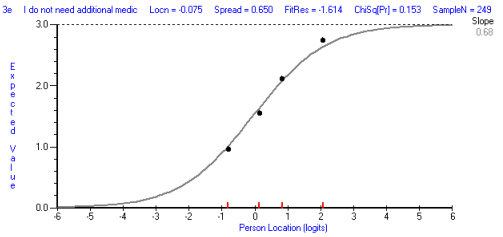
Item 3a



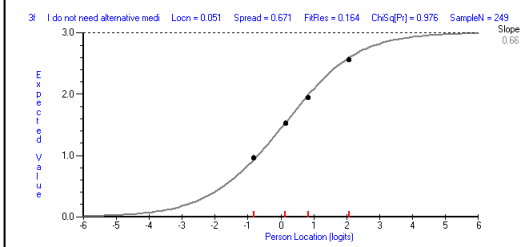
Item 3c



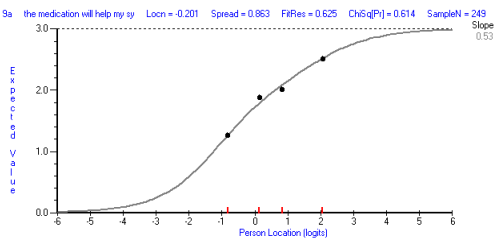
Item 3d



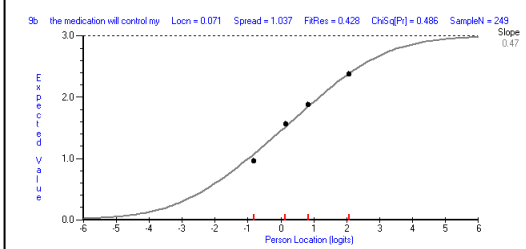
Item 3e



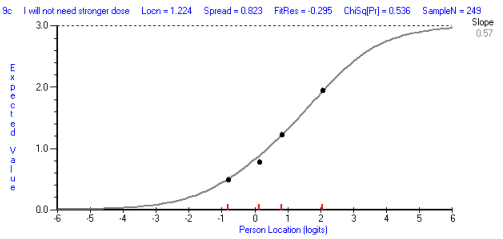
Item 3f



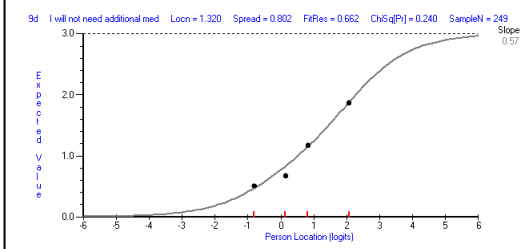
Item 9a



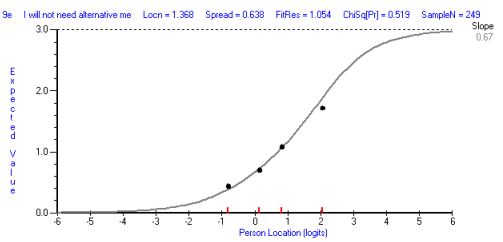
Item 9b



Item 9c



Item 9d



Item 9e

5.5.4.2.3 How has the sample been measured?

The person separation index (PSI) was increased to 0.86, indicating the scale`s good ability to separate the sample and the lower level of random error compared to the incomplete version of the scale which was evaluated in the first field test (Table 5.21). The scale displayed the poorest validity of sample measurement of the five scales as the person fit residuals ranged from -8.661 to 4.272 logits, whilst residuals for 25 participants, 9% of the sample, fell outside the “rule of thumb” range of -2.5 to +2.5. Twenty of these participants (7.2%) produced a negative fit residual, indicating observed scores were significantly lower than expected (residual = observed – expected) whilst five (1.8%) were positive residuals (>+2.5).

Figure 5.11 shows the relationship between the raw ordinals cores and the interval (logit) measurement they imply. An S-shaped relationship instead of an absolute linear one is revealed by this graph, a relationship that appears stronger at the lower end of the axes. The relationship is also displayed numerically through the transformed raw scores (Table 5.10). A change of ten points of the total raw score between 0 and 10 is related to an approximate change of 3 logits, and similarly between 26 and 36 to approximately 3.5, whereas a change of ten points between the total score of 10 and 20 is related to a change of approximately 1 logit. This information indicates that interpretations made on the basis of raw total scores are sub-optimal as implications of changes at the extremes are greater than toward the centre of the scale. This however was an expected finding considering the stringent mathematical criteria of the RMT (517). Additional RMT result outputs are presented in Appendix 5.7.

Table 5.10 PCQ 2nd Draft PCQ *Medication* Scale: Transformed Raw Scores

Raw Score (ordinal)	Logit (interval)	0-100 Transformation	Raw Score (ordinal)	Logit (interval)	0-100 Transformation
0	-4.158	0*	19	-0.012	50
1	-3.382	13	20	0.136	51
2	-2.869	19	21	0.289	53
3	-2.531	23	22	0.448	55
4	-2.274	25	23	0.613	57
5	-2.062	28	24	0.785	58
6	-1.877	30	25	0.965	60
7	-1.709	32	26	1.153	62
8	-1.552	33	27	1.35	65
9	-1.402	35	28	1.556	67
10	-1.258	36	29	1.773	69
11	-1.117	38	30	2.004	72
12	-0.979	39	31	2.254	74
13	-0.842	41	32	2.531	77
14	-0.707	42	33	2.852	81
15	-0.571	44	34	3.252	85
16	-0.435	45	35	3.819	91
17	-0.297	47	36	4.624	100*
18	-0.156	48			

extrapolated values due to asymmetry of data

Figure 5.11 PCQ 2nd Draft *Medication* Scale: Total Raw Score to Logit Transformation

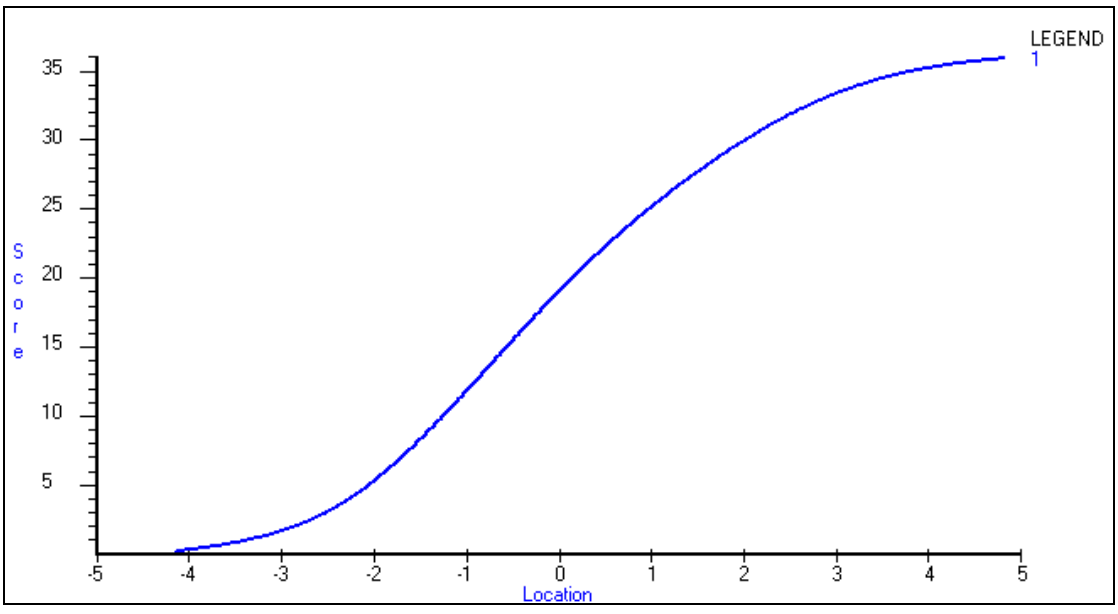


Figure 5.11: *The x-axis represents the construct as an interval logit score and the y-axis raw score on the Medication Scale*

5.5.4.3 PCQ 2nd Draft *Trust in Doctor* Scale Summary Results

The second draft of the *trust in doctor* scale comprised 8 items related to a single sub-domain reflecting patients` certainty in their doctor`s knowledge.

5.5.4.3.1 How adequate was the sample to scale targeting?

Sample to scale targeting was marginally better than the first field test (Table 5.21). The person location range was narrower by approximately 0.7 logits (range -2.861 to 3.549 logits), whereas the item threshold and item location range were marginally wider (range: -3.160 to 2.727 logits, mean=0.00) (range: -1.163 to 1.723 logits) respectively. The range of certainty in the sample and the range of certainty covered by the scale items were more closely matched. The sample was sufficient for evaluating but the scale items were still sub-optimal for assessing the range of certainty in the sample, as some items gaps are evident in Figure 5.12B. Precision of measurement as denoted by the information function curve was poor as many person measurement estimates fell outside the information function curve suggesting that their measurement was associated with greater standard error, particularly in the middle and higher end of ability. This denotes that measurement for these person measurements was less precise and possibly the insufficiency of existing scale items to measure certainty at these levels of ability.

Figure 5.12 PCQ 2nd Draft *Trust in Doctor* Scale: Targeting of Sample to Scale

Figure 5.12A

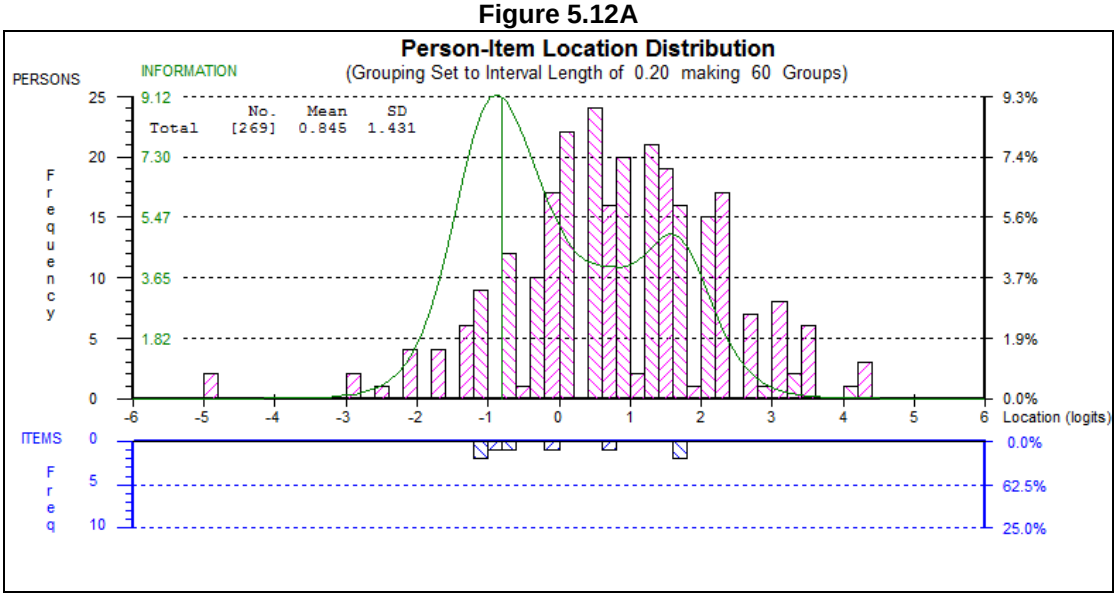


Figure 5.12 (Cont`d)

Figure 5.12B

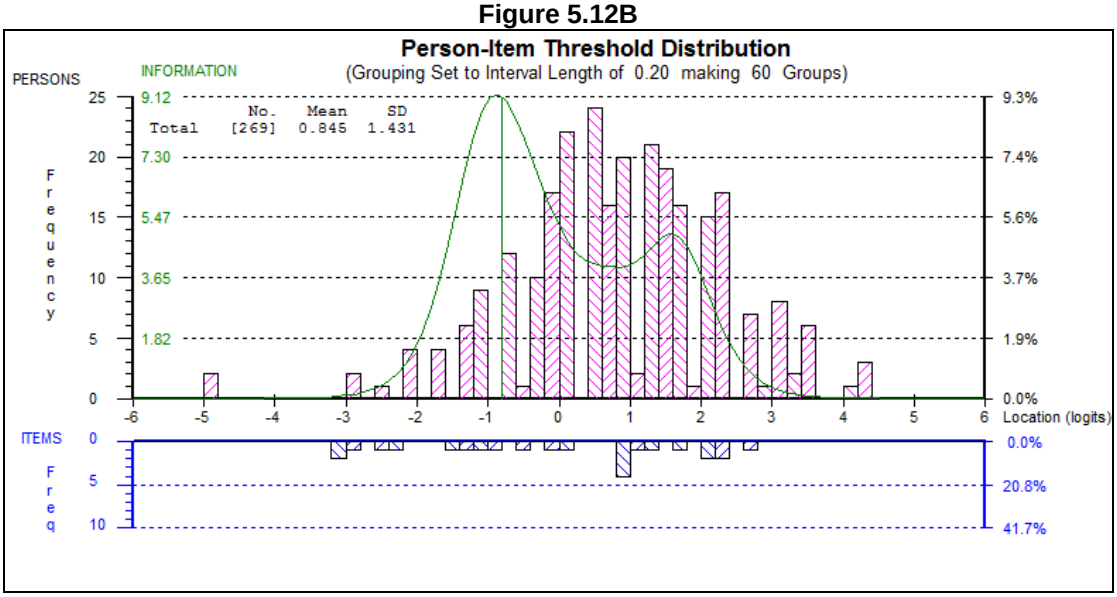


Figure 5.12: *the pink blocks represent the sample distribution for the trust in doctor scale and the blue blocks represent the scale distribution of the 8 items on the same measurement continuum. The green curve shows the location on the continuum the scale performs at its best, indicating that the location of item thresholds and persons is well matched.*

5.5.4.3.2 To what extent has a measurement continuum been constructed successfully?

Response categories for all items worked as expected as response thresholds were ordered in sequence (Table 5.11). The item location histograms (Figure 5.12) indicated some evident item gaps, also evident when reviewing the item location logits as items 4f and 4h were located approximately 1 logit apart (Table 5.12). Item difficulty, suggested in the ordering of items in the first field test, was confirmed to a large extent as the ordering of items was in sequence, except for items 4h and 4g which were reversed but only 0.1 logit apart.

Item goodness of fit was also consistent with the first field test (Table 4.15), and two items (4a & 4b) produced negative residuals marginally outside the lower expected level (-2.5) and subsequent significant chi square probability. Item 4g produced a positive fit residual correlation and likewise a significant chi square probability (Table 5.12). Review of the ICCs for these items (Figure 5.13 & 5.14) indicated that only one of the four class intervals produced observed scores misfitting the equivalent expected scores for items 4a and 4b. Observed scores (black dots) for item 4g however created a line which was much flatter than the expected curve, suggesting the item was under-

estimating the trait (i.e. producing higher scores than expected at lower levels of the trait and lower than expected at higher levels of the trait). Despite this, the item fit skewness statistic (0.417) fell within the expected range of -1 to 1 (Table 5.21).

Consistent with the first field test items, two items relating to medication choice and medication dosage (4a & 4b) produced a significantly high residual correlation coefficient indicating response bias (Table 5.12). The remaining items produced residual correlations below the expected criterion of 0.30. The items were also stable across the two condition groups and seven age and disease duration groups, as no significant DIF was displayed.

Table 5.11: PCQ 2nd Draft *Trust in Doctor* Scale: Item Threshold Location

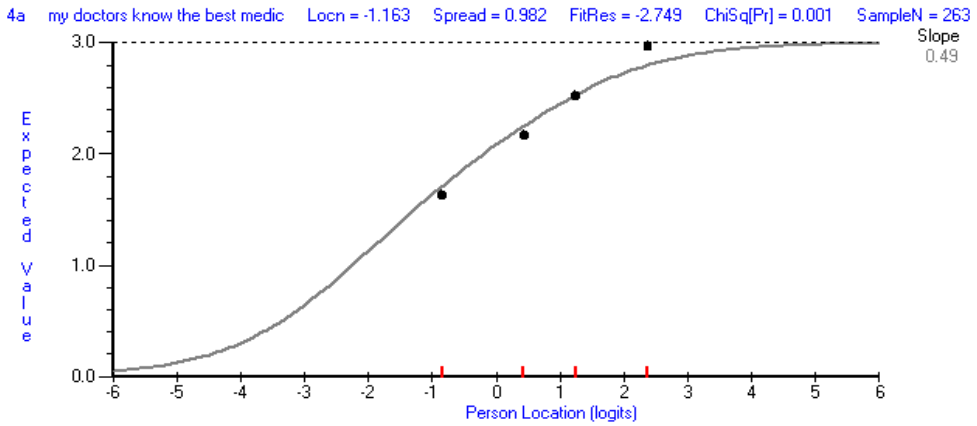
Index	Item	τ1	τ2	τ3
4a	Doctor knows best medication dose	-2.99	-1.44	0.94
4b	Doctor knows which medication works best	-3.16	-1.33	1.18
4c	Doctor knows exactly how physically active I should be	-3.05	-0.91	1.33
4d	Doctor knows exactly what's wrong with me.	-2.41	-0.41	0.82
4e	Doctor knows exactly how physically active I should be.	-2.37	0.10	1.69
4f	Doctor knows how to help the non-physical aspects	-1.16	0.96	2.21
4g	Doctor knows what caused my lupus/arthritis.	0.85	2.06	2.26
4h	Doctor knows exactly how my condition will progress	-0.04	2.14	2.73

Table 5.12 PCQ 2nd Draft *Trust in Doctor* Scale: Item Fit Statistics Ordered by Location

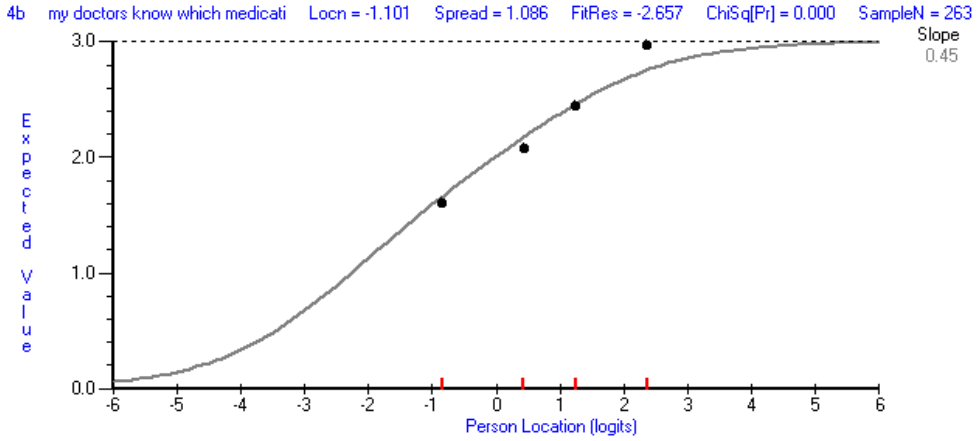
Item	Threshold	Loc	SE	FitRes	Chi Sq Prob	Res.r	DIF prob.		
							C	A	D
4a	Ordered	-1.16	0.11	-2.75	0.00	0.714	0.26	0.05	0.04
4b	Ordered	-1.10	0.11	-2.66	0.00	0.714	0.12	0.31	0.00
4c	Ordered	-0.88	0.10	-1.15	0.02	<0.30	0.02	0.15	0.68
4d	Ordered	-0.67	0.10	0.37	0.26	<0.30	0.14	0.34	0.35
4e	Ordered	-0.19	0.10	-1.59	0.05	<0.30	0.67	0.03	0.15
4f	Ordered	0.67	0.09	1.28	0.70	<0.30	0.65	0.07	0.39
4h	Ordered	1.61	0.09	1.63	0.68	<0.30	0.04	0.08	0.41
4g	Ordered	1.72	0.08	**4.23**	**0.00***	<0.30	0.68	0.46	0.16

Loc location; SE standard error; FitRes fit residual; ChiSq prob chi square probability; Res. r residual correlations; DIF prob differential item functioning probability; C condition; A age; D disease duration *significant with Bonferroni adjustment

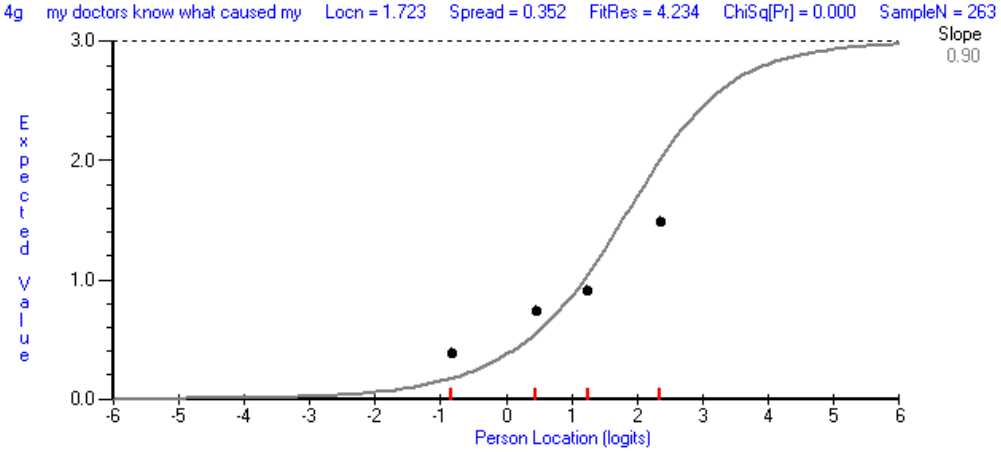
Figure 5.13 PCQ 2nd Draft *Trust in Doctor* Scale: Item Characteristic Curves (items displaying misfit)



Item4a: I can tell straight away when experiencing a symptom



Item 4b: I can tell apart everyday symptoms from flares



Item4g: I know all the different symptoms related to my condition

Figure 5.13: *The y-axis represents the person scores and the x-axis represents the person location logits. The curve denotes the expected score across the range of person locations. The black dots represent the observed scores in each of the four class intervals (class intervals of person location).The graph indicates that item 4g under-discriminates the trait as the line indicated by the dots is flatter than the expected curve. Graphs for items 4a and 4b do not indicate significant misfit as only one of the four dots lies away of the expected curve suggesting border line over-estimation of the trait.*

Figure 5.14 PCQ 2nd Draft *Trust in Doctor* Scale: Item Characteristic Curves

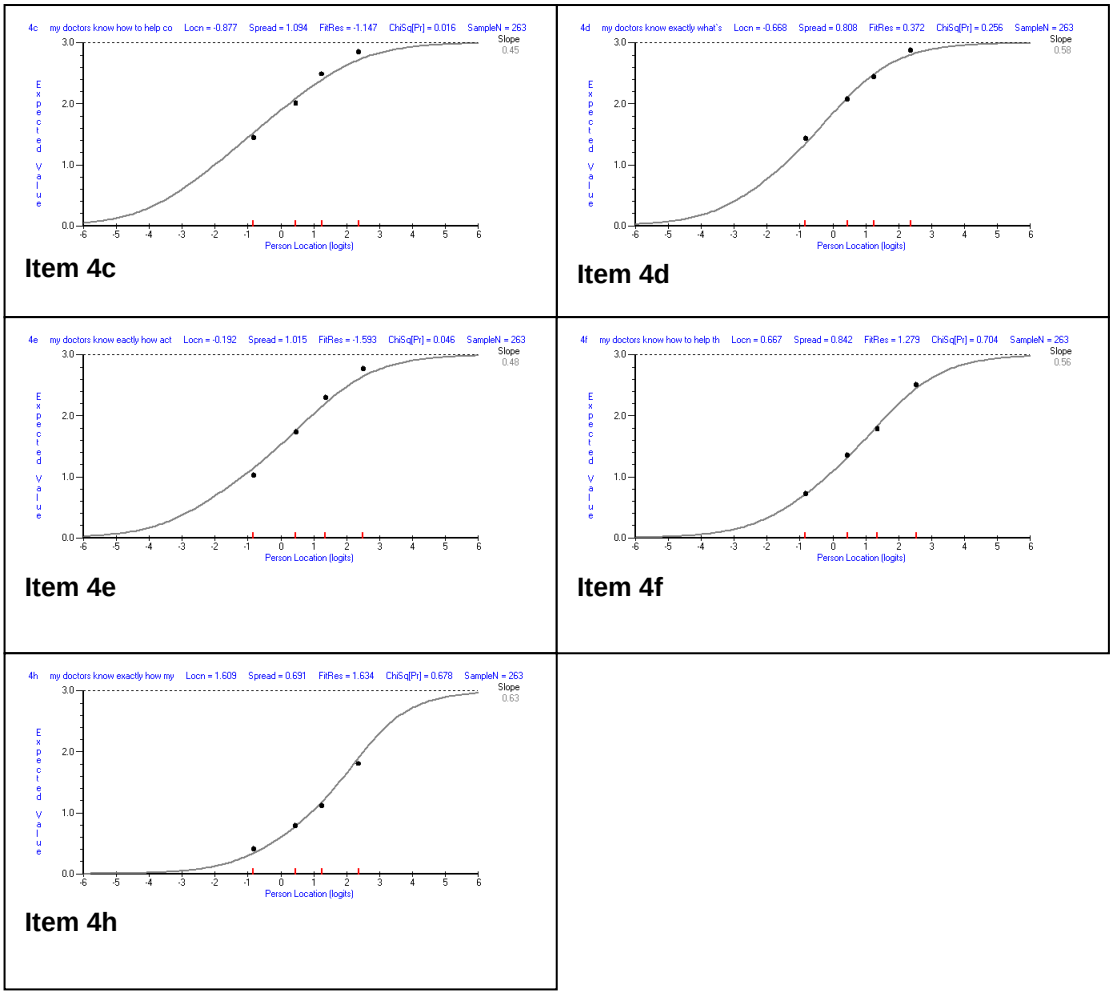


Figure 5.14: *The x-axis represents the person location logits, the y-axis the expected value and the dots represent the observed scores in the four class intervals. None of the items displays misfit as the black dots lye very closely on the expected curve.*

5.5.4.3.3 How has the sample been measured?

Similar to the first field test, the person separation index (PSI) was 0.83, indicating that the separation of the sample by the scale was good and that the random error was low (Table 5.21). Person fit residuals ranged from -3.178 to 3.446 logits, whilst 3.6% of the sample (10 participants) fell outside the “rule of thumb” range of -2.5 to +2.5. Seven of these participants (2.5%) produced a negative fit residual, indicating observed scores were significantly lower than expected (residual = observed – expected), whilst three (1.1%) were positive residuals (>+2.5). Scale measurement was sub-optimal but consistent with the first field test, when exactly the same percentage of the sample fell outside the “rule of thumb” (See section 4.5.4.5).

Figure 5.15 shows the relationship between the raw ordinal scores and the interval (logit) measurement they imply. The relationship of raw scores with linear

measurement was not absolute; however scores of the *trust in doctor* scale displayed the closer proximity to interval measurement. Raw scores spanned over 25 points (Table 5.13), where 5 points (raw score) spanned over approximately 2 logits at the two ends of the scale and approximately 1 logit in the middle of the scale. This information indicates that interpretations made on the basis of raw total scores are sub-optimal as implications of changes at the extremes are greater than toward the centre of the scale. This however was an expected finding considering the stringent mathematical criteria of the RMT (517). Additional RMT result outputs are presented in Appendix 5.8.

Table 5.13 PCQ 2nd Draft *Trust in Doctor* Scale: Transformed Raw Scores

Raw Score (ordinal)	Logit (interval)	0-100 Transformation	Raw Score (ordinal)	Logit (interval)	0-100 Transformation
0	-4.903	0*	13	0.452	55
1	-4.024	9	14	0.719	57
2	-3.361	16	15	0.981	60
3	-2.861	21	16	1.239	63
4	-2.435	25	17	1.496	65
5	-2.05	29	18	1.755	68
6	-1.69	33	19	2.021	71
7	-1.347	36	20	2.306	74
8	-1.018	40	21	2.623	77
9	-0.701	43	22	3.009	81
10	-0.3997	46	23	3.549	86
11	-0.105	49	24	4.305	100*
12	0.178	52			

extrapolated values due to asymmetry of data

Figure 5.15 PCQ 2nd Draft *Trust in Doctor* Scale: Total Raw Score to Logit Transformation

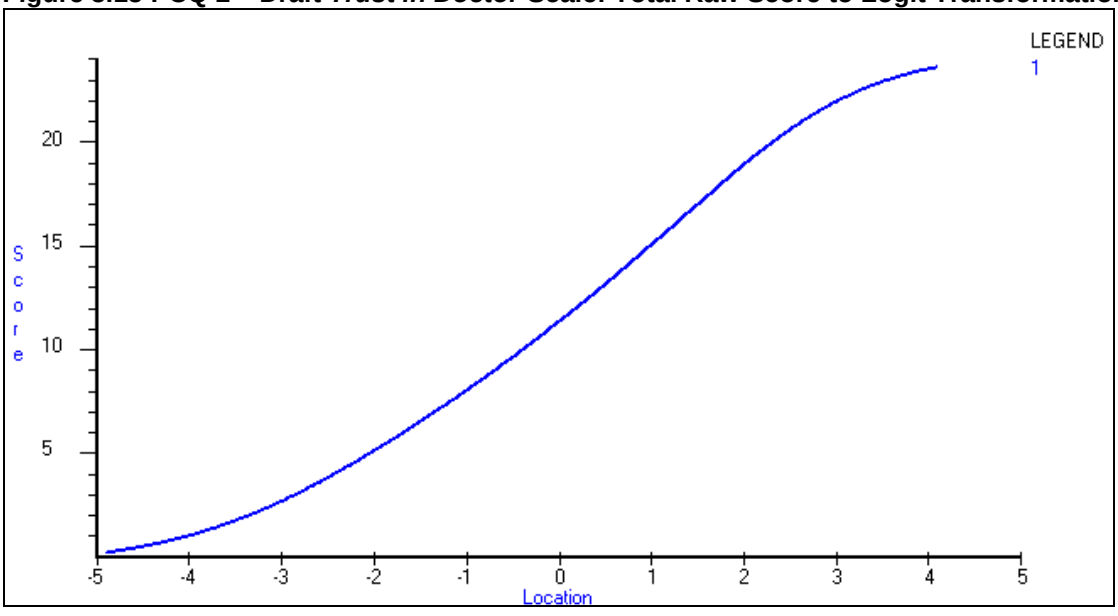


Figure 5.15: *The x-axis represents the construct as an interval logit score and the y-axis raw score on the Trust in Doctor Scale*

5.5.4.4 PCQ 2nd Draft: *Self-management* Scale Summary Results

The second draft of the *self-management* scale comprised 6 items related to the control and management sub-domains.

5.5.4.4.1 How adequate was the sample to scale targeting?

Sample to scale targeting was sub-optimal and consistent with that of the first field test (Table 5.21). The person locations covered the scale items (range -3.508 to 0.4.044 logits, mean=1.276), indicating the sufficiency of the sample for the scale evaluation. The item range was suboptimal, ranging across less than 1 logit (Range -0.523 to 0.434, mean=0.000), whereas the item thresholds matched the person distributions somewhat better (range: -1.953 to 2.652). Figure 5.16A indicates the insufficiency of the items to cover the person range. In other words, the range of certainty measured by the scale did not sufficiently match the range of certainty reported in the sample. The sub-optimal targeting is also displayed by the consistently high person mean reported in both field tests (Table 5.21). This finding suggests that the majority of the sample is located on higher levels of the measurement continuum (Figure 5.16A), i.e. at higher certainty levels than the certainty assessed by the items. Precision of measurement as denoted by the information function curve was sub-optimal as many person measurement estimates (particularly at high ability levels) fell outside the information function curve suggesting that their measurement was associated with greater standard error. This denotes that measurement for people with higher level of certainty was less precise.

Figure 5.16 PCQ 2nd Draft *Self-management* Scale: Targeting of Sample to Scale

Figure 5.16A

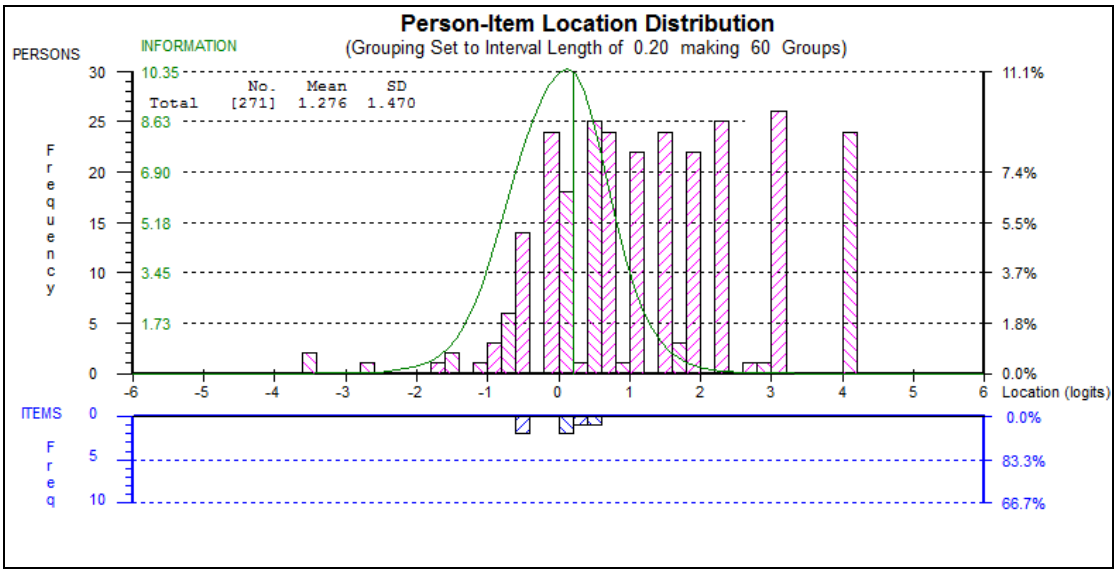


Figure 5.16 (cont`d)

Figure 5.16B

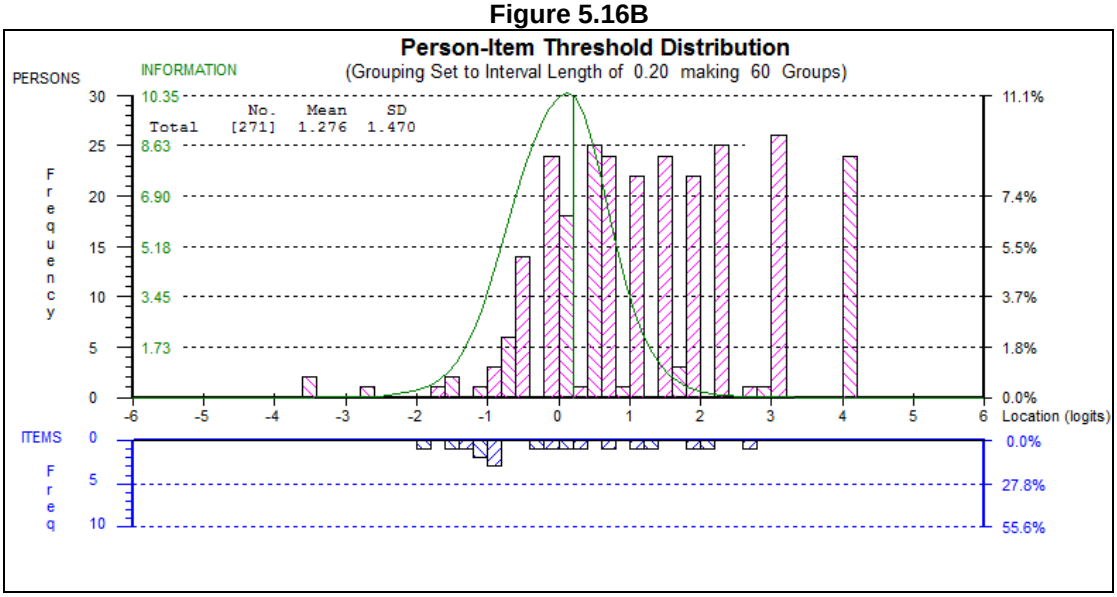


Figure 5.16: *the pink blocks represent the sample distribution for the self-management scale and the blue blocks represent the scale distribution of the 6 items on the same measurement continuum. The green curve shows the location on the continuum the scale performs at its best, indicating that the location of item thresholds and persons is well matched.*

5.5.4.4.2 To what extent has a measurement continuum been constructed successfully?

Response categories were ordered in sequence as expected for all items apart from item 5a, which was also disordered in the first field test (Table 4.17). Threshold location logits (Table 5.14) indicate that the probability of endorsing the middle response categories of “somewhat uncertain” and “somewhat certain” was located on a lower location logit than the two uncertain categories “very uncertain” and “somewhat uncertain”. This misfit to the RMT expectations is also displayed through the category probability curve of item 5a (Figure 5.17), which shows how the probability curve “1: somewhat uncertain” was not the most probable response at any level of the certainty.

Similar to the first draft of the scale the large item gap span across 0.6 logits between items 5a and 5c; whereas, the range of logits was relatively narrow compared to other scales (Table 5.15). The ordering/difficulty of items, was in line with the first field test apart from items 5c and 5b which were reversed. Items displayed a very good goodness of fit as results for all items satisfied the RMT expectations. All item fit residuals fell within the “rule of thumb” range, and no significant difference was displayed in the item-trait interaction assessed by the chi square statistic. The ICCs for all items were also satisfactory (Figure 5.18), thus indicating no major deviation from expected scores. Furthermore there was no response bias between the items as all

residual correlation coefficients were below 0.30 and the items were stable between the condition age and disease duration groups as no significant DIF was reported (Table 5.15).

Table 5.14 PCQ 2nd Draft *Self-management* Scale: Item Threshold Location

Index	Item	τ1	τ2	τ3
5a	I understand questions and recommendations	-0.98	-1.33	0.74
5b	I understand what test results mean	-1.12	-0.37	1.83
5c	I know which symptoms to report	-1.95	-0.92	1.40
5d	I know which types of physical activity I should avoid	-1.04	0.36	1.13
5e	I know exactly how to manage my condition	-1.60	-0.11	2.65
5f	There are things I can do to help control my condition	-0.90	0.14	2.06

Figure 5.17 PCQ 2nd Draft *Self-management* Scale: Category Probability Curve (item 5a displaying disordered thresholds)

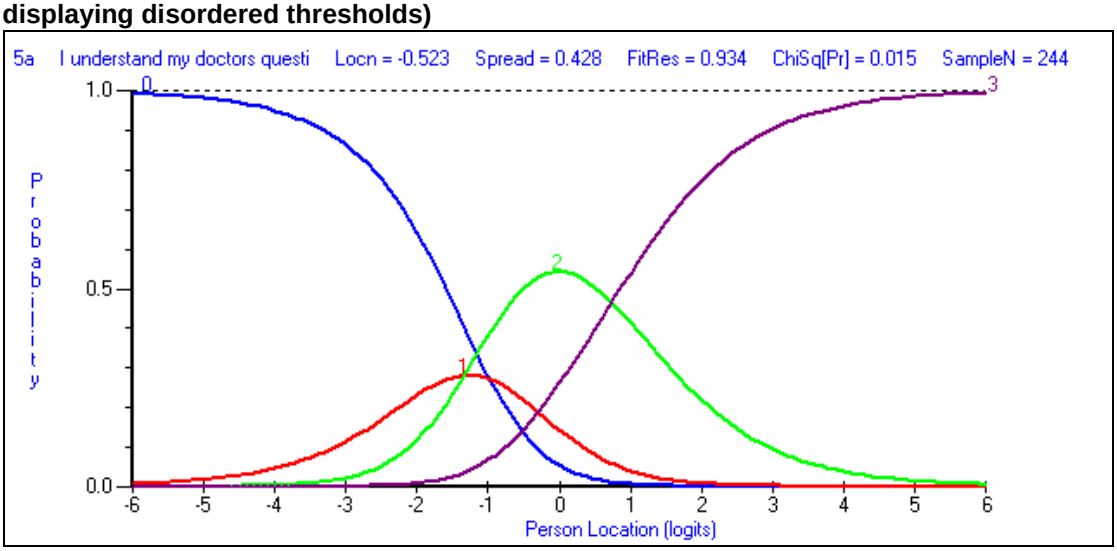


Figure 5.17: *The x-axis represents the measurement continuum of the trait (certainty), with increasing ability from left to right and the y-axis represents the probability of choosing each of the four response categories. The blue line represents 'Very Uncertain'; the red 'Somewhat Uncertain"; the green 'Somewhat Certain' and the purple "Very Certain". Thresholds (τ1, τ2, τ3) represent the points where each pair of probability curves meet. Item 5a displays disordering as the curves and thresholds are not ordered consecutively on the measurement continuum.*

Table 5.15 PCQ 2nd Draft *Self-management* Scale: Item Fit Statistics Ordered by Location

Item	Thresh.	Loc	SE	FitRes	ChiSq Prob	Res.r	DIF prob.		
							C	A	D
5a	Disord.	-0.52	0.10	0.93	0.02	<0.30	0.44	0.03	0.83
5c	Ordered	-0.49	0.11	-0.56	0.30	<0.30	0.02	0.29	0.60
5b	Ordered	0.11	0.09	0.91	0.30	<0.30	0.01	0.22	0.44
5d	Ordered	0.15	0.09	0.10	0.61	<0.30	0.79	0.45	0.46
5e	Ordered	0.32	0.10	-1.11	0.02	<0.30	0.03	0.07	0.29
5f	Ordered	0.43	0.09	0.93	0.06	<0.30	0.10	0.00	0.99

Loc location; SE standard error; FitRes fit residual; ChiSq prob chi square probability; Res. r residual correlations; DIF prob differential item functioning probability; C condition; A age; D disease duration *significant with Bonferroni adjustment

Figure 5.18 PCQ 2nd Draft *Self-management* Scale: Item Characteristic Curves

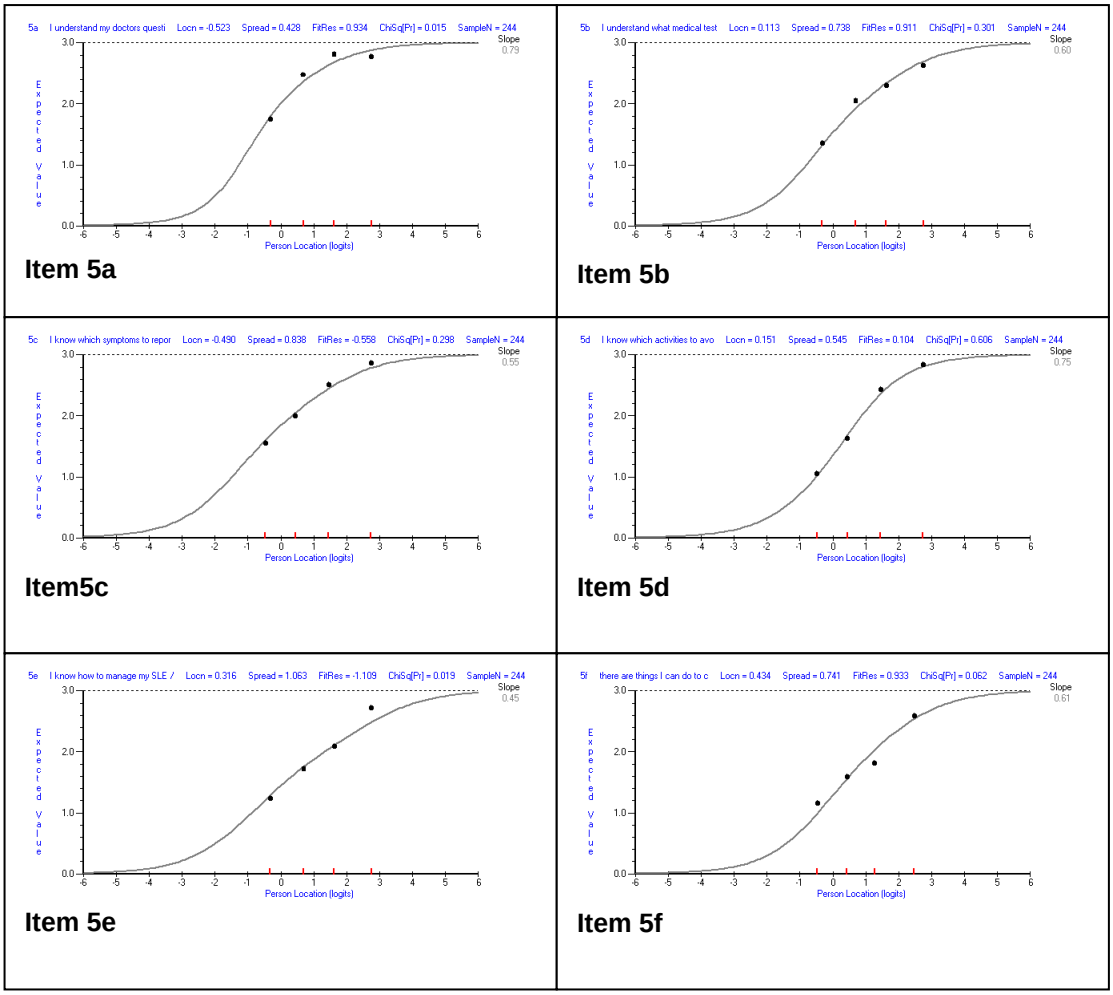


Figure 5.18: *The x-axis represents the person location logits, the y-axis the expected value and the dots represent the observed scores in the four class intervals. None of the items displays misfit as the black dots lye very closely on the expected curve.*

5.5.4.4.3 *How has the sample been measured?*

The person separation index (PSI) was the lowest of all scales but was still high enough (0.73) to guarantee the scales good ability to separate the sample and retain the random error at low levels, which was consistent with the first field test results (Table 5.21). The validity of sample measurement was the best of all scales as the person fit residuals ranged from -3.579 to 1.904 logits. Residuals for only 5 participants, 1.79% of the sample, fell below the expected level of -2.5 producing negative fit residuals, indicating that observed scores were significantly lower than expected (residual = observed – expected). Scale measurement was therefore satisfactory.

Figure 5.19 shows the relationship between the raw ordinal scores and the interval (logit) measurement they imply. The relationship deviated from the expected linear line, particularly at the higher levels of the total score. Total raw scores for this scale

spanned over 19 points (Table 5.15). A change of 5 points at the two ends of the continuum is related to approximately 2 logits, whereas a change of 5 points in the middle of the continuum is related to approximately 1 logit in the transformed scores. This information indicates that interpretations made on the basis of raw total scores are sub-optimal as implications of changes at the extremes are greater than toward the centre of the scale. This however was an expected finding considering the stringent mathematical criteria of the RMT (517). Additional RMT result outputs are presented in Appendix 5.9.

Table 5.16 PCQ 2nd Draft *Self-management* Scale: Transformed Raw Scores

Raw Score (ordinal)	Logit (interval)	0-100 Transformation
0	-3.508	0*
1	-2.716	16
2	-2.159	23
3	-1.768	28
4	-1.451	32
5	-1.173	35
6	-0.912	39
7	-0.659	42
8	-0.405	45
9	-0.144	48
10	0.127	52
11	0.413	55
12	0.72	59
13	1.054	63
14	1.428	68
15	1.861	73
16	2.388	80
17	3.095	88
18	4.044	100*

extrapolated values due to asymmetry of data

Figure 5.19 PCQ 2nd Draft *Self-management* Scale Data: Total Raw Score to Logit Transformation

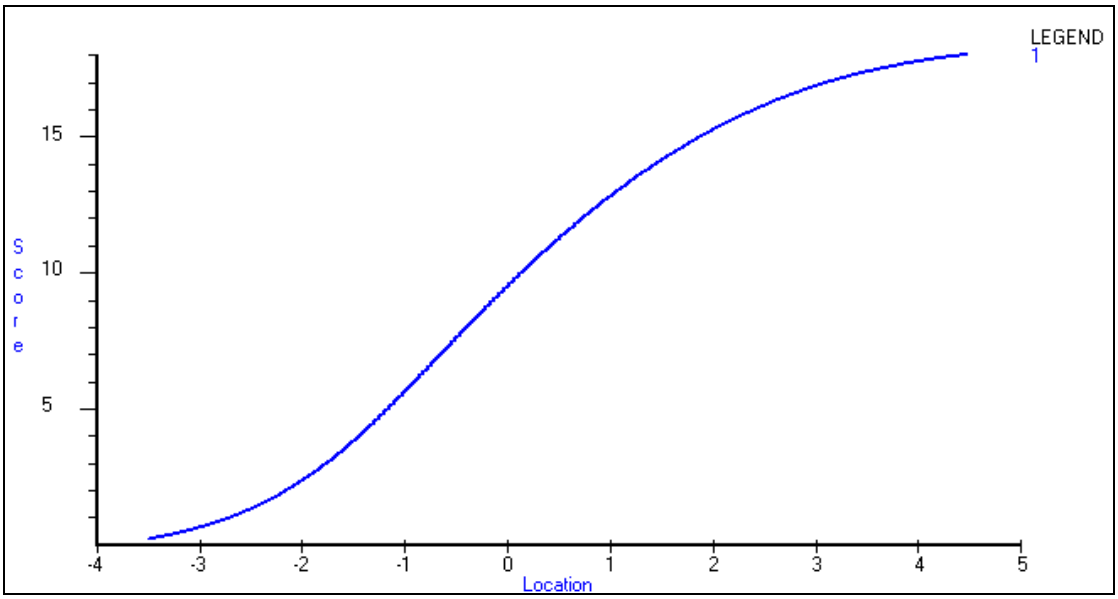


Figure 5.19: *The x-axis represents the construct as an interval logit score and the y-axis raw score on the self-management scale*

5.5.4.5 PCQ 2nd Draft: *Impact* Scale Summary Results

The second draft of the *impact* scale comprised 10 items resulting from the integration of the first draft of the items. Items reflected five sub-domains of planning, functionality, occupation, relationships and children impact. Due to the integration, the second draft scale was not possible in the first field test. This constituted the first psychometric evaluation of this version of the scale. Results will be compared to the first draft of the scale.

5.5.4.5.1 How adequate is the sample to scale targeting?

Sample to scale targeting of the 10 *impact* items was satisfactory and improved from the first draft of the scale (Table 5.21). The person location spanned over 9 logits (range 4.744 to 4.309 logits) and was relatively well matched by the item locations that were wider than the first draft (threshold range: -3.041 to 2.555 logits, mean=0.00; location range: 1.239 to 0.987 logits). Therefore, items in the scale covered the range of certainty in the sample more sufficiently than the first draft items. Reviewing the person-to-item distribution histograms (Figure 5.20) also indicates the sufficiency of the sample for evaluating this scale, as the range of certainty in the sample (Figure 5.20A) covers the range of certainty measured by the items (Figure 5.20B). Precision of measurement as denoted by the information function curve was sub-optimal as many person measurement estimates (particularly at low ability levels) fell outside the information function curve suggesting that their measurement was associated with greater standard error. This denotes that measurement for people with higher level of certainty was less precise.

Figure 5.20: PCQ 2nd Draft *Impact* Scale: Targeting of Sample to Scale

Figure 5.20A

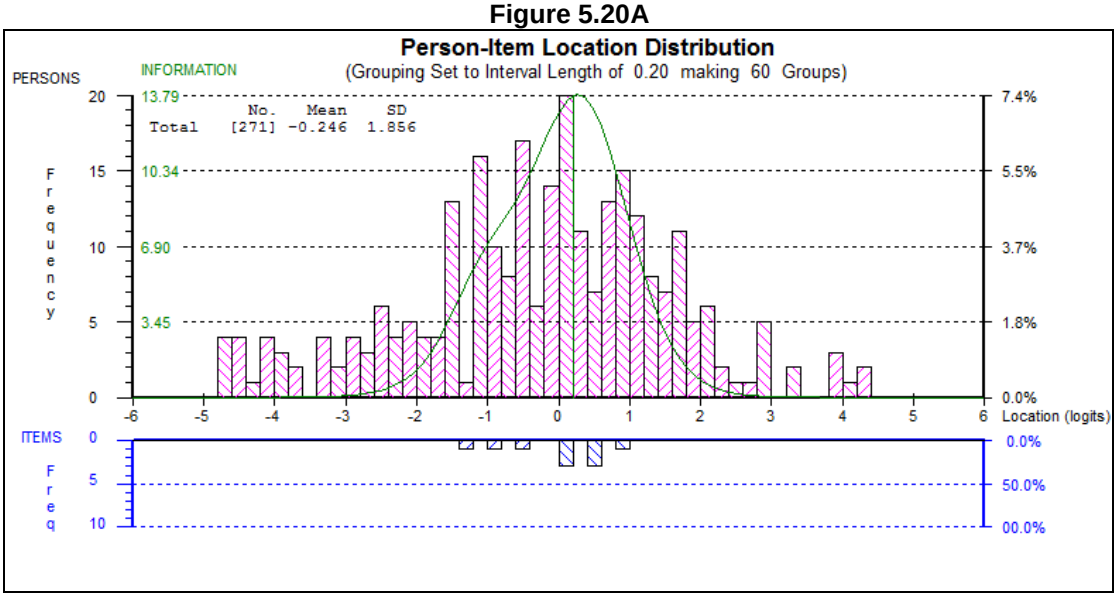


Figure 5.20B

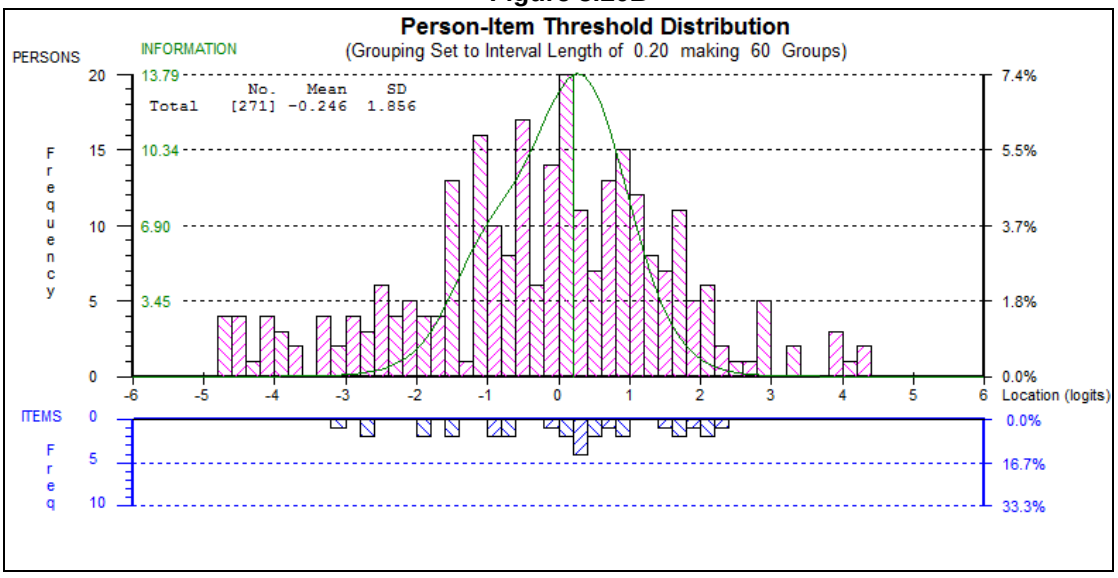


Figure 5.20: *the pink blocks represent the sample distribution for the impact scale and the blue blocks represent the scale distribution of the 10 items on the same measurement continuum. The green curve shows the location on the continuum the scale performs at its best, indicating that the location of item thresholds and persons is well matched.*

5.5.4.5.2 To what extent has a measurement continuum been constructed successfully?

Response categories were ordered in sequence as expected for all items apart from item 15j (Table 5.17). This is a finding which is consistent with the first field test, where item 26o related to pregnancy was also disordered. Threshold location logits indicate that the probability of endorsing the middle response categories of “somewhat uncertain” and “somewhat certain” was located on higher location logits (1.72), or in other words at higher levels of the trait than the probability of endorsing the “somewhat

certain" and "very certain" categories. This misfit to the RMT expectations is also displayed through the category probability curve of item 15j (Figure 5.21), which shows how the probability curve "2: somewhat certain" was not the most probable response at any level of the certainty.

The item location histograms (Figure 5.20) indicated some item gaps, however when reviewing the location logits of all 10 items the largest item gap revealed was 0.45 logits between items 15h and 15j which was not large compared to the remaining scales (Table 5.18). Item goodness of fit of the final scale improved from the first draft of the scale. The fit residual range was improved (Table 5.21), but two items (15e & 15j) still displayed fit residuals outside the "rule of thumb" range of -2.5 to +2.5 (Table 5.18) and significant Chi square correlations, as did item 15c. Reviewing the graphical representation of the item-trait relationship for these three items (Figure 5.22) shows that item 15j displays the strongest misfit, indicating an underestimation of certainty. Observed scores (black dots) for items 15c and 15e lay marginally away from the expected curve. The remaining seven items displayed optimal ICCs curves (Figure 5.23).

Response bias was greatly improved from the first draft of the scale (Table 4.11) as the higher residual correlation coefficient was 0.315, indicating no significant item dependency (Table 5.18). The stability of the scale also improved as only one item reported DIF between the two conditions, as the observed scores of the SLE sample were higher than expected, and they were lower than expected for the RA sample.

Table 5.17 PCQ 2nd Draft *Impact* Scale: Item Threshold Location

Index	Item	τ1	τ2	τ3
15a	Will not affect my ability to plan my life	-1.95	0.30	1.70
15b	Will not affect my education	-3.04	-0.68	0.00
15c	Will not affect my relationship	-2.65	-0.60	0.52
15d	Will not affect my ability to care for my children	-2.62	0.19	0.85
15e	Will not affect my functionality	-1.82	0.30	1.88
15f	Will not affect my finances	-1.46	0.07	1.46
15g	Will not affect my ability to exercise	-1.52	0.79	2.11
15h	Will not affect my job prospects	-0.89	0.27	2.26
15i	Will not affect my mobility	-1.00	0.43	2.17
15j	Will not affect my pregnancy	0.32	1.72	0.92

Figure 5.21 PCQ 2nd Draft *Impact* Scale: Category Probability Curve (item 15j displaying disordered thresholds)

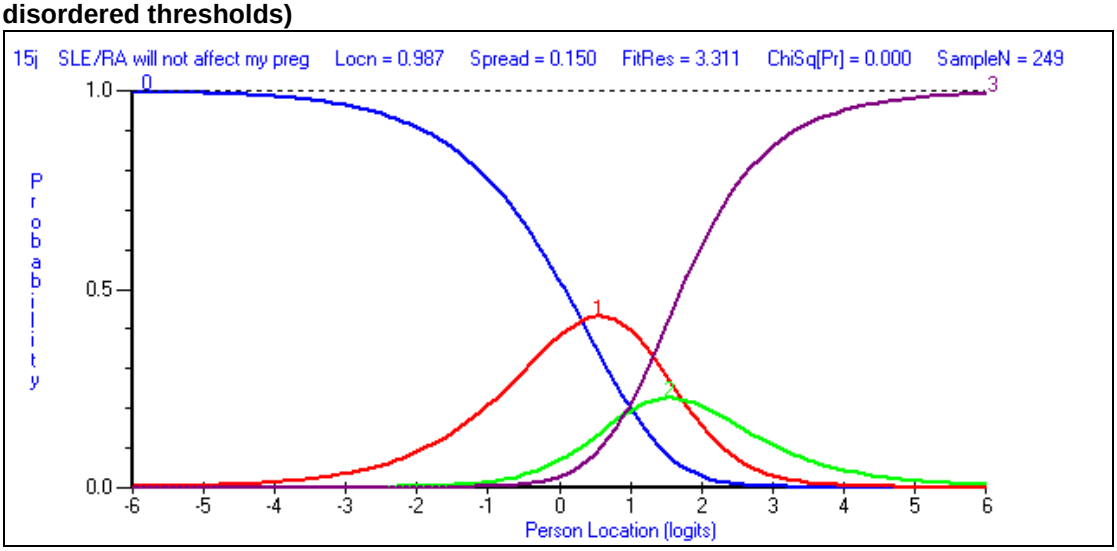


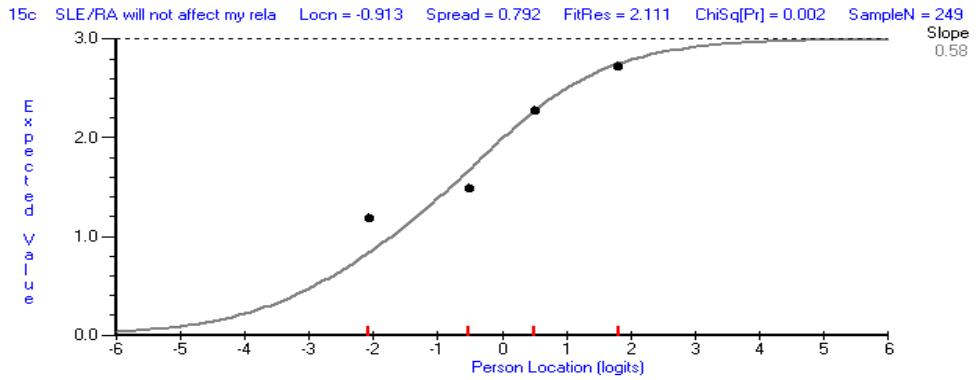
Figure 5.21: *The x-axis represents the measurement continuum of the trait (certainty), with increasing ability from left to right and the y-axis represents the probability of choosing each of the four response categories. The blue line represents 'Very Uncertain'; the red 'Somewhat Uncertain"; the green "Somewhat Certain" and the purple "Very Certain". Thresholds (τ1, τ2, τ3) represent the points where each pair of probability curves meet. Item 15j displays as the curves and thresholds are not ordered consecutively on the measurement continuum.*

Table 5.18 PCQ 2nd Draft *Impact* Scale: Item Fit Statistics Ordered by Location

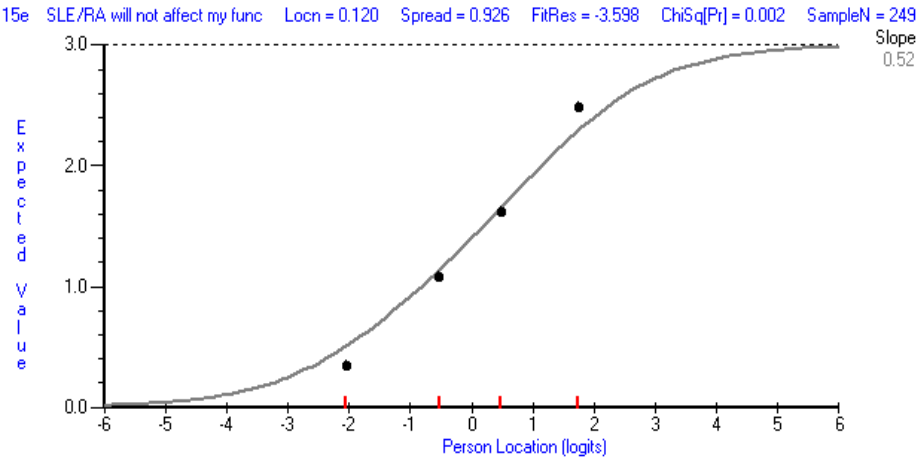
Item	Thresh	Loc	SE	FitRes	ChiSq Prob	Res.r	DIF prob.		
							C	A	D
15b	Ordered	-1.24	0.16	0.56	0.75	<0.30	0.49	0.47	0.37
15c	Ordered	-0.91	0.10	2.11	**0.00***	0.315	0.00	0.01	0.17
15d	Ordered	-0.53	0.13	1.66	0.15	0.315	0.04	0.02	0.74
15a	Ordered	0.01	0.10	-1.92	0.00	<0.30	0.12	0.85	0.44
15f	Ordered	0.02	0.09	1.10	0.63	<0.30	0.97	0.01	0.02
15e	Ordered	0.12	0.10	**-3.60**	**0.00***	<0.30	**0.00***	0.02	0.24
15g	Ordered	0.46	0.10	0.48	0.69	<0.30	0.44	0.56	0.14
15i	Ordered	0.54	0.09	-1.36	0.07	<0.30	0.01	0.00	0.21
15h	Ordered	0.54	0.11	-0.58	0.13	<0.30	0.33	0.01	0.04
15j	Disorder.	0.99	0.16	**3.31**	**0.00***	<0.30	0.58	0.04	0.07

Loc location; SE standard error; FitRes fit residual; ChiSq prob chi square probability; Res. r residual correlations; DIF prob differential item functioning probability; C condition; A age; D disease duration *significant with Bonferroni adjustment

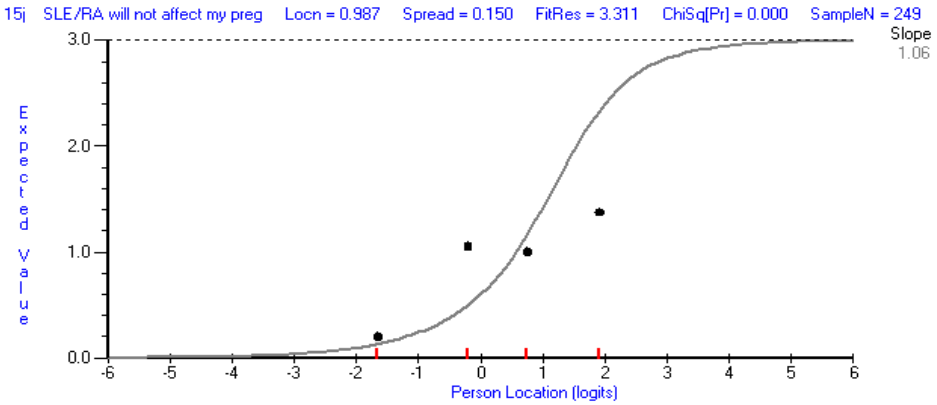
Figure 5.22 PCQ 2nd Draft *Impact* Scale: Item Characteristic Curves (items displaying misfit)



Item 15c: Lupus/arthritis will not affect my relationship



Item 15e: Lupus/arthritis will not affect functionality



Item 15j: Lupus/arthritis will not affect pregnancy

Figure 5.22: *The y-axis represents the person scores and the x-axis represents the person location logits. The curve denotes the expected score across the range of person locations. The black dots represent the observed scores in each of the four class intervals (class intervals of person location). Item 15j displays under discrimination of the trait as the line indicated by the dots is flatter than the expected curve. Dots for items 15c display marginal under estimation and for item 15e marginal over estimation of the trait as they lye close to the expected curve.*

Figure 5.23 PCQ 2nd Draft Impact Scale: Item Characteristic Curves

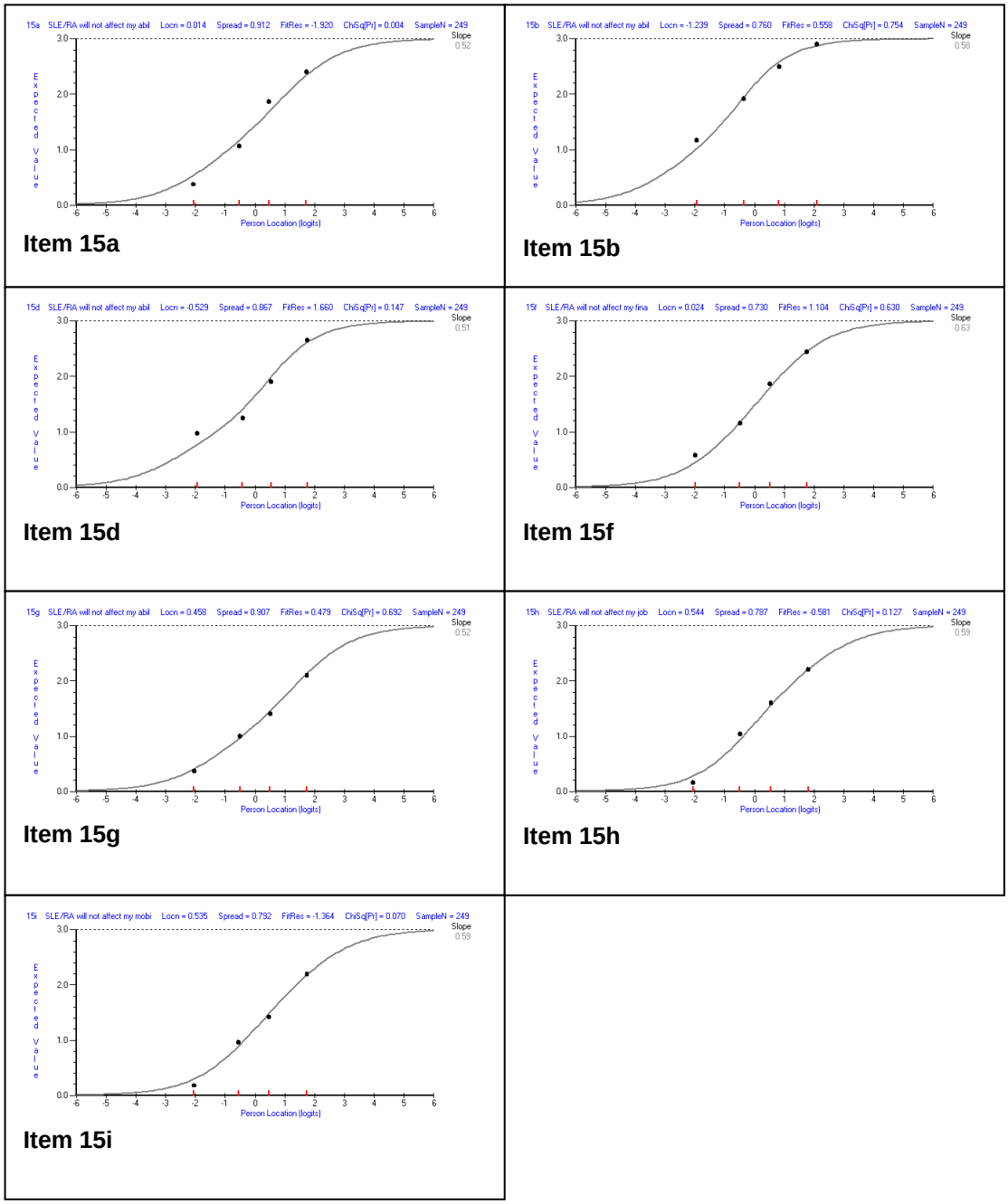


Figure 5.23: *The x-axis represents the person location logits, the y-axis the expected value and the dots represent the observed scores in the four class intervals. None of the items displays misfit as the black dots lye very closely on the expected curve.*

5.5.4.5.1 How has the sample been measured?

The person separation index (PSI) was slightly lower than the first draft but still remained high at 0.87, indicating that the separation of the sample by the scale was good and the random error was low (Table 5.21). Person fit residuals ranged from -5.415 to 2.904 logits, whilst residuals for 18 participants, 6.45% of the sample, fell outside the “rule of thumb” range of -2.5 to +2.5. Sixteen of these participants (5.73%) produced a negative fit residual, thus indicating observed scores were significantly lower than expected (residual = observed – expected), whilst two (0.7%) were positive

residuals (>+2.5). Scale measurement was sub-optimal but improved from the first draft of the scale, where 14.6% of the sample fell outside the “rule of thumb”.

Figure 5.24 shows the relationship between the raw ordinal scores and the interval (logit) measurement they imply. An S-shaped relationship instead of an absolute linear one is revealed by this graph, a relationship that appears stronger at the lower end of the axes. The relationship is proven numerically through the transformed raw scores (Table 5.19). A change of ten points of the total raw score between 0 and 10 is related to an approximate change of 4 logits, and similarly between 20 and 30 to approximately 3.3, whereas a change of ten points between the total score of 10 and 20 is related to a change of approximately 1.5 logits. This information indicates that interpretations made on the basis of raw total scores are sub-optimal as implications of changes at the extremes are greater than toward the centre of the scale. This however was an expected finding considering the stringent mathematical criteria of the RMT (517). Additional RMT result outputs are presented in Appendix 5.10.

Table 5.19: PCQ 2nd Draft Impact Scale: Transformed Raw Scores

Raw Score	Logit	Logit 0-100 Transformation	Raw Score	Logit	Logit 0-100 Transformation
0	-4.744	0*	16	0.291	53
1	-3.856	9	17	0.459	55
2	-3.207	16	18	0.627	57
3	-2.733	21	19	0.794	58
4	-2.347	25	20	0.964	60
5	-2.016	29	21	1.136	62
6	-1.724	32	22	1.314	64
7	-1.462	35	23	1.501	66
8	-1.222	37	24	1.703	68
9	-1	39	25	1.927	70
10	-0.792	42	26	2.184	73
11	-0.596	44	27	2.494	76
12	-0.408	46	28	2.894	81
13	-0.227	48	29	3.472	87
14	-0.051	49	30	4.309	100*
15	0.121	51			

extrapolated values due to asymmetry of data

Figure 5.24 PCQ 2nd Draft Impact Scale: Total Raw Score to Logit Transformation

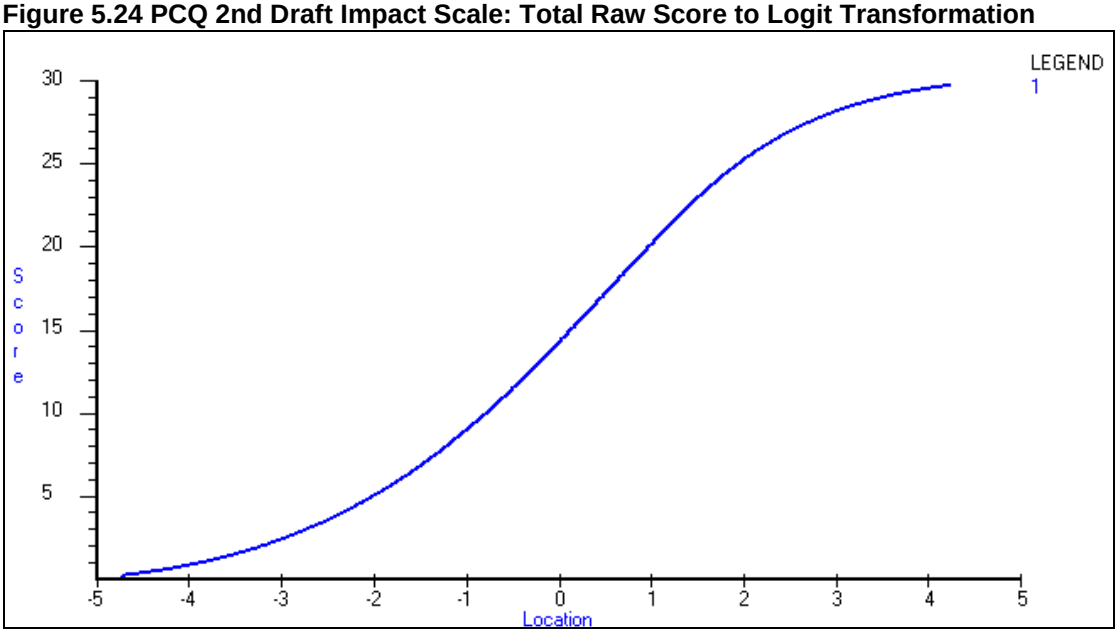


Figure 5.24: *The x-axis represents the construct as an interval logit score and the y-axis raw score on the Impact Scale*

5.5.4.6 Comparison of RMT results between the two field tests.

As discussed in section 5.5.2, the sample of external sites (RBH, RJAH & LRI) was not entirely independent from that of the first field test. A ratio of 35% of participants recruited by external sites included participants completing the first field test as well, but no further details were available. Due to this factor the combined sample (n=662) was not used as the main evaluation dataset for these scales, but only as an informative comparison. Data for three of the five PCQ scales were available in both field tests, therefore datasets of both field tests were combined in order to compare and contrast scale evaluation in the total sample compared to the first and second field test sample.

Scale-level results for these three scales (*symptoms & flares*; *trust in doctor & self-management*) using the first, second and combined dataset are presented in Table 5.21. Scale performance was consistent across these datasets for all three scales on all parameters including power, PSI, person and item location ranges and person mean values. There was one minor inconsistency in the *symptoms and flares* 14-item scale as the item fit skewness statistic (1.026) was marginally above the criterion level (+1) in comparison to the second and combined datasets, where item skewness fell within the expected criteria.

Item-level results for the combined dataset are presented in Appendix 5.11. For the *symptom and flares* scale item performance was relatively consistent with the second field test results (Table 5.6). Item ordering was replicated in the same sequence and

only one item (1a) showed some misfit of expected and observed scores as reported in the second field test. Consistent response bias results were indicated as the same items (7c-7f) produced residual correlations coefficients above the 0.4 criterion. Item stability was also consistent. DIF between the two conditions for items 1a and 7c which approached significance in the second field test was significant with the Bonferroni correction in the combined field test. The only major inconsistency was the reversed response thresholds for item 1h in the SLE sample.

Combined dataset results for the *trust in doctor* items (Appendix 5.12) were entirely consistent with the second field test results (Table 5.12). Items were ordered in the same difficulty sequence, and response thresholds were ordered in both analyses. Item 4g displayed underestimation with significant chi square probability and a fit residual above the +2.5 level in both datasets. Items 4a and 4b were marginally misfitting and indicating response bias with consistently high residual correlation coefficient. Item performance was stable across condition groups, age categories and disease duration groups in both analyses.

Combined dataset results for the *self-management* items (Appendix 5.13) were to a great extent consistent with the second field test results (Table 5.15). The sequence of item ordering was identical and the same item (5a) displayed reversed response thresholds. All items displayed goodness of fit in terms of fit residuals and chi square probabilities, and no response bias was displayed in either analysis. The only inconsistency between the two dataset analyses was the instability displayed by two items (5b, 5f) between the two conditions and by one item (5f) between the age groups in the combined dataset.

In addition to these analyses, the scale items in the combined dataset were evaluated for performance stability between the two field tests. Table 5.20 displays the results of DIF between the two field tests for the 28 items comprising the three scales. Two of these items (4g & 5b) reported significant DIF. The graphs of these items (Figure 5.25) display how observed scores for both items were lower than expected in the second field test (red line) and higher than expected in the first field test (blue line). However, this relationship was not judged to be substantial as lines of both field tests lay relatively close to each other. The sample composition of the two field tests could also account for this differential result as 55% of the first sample were RA participants (n=210), whereas only 41% of the second sample were RA patients (n=114).

Table 5.20 Differential Item Functioning by Field Test

Item	MS	F	DF	Field Test	Item	MS	F	DF	Field Test
Symptoms & Flares					**Trust in Doctor**				
1a	0.08	0.10	1.00	0.75	**4a**	0.29	0.46	1.00	0.50
1b	4.61	5.04	1.00	0.03	**4b**	1.30	1.94	1.00	0.16
1c	1.98	2.37	1.00	0.12	**4c**	3.65	4.84	1.00	0.03
1d	0.51	0.57	1.00	0.45	**4d**	3.73	4.25	1.00	0.04
1e	0.08	0.08	1.00	0.77	**4e**	7.43	8.97	1.00	0.00
1f	4.55	4.01	1.00	0.05	**4f**	0.57	0.62	1.00	0.43
1g	11.02	13.17	1.00	0.00	**4g**	21.61	19.05	1.00	**0.00***
1hRA	1.44	1.55	1.00	0.21	**4h**	7.97	8.47	1.00	0.00
1hSLE	4.80	5.09	1.00	0.02	**Self-management**				
1i	0.42	0.50	1.00	0.48	**5a**	1.68	1.76	1.00	0.19
7b	0.21	0.19	1.00	0.67	**5b**	11.94	12.92	1.00	**0.00***
7c	0.24	0.28	1.00	0.60	**5c**	0.01	0.01	1.00	0.92
7d	2.90	3.52	1.00	0.06	**5d**	0.38	0.45	1.00	0.50
7e	3.95	3.74	1.00	0.05	**5e**	4.98	7.19	1.00	0.01
7f	0.62	0.65	1.00	0.42	**5f**	5.52	6.35	1.00	0.01

significant with Bonferroni correction at p<0.01 level

Figure 5.25: PCQ 2nd Draft: Differential Item Functioning by Field Test

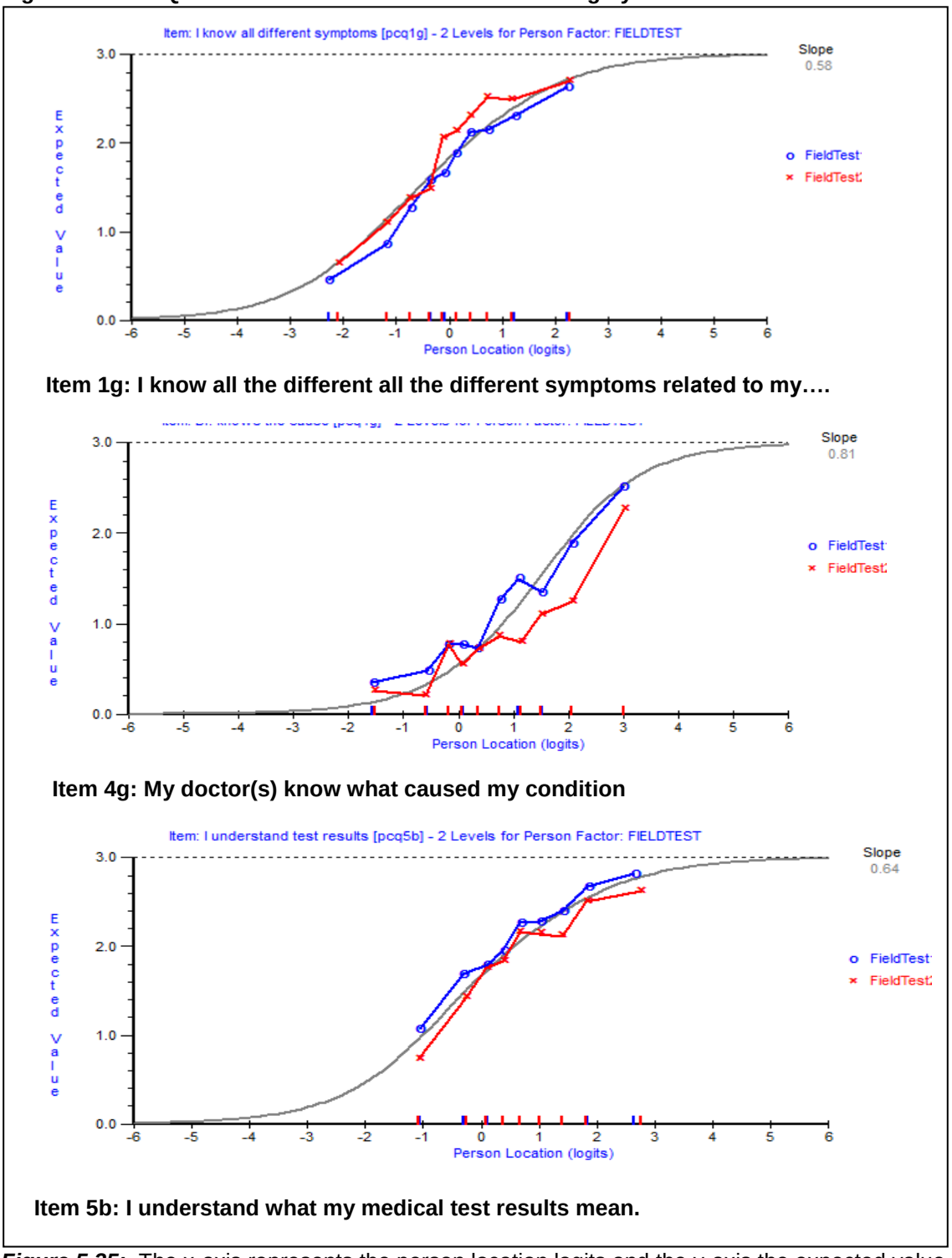


Figure 5.25: The x-axis represents the person location logits and the y-axis the expected value of scores. The blue line represented the observed scores in the first field test and the red line the observed scores in the second sample, plotted against the curve of expected scores for the combined sample. Graphs for items 4g and 5b displayed the greatest DIF statistically (Table 5.20) indicate that observed scores in the first field test were consistently higher than expected whilst in the second field test lower than the expected curve. The opposite is displayed for item 1g, although both lines lye closer to the expected curve in comparison with items 4g and 5b where graphically DIF appears more significant. 1j.

Table 5.21 Rasch Analysis Scale-Level Summary Statistics

	PSI		Person-Item Distribution (targeting)			Item fit				Person fit			
Field Test	With extremes	No extremes	Person location range	Item location range	Item threshold range	Mean (SD)	Fit Res. Mean (SD)	Skewn.	Fit Res. range	Mean (SD)	Fit Res. Mean (SD)	Skewn.	Fit Res. range
Symptom & Flares 16 items													
1	0.906	0.896	-5.216 – 5.073	-1.579 – 1.997	-3.213 – 3.566	0.000 (1.149)	0.208 (1.689)	1.485	-1.775 - 5.073	0.050 (1.299)	-0.298 (1.325)	0.092	-4.306 - 4.547
2	0.908	0.892	-4.702 – 5.638	-1.691 – 2.433	-4.077 – 4.203	0.000 (1.327)	0.298 (1.506)	0.249	-2.134 - 3.075	0.115 (1.453)	-0.222 (1.283)	-0.057	-4.366 - 4.121
Symptom & Flares 14 items													
1	0.899	0.888	-5.273 - 5.060	-1.617 – 2.021	-3.254 – 3.603	0.000 (1.221)	0.228 (1.318)	1.026	-1.342 - 3.582	0.038 (1.377)	-0.327 (1.297)	0.072	-4.079 - 4.567
2	0.907	0.891	-5.797 - 5.892	-1.815 - 2.569	-4.337 – 4.490	0.000 (1.383)	0.271 (1.308)	0.118	-1.998 – 2.351	0.067 (1.511)	-0.265 (1.295)	-0.100	-4.096 - 4.061
1 & 2	0.901	0.889	-5.389 – 5.206	-1.699 – 2.135	-3.554 – 3.762	0.000 (1.253)	-1.007 (1.667)	0.586	-3.311 - 2.316	0.012 (1.393)	-0.325 (1.252)	-0.116	-4.223 - 4.669
Trust in Doctor													
1	0.836	0.818	-3.514 – 3.541	-1.169 – 1.216	-2.724 – 2.612	0.000 (0.917)	0.015 (1.227)	-0.082	-1.878 - 1.938	0.970 (1.594)	-0.366 (1.194)	-0.345	-4.099 - 2.914
2	0.831	0.809	-2.861 – 3.549	-1.163 – 1.723	-3.160 – 2.727	0.00 (1.184)	-0.078 (2.424)	0.417	-2.749 – 4.234	0.845 (1.431)	-0.352 (1.142)	0.175	-3.178 - 3.446
1 & 2	0.841	0.821	-3.113 – 3.543	-1.162 – 1.420	-2.868 – 2.632	0.000 (1.027)	-0.240 (2.435)	0.403	-3.326 - 4.276	0.904 (1.542)	-0.361 (1.166)	-0.225	-4.023 - 3.185
Self-management													
1	0.754	0.691	-2.177 – 4.242	-0.967 – 0.797	-1.760 – 2.895	0.000 (0.656)	0.150 (1.330)	-0.337	-1.676 - 1.449	1.023 (1.416)	-0.374 (1.131)	-0.368	-3.668 - 2.188
2	0.734	0.679	-3.508 – 4.044	-0.523 – 0.434	-1.953 – 2.652	0.000 (0.409)	0.203 (0.881)	-0.380	-1.109 - 0.934	1.276 (1.470)	-0.301 (1.012)	-0.293	-3.579 - 1.904
1 & 2	0.740	0.685	-2.634 – 3.119	-0.780 – 0.651	-1.387 – 2.739	0.000 (0.534)	-0.845 (1.782)	-0.169	-3.040 - 1.162	1.108 (1.423)	-0.343 (1.073)	-0.432	-3.789 - 2.124

Field Tests 1 N=383; 2 N=279; 1 & 2 N

Table 5.21 (cont`d)

	PSI		Person-Item Distribution (targeting)			Item fit				Person fit			
Field Test	With extremes	No extremes	Person location range	Item location range	Item threshold range	Mean (SD)	Fit Res. Mean (SD)	Skewn.	Fit Res. range	Mean (SD)	Fit Res. Mean (SD)	Skewn.	Fit Res. range
Medication													
1*	0.761	0.721	-4.008 – 4.038	-1.107 – 0.906	-2.601 – 2.329	0.000 (0.759)	0.087 (1.552)	-0.002	-1.878 - 1.938	1.643 (1.745)	-0.425 (1.180)	-0.180	-3.726 - 2.767
2	0.864	0.831	-4.106 – 4.620	-1.536 – 1.368	-2.119 – 2.619	0.000 (0.904)	-0.004 (1.164)	0.585	-1.693 - 2.578	0.675 (1.435)	-0.513 (1.501)	-0.526	-8.661 –4.272
Impact													
1*	0.893	0.883	-4.598 – 4.556	-0.745 – 0.803	-1.935 – 2.353	0.000 (0.516)	0.298 (2.137)	0.810	-2.636 –5.771	-0.011 (1.490)	-0.538 (1.855)	-0.369	-6.634 –3.993
2	0.870	0.845	-4.744 – 4.309	-1.239 - - 0.987	-3.041 – 2.555	0.000 (0.702	0.176 (2.067)	-0.281	-3.598 - 3.311	-0.246 (1.856)	-0.421 (1.423)	-0.611	-5.415 - 2.904

1st draft of the scale of the scale; Field Tests 1 N=383; 2 N=279; 1 & 2 N=662

5.5.5 Traditional Psychometrics: Validity Results

Convergent validity was evaluated through an examination of the correlations between scale total scores (Table 5.22). All but three of the correlations fell between the expected criterion range of 0.30 – 0.70 apart from the *symptoms and flares* and *medication* association, as well as the association of the *impact* with the *symptoms and flares* and *self-management* scales, the correlation of which fell <0.30 indicating that the association between these scales was weaker than expected. These relationships were further explored in the two samples independently to explore these unexpected findings.

Table 5.22: Convergent Validity Pearson Correlations

	Total Sample	**1**	**2**	**3**	**4**	**5**
1	Symptoms – Flares	1				
2	Medication	0.20	1			
3	Trust in Doctor	0.352	0.504	1		
4	Self-manage.	0.536	0.446	0.442	1	
5	Impact	0.13	0.453	0.559	0.12	1
	SLE sample	**1**	**2**	**3**	**4**	**5**
1	Symptoms & Flares	1				
2	Medication	0.03	1			
3	Trust in Doctor	0.19	0.41	1		
4	Self-management	0.31	0.37	0.28	1	
5	Impact	0.03	0.48	0.48	0.26	1
	RA sample	1	2	3	4	5
1	Symptoms & Flares	1				
2	Medication	0.41	1			
3	Trust in Doctor	0.58	0.39	1		
4	Self-management	0.40	0.32	0.43	1	
5	Impact	0.27	0.37	0.39	0.26	1

Convergent validity tests within the SLE sample revealed that the association between all scales within the expected criterion range apart from the *symptoms and flares* that only displayed the expected relationship with the *self-management* scale (r = 0.31). The association between the *self-management* and *impact* scales (r = 0.26) fell marginally below the lower criterion of 0.30 in both patient groups, similar to the association between the self-management and trust in doctor in the SLE sample (r = 0.28) and the association between the symptoms and flares and impact scale in the RA sample only (r = 0.27). The PCQ scales displayed stronger convergent validity within the RA sample with more scales

showing an association within the expected criterion range (Table 5.22).

External validity of the final PCQ scales was also associated through association with demographic variables (Table 5.23). Certainty in all of the five scales was not associated with participants` gender or age. Longer disease duration was associated with increased certainty with relation to *medication* and *self-management*. Ethnicity group was marginally associated with certainty of *symptoms and flares* and *self-management*, but no other significant association was revealed between the remaining demographic variables and the five PCQ scales. The association of the illness trajectory (SLE/RA) with the different scales as well as the demographic associations with certainty levels within each condition group will be presented in Chapter 6.

Table 5.23 PCQ Scales Association with Demographic Variables

	Symptoms – Flares	Medication	Trust in Doctor	Self-management	Impact
Gender					
t-test p value	0.778	0.760	0.154	0.742	0.216
Age					
Pearson correlation coefficient	0.02	0.24	0.100	0.063	0.206
Disease duration					
Pearson correlation coefficient	0.106	0.166	0.114	0.214	0.205
Age categories					
One-way ANOVA p-value	0.821	0.415	0.339	0.924	0.540
Disease duration categories					
One-way ANOVA p-value	0.240	**0.018***	0.137	**0.034***	0.648
Ethnic group					
One-way ANOVA p-value	**0.010***	0.176	0.570	**0.022***	0.040
Employment status					
One-way ANOVA p-value	0.179	0.161	0.582	0.877	0.819
Living situation					
One-way ANOVA p-value	0.056	0.368	0.348	0.292	0.489
Education					
One-way ANOVA p-value	0.607	0.787	0.036	0.231	0.410

*significant at p<0.05, **significant at p<0.01 level

5.5.6 Review of Single Items

At the completion of this analysis the research team addressed and reviewed the ten single items (Table 5.24) resulting from the item reduction in Chapter 4. Initially they were retained in the second draft of the PCQ as single descriptive parameter indicators that would be assessed in addition to the scales as they failed to perform well within scales. They could not be analysed further or used as scales representing distinct

constructs. It was therefore only possible to evaluate them psychometrically using traditional psychometrics, as the RUMM2030 and RMT analysis only deals with scales and not single parameters.

Results indicate that single items did not always show the strongest association with PCQ scale derived from the same conceptual domain. E.g. item 2 derived from the symptoms and prognosis original domain and scale showed no association (r = 0.06) with the *symptoms and flares* scale; whereas, its association with remaining scales fell within the convergent validity criterion range (0.30 to 0.70) suggesting conceptually similar constructs. Items 6 and 14 were derived from the social functioning scale (the only scale eliminated from the final version of the PCQ) and did not produce any strong association with any of the other scales as all their correlations fell below the 0.30 minimum convergent validity criterion. Reviewing the single items association with the PCQ scales (Table 5.24) it was decided to exclude them from further analyses of this thesis as they could not be utilized to represent or quantify a distinct domain or construct.

Table 5.24 Single Items Association with PCQ Scales

Item	**Conceptual Domain**	**Symptoms - Flares**	**Medication**	**Trust in Doctor**	**Self-management**	**Impact**
2	Symptoms & Prognosis	0.06	0.61	0.32	0.28	0.42
6	Social Function.	0.27	0.09	0.19	0.17	0.04
8a	Symptoms & Prognosis	0.33	0.29	0.33	0.25	0.30
8b	Symptoms & Prognosis	0.26	0.24	0.29	0.28	0.33
8c	Symptoms & Prognosis	0.35	0.34	0.34	0.25	0.46
10	Medical management	0.00	0.30	0.23	0.10	0.47
11	Medical management	0.11	0.30	0.31	0.21	0.42
12	Medical management	0.03	0.00	-0.08	0.00	0.12
13	Self-management	0.02	0.45	0.29	0.27	0.53
14	Social functioning	-0.01	0.14	0.22	0.17	0.16

5.6 Psychometric Evaluation Conclusions

The second draft of the PCQ scales performed consistently well in the second field test as in the first**,** whereas further revisions were only necessary in the symptoms and flares scale.

Sample to scale targeting was satisfactory in all scales apart from *self-management* where, consistent with the first field test, a sub-optimal item location range was reported (see section 4.5.4.8). In other words, the range of the trait measured by all scales except for the *self-management* one matched the range of the trait in the sample well. As discussed in Chapter 4, the breadth of qualitative data was exhausted by the six items comprising the *self-management* scale. There were therefore no further potential item additions suggested by the qualitative data that could be made to improve scale targeting. The precision of measurement can be further improved as the information function curves denoted that many person measurement estimates fell outside the best functioning of the scales as they were associated with higher standard error and for some scales e.g. the *trust in doctor* scale the potential need for additional items to be included to address ability at all levels of measurement.

The performance of the five measurement continuums was also satisfactory and consistent with the first field test, as was the ordering of items to a large extent. All item response categories were ordered in sequence apart from three items; one (5a) of the *self-management* scale that was consistently disordered in the first field test and another two items (3Bra & 15j) of the *medication* and *impact* scales evaluated for the first time in this field test. Two items were reportedly underestimating the trait, 4g of the *trust in doctor* scale and 15j of the *impact* scale, however overall the goodness of fit was optimal as all item skewness statistics (Table 5.21) fell within the range criterion (-1 to 1).

Extensive response bias was revealed in the *medication* items that were first evaluated in this field test. Another two pairs of items of the *trust in doctor* (4a & 4b) and *symptoms and flares* (7e & 7f) produced high residual correlation coefficients which were consistent with the first field test. These findings indicate that performance of the scale could benefit by the integration of these items in a further revision of the scale, however evaluating suggested item integrations was not possible with the dataset available in this field test.

The performance of the scale items was to a large extent stable across SLE and RA and the different age and disease duration groups. All scales produced high PSI (073 – 0.91), thus confirming their ability to separate the sample. However, the validity of sample measurement across all the scales was sub-optimal as person fit residuals outside the “rule of thumb” range ranged between 1.79% and 9%.

Validity results supported the arguments put forward by the health care professionals (HCPs) regarding the sources and association of patient uncertainty to some extent (see section 3.3.4.1). Gender had no effect on the level of certainty within any of the five scales, whereas longer disease duration was associated with higher levels of *self-management* and *medication*. Age on the other hand did not display a significant association with any of the PCQ scales.

The relationship between the different PCQ scales was also explored with the expectation that positive associations would be found between levels of certainty in the symptoms and flares and trust in doctor domains, and levels of uncertainty in the medication and impact domains subsequently. In line with the HCPs suggestions, convergent validity was reported between the five PCQ scales, with the trust in doctor scale displaying the strongest associations. Contrary to HCPs suggestions though, no significant association was reported between the impact and symptoms and flares scales.

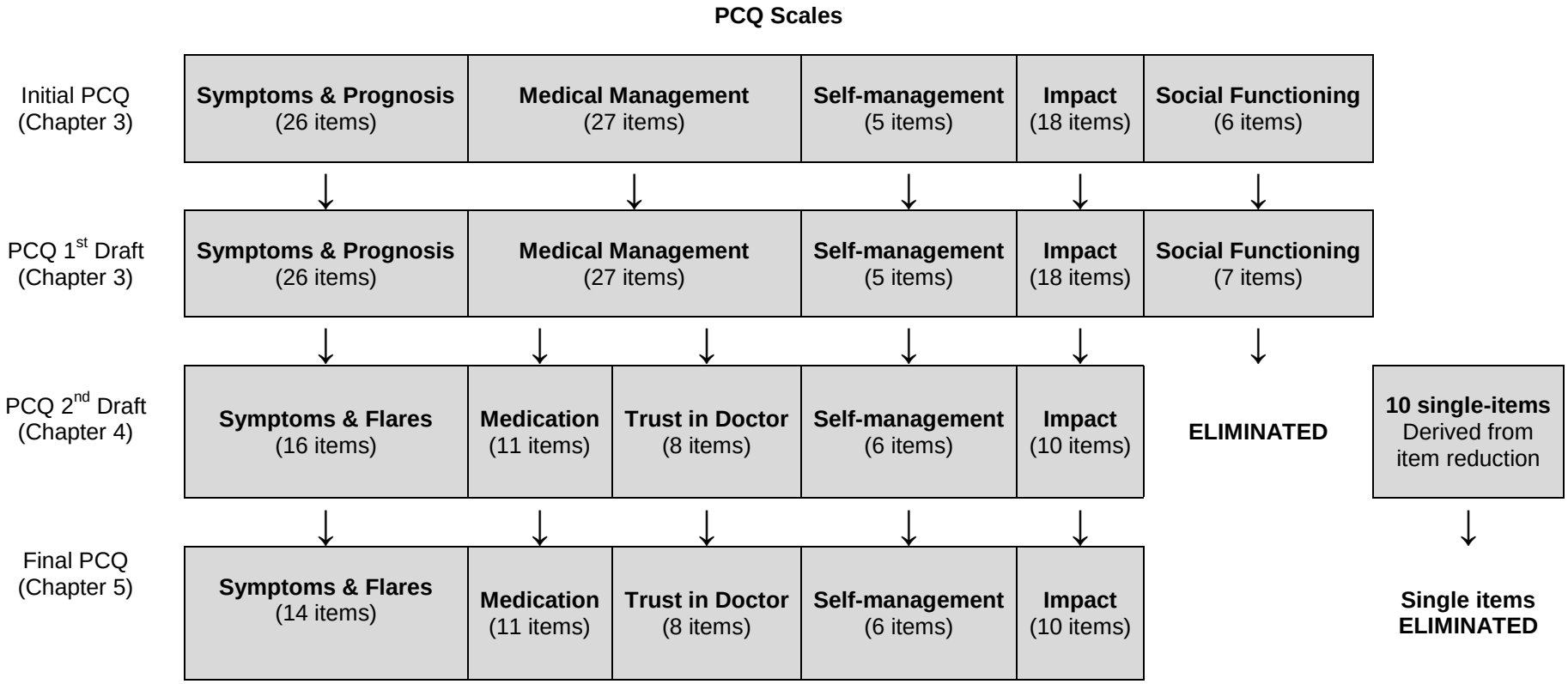
This hypothesis regarding convergent validity between the abovementioned PCQ scales was supported in the RA sample. However, mixed support for the associations between the different patient uncertain domains was provided by the SLE sample. Even though the trust in doctor scale satisfied the convergent validity criteria with the other scales, the symptoms and flares domain did not manifest the expected associations. Levels of certainty in relation to symptom interpretation and flare prediction did not appear to be associated significantly with certainty in any of the other scales failing to support the convergent validity expectations.

Reviewing the potential use and additive value of the ten single items resulting from item reduction in the first field test, the research group decided to exclude them from further analyses in this thesis. The final version of the PCQ scales (Table 5.25) consisted of five scales; *symptoms and flares*, *medication*, *trust in doctor*, *self-management* and *impact*. The RMT analysis results indicated that the measurement properties of these scales were satisfactory despite some minor deviations from the RMT expectations, which are anticipated as the mathematical expectations are stringent (517).

5.7 Chapter 5 Summary

The second field test resulted in the final revision of the PCQ scales. Rasch analysis indicated that the sample to scale targeting was satisfactory for all scales except self-management which displayed sub-optimal targeting. The measurement continuums were constructed successfully to a large extent for all scales, and sample measurement was also adequate considering the stringent criteria of RMT. The convergent and discriminant validity of the final PCQ scales was further explored providing mixed support for the hypotheses which were based on previous findings. Chapter 6 presents the first application of the PCQ in a cross-sectional exploratory cohort study in SLE and RA.

Table 5.25 PCQ Item Revisions



Chapter 6: Patient Uncertainty in SLE and RA

6.1 Chapter 6 Overview

Chapter 6 presents an extended validity evaluation of the final PCQ scales and an initial exploration of the association of patient uncertainty in SLE and RA with other patient outcomes. The aims of the studies presented here were to examine the construct validity of PCQ further with regards to the suggested sources of patient uncertainty first of all, and secondly to investigate the association of patient uncertainty with patient outcomes, including treatment adherence, mood and health related quality of life in SLE and RA. The hypotheses regarding these aims were guided by previous study findings and the current literature.

6.2 Background

The studies presented in this chapter constitute the first exploration of patient uncertainty in SLE and RA as quantified by the newly developed PCQ instrument. The PCQ instrument consists of five scales measuring patient uncertainty across five domains which are uncertainty related to *symptoms and flares*, medication, *trust in doctor*, *self-management* and *impact*. The literature presented in Chapters 1 and 2 and the qualitative investigation findings presented in Chapter 3 were used to guide these analyses. A brief summary of these is presented below in order to set the background for the analysis of this chapter.

The first aim of the studies presented in this chapter was to explore the construct validity of the five patient uncertainty scales further, beginning with the differences of patient uncertainty levels reported in the two illness trajectories (SLE & RA). Both the qualitative (34, 55, 56, 87) and quantitative (44, 71) studies reviewed suggested the role of illness characteristics in both the level and types of uncertainty experienced by patients respectively. When questioned directly about the role of illness trajectory, health care professionals (HCPs) provided mixed responses as to whether the greater heterogeneity of SLE leads to greater levels of patient uncertainty when compared to RA (see section 3.3.4.1). Even though there was a general consensus on the inherent increased complexity of SLE, some HCPs argued against the causal role of illness trajectory in the expression of patient uncertainty. The subsequent patient interviews indicated that patients with SLE and RA experience the same overarching domains of patient uncertainty, but nevertheless patients with SLE displayed heightened

uncertainty on a sub-domain level, particularly with regards uncertainty to illness progression and unpredictability.

Chapter 6 presents studies exploring the above in each condition (SLE & RA) separately. The association of current disease activity with patient uncertainty levels was also explored as HCPs provided mixed arguments regarding the association of illness severity and levels of patient uncertainty.

Apart from the demographic and illness variables, the HCPs interview findings indicated the links between the different domains of patient uncertainty. In particular, it was suggested that heightened uncertainty with regards to the *trust in doctor* and *symptom and flares* domains is linked with higher uncertainty in the *medication* and *impact* domains. Additionally, HCPs suggested the role of personal characteristics and particular coping styles in the level of patient uncertainty expressed by patients. Adaptive coping strategies and higher levels of social support were also identified in the literature review as variables linked with lower levels patient uncertainty (29, 94, 104, 114, 121). These suggestions are also explored in this chapter.

The second aim of the studies presented in this chapter was to explore the association of patient uncertainty with other patient outcomes. The health care professionals (HCPs) and patient qualitative interviews concluded that patient uncertainty is a subjective perception. Patient uncertainty was further portrayed as an aversive variable which has negative consequences on both behavioural and psychosocial outcomes (see section 3.3.6). These findings supported the literature review findings suggesting that patient uncertainty levels quantified with the generic Mishel Uncertainty in Illness (MUIS/MUIS-C) scales contributed to psychological distress and patient adjustment in asthma (121, 123), mood and anxiety levels in heart conditions (43, 132) and multiple sclerosis (116, 138).

The qualitative findings of this thesis support the bio-psychosocial model of health and illness (147, 150, 155) outlined in section 2.4.4. The model postulates that variables such as patient beliefs, coping and social support contribute to and moderate the relationship between disease and physical, psychosocial and behavioural outcomes in SLE and RA. Furthermore, the bio-psychosocial model of rheumatic conditions (155) indicated that coping strategies affect stressors and cognition (e.g. patient beliefs/perceptions) impact on physical functioning (see section 1.3.) (157-160, 531). By investigating the association of patient uncertainty as a subjective perception

patients hold, with other outcomes, and this is in line with these integrative models of illness.

The studies described in this chapter specifically investigated the association of patient uncertainty with treatment adherence and mood and health related quality of life (HRQoL). Poor treatment adherence was explicitly suggested by the HCPs as a consequence and signal of heightened patient uncertainty (see section 3.3.4.1.5). Patient beliefs about the cause and control of illness and illness flares, use of medications, dissatisfaction with health care, patient self-efficacy and depression levels have been reported to contribute to intentional non-adherence in both SLE and RA (343, 459-462). The association of patient uncertainty to treatment adherence as a patient perception has never been explored in these conditions.

Patient quotations related to uncertainty were often expressed with an apparent sense of worry and anxiety (see section 3.3.4.2), an issue that was also indicated by HCPs (see section 3.3.4.1.5). Literature findings have indicated that anxiety is associated with the challenge of being diagnosed and adjusting to a new condition and is therefore heightened during the early phases of diagnosis (343, 447, 449), whereas depression levels have been found to increase progressively, thus reflecting the overall burden of an illness (343, 448, 449). In addition, studies have indicated that patient beliefs have a dynamic association with mood in SLE and RA (88, 448, 453), and one study has further indicated the association of patient uncertainty as assessed with the generic one-dimensional MUIS-C instrument (89) with psychological distress in SLE (97). The association of patient uncertainty with depression and anxiety was therefore explored.

Finally, the studies presented in this chapter explored the association of patient uncertainty with HRQoL in SLE and RA. HRQoL refers to a patients` own perception of the impact of an illness and its treatment on his/her physical, mental and social functionality (302, 389). HRQoL is one of the three recommended outcomes in SLE (532) and is widely recognised as a key outcome in all chronic conditions, particularly as it is not associated with clinical parameters of disease (180, 181, 343). Literature findings have suggested that other non-clinical patient outcomes such as psychological distress, patient beliefs, self-efficacy, coping strategies and social support contribute to HRQoL in SLE (300, 391, 410, 425) and mood and social support in RA (361, 428). HRQoL is relatively poor in both SLE and RA and displays a modest association with disease parameters (300, 343, 400, 401), nevertheless the potential contribution of a patient perceptions like uncertainty to lower HRQoL has never been explicitly assessed in rheumatology.

Non-clinical moderating variables such as beliefs, coping and social support have been reported to contribute to treatment adherence, mood and HRQoL, moderating the relationship between disease and treatment variables with these outcomes (see section 2.4.4). This chapter offers a preliminary exploration of the association of patient uncertainty with these outcomes, in the absence of full information on disease and treatment variables that would allow a complete moderation analysis. In addition to the association of patient uncertainty with the above variables, these analyses examined how this association compares to other cognitive, behavioural and psychosocial variables that have been previously reported to predict these patient outcomes.

6.2.1 Aims

The studies presented in this chapter aimed to (i) assess the construct validity of the final PCQ scales more extensively, and (ii) explore the association of patient uncertainty with other patient outcomes in SLE and RA. As this was the first quantitative investigation of patient uncertainty using the newly developed PCQ instrument in SLE and RA, the explorations were guided by the literature and qualitative findings but remained exploratory. The specific objectives were the following:

I. Construct Validity Exploration

i. Is there a difference between the levels of patient uncertainty in SLE and RA?

ii. Is patient uncertainty associated with gender, age, disease duration and illness severity?

iii. Is patient uncertainty associated with social support and any specific coping strategies?

II. The Association of Patient Uncertainty with Patient Outcomes

i. Are higher levels of patient uncertainty associated with lower levels of treatment adherence?

ii. Are higher levels of patient uncertainty associated with higher levels of depression and anxiety?

iii. Are higher levels of patient uncertainty associated with poorer HRQoL (generic & disease specific)?

Considering this was an exploratory analysis and the first quantitative assessment of patient uncertainty using the PCQ in SLE and RA, the research questions within the above objectives were not made explicit to any of the five specific domains of patient

uncertainty (i.e. *symptoms and flares*, *medication*, *trust in doctor*, *self-management*, or *impact*). Results were analysed in each of the two samples (SLE & RA) separately but are presented in parallel.

6.3 Methods

This chapter constitutes an extended and additional analysis of the observational study presented in Chapter 5.

6.3.1 Study design

A cross-sectional observational study was set up across four hospital sites. This design was described in section 5.3.1. Contrary to Chapter 5, the SLE and RA were analysed independently.

6.3.2 Participants

The participant eligibility sampling and recruitment was described in sections 5.3.3 and 5.3.4.

6.3.3 Materials

In addition to the brief demographic questionnaire and the PCQ instrument described in section 5.3.5, another nine instruments were used in this chapter`s analysis as well as a measure of disease activity. License permissions were obtained for all instruments used. These questionnaires were completed during the second field test but were not utilised or presented in the analysis of Chapter 5. The instruments were chosen on the basis of their use in the SLE and RA literature as well as considering logistical issues e.g. instrument length – minimising participant burden. All instruments used are described below.

6.3.3.1 Demographic & Disease Variables

In addition to the brief demographics questionnaire recording details of participant age, year of diagnosis, gender, ethnic group, employment status, living status and highest level of education, SLE disease activity was also recorded. It was not logistically possible to collect disease activity scores for the RA sample.

SLE disease activity was assessed using the British Isles Lupus Assessment Group (BILAG) system (297, 533). The original BILAG consists of 86 feature items related to eight different systems, including constitutional, mucocutaneous, neurological, musculoskeletal, cardiorespiratory, vasculitis, renal and haematological systems including items capturing symptoms, signs and laboratory results. Physicians are instructed to score each of the 86 features as absent or present, and if present whether that feature is new, worse, the same, or better over the previous 4 weeks. Physicians are instructed to score features that are attributable to SLE disease activity and not due

to damage, infection, or other conditions. Disease activity is defined as a disease process which is reversible, while damage refers to permanent and irreversible.

Physicians are then instructed to score the eight overarching organs/systems on the basis of “intention to treat” using a score from A to E. An A score conveys the need for major immunosuppressant’s or steroids >20mg/day, B the need for modest doses of steroids, C a low dose of steroids or non-steroidal drugs, while D conveys that disease in that system is no longer active and E conveys that disease was never active in that system (534).

Even though a total score was not initially intended, a scoring system of A=9, B=3, C=1, D and E=0 was originally used (535) which produces a BILAG global score. Possible scores range between 0 and 72, with higher scores indicating more active disease. The BILAG index has been shown to correlate well with other disease activity measures and has high between-rater and within-rater reliability (533) and sensitivity to change (536). BILAG scores for the University College Hospital sample were retrieved from the computer programme called the BLIPS (British Lupus Integrated Program), where routinely collected BILAG scores are uploaded. Scores for the Royal Blackburn Hospital sample were recorded by the local collaborating consultant (LST).

6.3.3.2 Patient Certainty Questionnaire (PCQ)

The final version of the PCQ instrument was derived after the second field test (Chapter 5) measuring levels of uncertainty across five scales including *symptoms & flares* (14 items), *medication* (11 items), *trust in doctor* (8 items), *self-management* (6 items) and *impact* (10 items). Items are scored on a 4-point Likert scale ranging from “1=very uncertain” to “4=very certain,” with higher scores reflecting more or less uncertainty. A “not applicable” response option is included in all but the *symptoms and flares* scale.

The PCQ instrument does not provide a total score, but instead offers a total score for each scale. Higher scores reflect lower patient uncertainty in all of the five scales. Specifically, lower patient uncertainty with regards to symptom interpretation and flare-prediction, the effectiveness, necessity and sufficiency of current and future medication, the trust in the doctors` knowledge/ability to treat SLE or RA, knowledge of how to self-manage one`s condition, and lastly lower uncertainty with regards to the lack of any future impact of SLE or RA on one`s life.

Total scores were computed using the RUMM2030 software before being transformed to SPSS. RUMM2030 accounts for missing data by computing class intervals on items and not on a person basis in order to control for any bias brought by missing data and also transforms scores into linear logit (see glossary) scores. Interval logit scores were then transformed to a 0 – 100 scale, with higher scores reflecting lower uncertainty.

6.3.3.3 Behavioural & Psychosocial Outcomes

Outcomes of treatment adherence, mood (depression and anxiety) and health related quality of life (generic and disease-specific) were assessed.

6.3.3.3.1 Treatment Adherence

Treatment adherence was assessed using the Compliance Questionnaire Rheumatology (458), currently the only rheumatology-specific adherence instrument. The CQR is a 19-item self-report instrument of patient compliance to drug regiments using a 4-point agreement Likert scale ranging from, 1 = don't agree at all to 4 =agree very much which is summed to provide a total score. Authors of the scale provide a formula for the transformation of scores from 0 (complete non-compliance) to 100 (perfect compliance).

A series of patient interviews and focus groups were conducted in order to develop the CQR items (537) that have shown moderate internal consistency (alpha 0.71) and a good test re-test reliability. Although a recent literature review of RA concludes that self-report measures overestimate non-adherence the CQR has been validated against the Medication Event Monitoring System (MEMS) electronic device that provides detailed information on medication taking behaviour (460), the CQR has been reported to compare well with MEMS over 6 months with a 98% sensitivity, 67% specificity and an estimated 78% ability to detect non-adherence (458, 460, 537).

6.3.3.3.2 Mood

Mood was assessed using the Hospital Anxiety & Depression Scale (HADS) (436). The HADS is a 14-item self-report instrument of depression and anxiety consisting of two 7-item sub-scales measuring how a person has been feeling in the past week. Each of the sub-scale scores range from 0-21, with higher scores indicating higher levels of anxious or depressed mood. A score of 0–7 for either subscale is regarded as being in the 'normal' range, a score of 8–10 is suggestive of the presence of moderate levels of anxiety or depression, and a score of >11 indicates 'caseness', a high likelihood that a person would be diagnosed to be suffering from clinical anxiety or clinical depression.

Authors of the scale noted that the depression items were based on the anhedonic state rather than anxiety on items of psychic manifestation of anxiety neurosis and personal research (436).The validity of the scale has recently been reviewed. A review of 71 studies utilising the HADs (538) concluded that the scale performs well in assessing the symptom severity and caseness of anxious and depressed mood in somatic, psychiatric and primary care patients and in the general population. More specifically, internal consistency scores ranged for HADS-anxiety from .68 to .93 and for HADS-depression from .67 to .90. Authors report the sensitivity and specificity for both sub-scales to be approximately 80%, however it is worth noting that a meta-analysis of depression studies in RA notes that the HADs scale led to an overestimation of depression compared to other scales (373).

6.3.3.3.3 Generic Health-related quality of life (HRQoL)

As described in Chapter 2, the Short Form-36 (SF-36) scale (175) is the most commonly used HRQoL instrument in SLE and RA. It is a generic instrument that assesses HRQoL in detail and enables the computation of two overarching component sub-scales that cover physical and mental quality of life. Using the SF-36 enables comparisons to be made with other chronic conditions and population based norms.

A shortened version of the SF-36, the SF-12v^2 was used in this study to reduce participant burden. The SF-12v^2, comprises 12 items of the original items across eight physical functioning dimensions, role limitations because of physical health problems, bodily pain, general health perceptions, vitality (energy/fatigue), social functioning, and role limitations because of emotional problems and general mental health (psychological distress and psychological well-being). Items are scored on 5-point Likert scales of frequency and severity and 3-point Likert scales of the extent limitation, with higher scores reflecting better HRQoL.

The UK version of the instrument was used (539) and total scores were computed for the two overarching component sub-scales, the physical component (PCS) and the mental component (MCS) sub-scale. Computation of scale scores was conducted using the Health Outcomes Scoring Software 4.0 (available with the licensed version of the scale) which produces transformed total scores ranging from 0 to 100 metric through item aggregation and transformation. It has been reported that both the PCS and MCS scores calculated by the SF-12 are virtually identical to those calculated from the SF-36 showing the same magnitude of HRQoL and change over time (540).

The SF-12 as it is a shorter version of the SF-36 instrument which has proved to be internally consistent and valid in SLE (541) and it was chosen so as to reduce participant burden whilst having the option of comparing the two composite scores with levels of HRQoL in the healthy population and other chronic conditions using the norms offered by the instrument developers (539, 540).

6.3.3.3.4 Disease-specific HRQoL

In addition to the SF-12v^2, disease specific instruments of HRQoL were also used as they target domains that are highly important to these specific patient groups which are not targeted by generic instruments.

6.3.3.3.4.1 Systemic Lupus Erythematosus Quality of Life - LupusQoL

The LupusQoL was the disease-specific HRQoL instrument chosen on the basis its empirical development (396) which improves its content validity in SLE. The authors of the LupusQoL having reviewed the existing SLE and HRQoL literature conducted qualitative interviews with SLE patients to develop the content of the LupuQoL (396). Refinement and psychometric validation of the LupusQoL were completed in several stages in the UK and specifically across two of the sites that participated in this study as well (Royal Blackburn Hospital and University College London) further ensuring its relevance for the sample assessed in this study.

This resulted in a multi-dimensional instrument covering domains and issues specifically important to SLE patients, which are not addressed by generic HRQoL instruments like the SF-12. The domains include physical health (assessing challenges with everyday physical activities), emotional health (assessing feelings of sadness, anxiety, worry, resentfulness and self-confidence), body image (assessing sense of attractiveness and body's interference with life), pain (assessing pain interference with activities, sleep and mobility), planning (assessing SLE interference with planning events), fatigue (assessing morning exhaustion, fatigue manifestations like lack of concentration), intimate relationships (assessing interest in sexual life) and the burden on others (assessing the extent of burden, stress and worry SLE brings to others). The eight domains reflect the diverse range of impact SLE can ultimately have on patients` lives and are comparable to the uncertainty impact sub-domains revealed in the conceptual framework of this study (Figure 3.1).

LupusQoL respondents are asked to respond to the items in relation to the past 4 weeks using a 5-point frequency scale ranging from 1=all the time to 5=never. Total scores are computed by summing the scores in each of the eight domains, with higher

scores reflecting better HRQoL. High internal consistency has been reported for all eight domains (0.88 – 0.96), good test re-test reliability (0.72-0.93), and demonstrated discriminant validity with levels of organ damage and disease activity as measured by BILAG, which was the chosen disease activity measure in this study as well. Despite being a disease-specific HRQoL, association between LupusQoL and disease activity is weak (178), suggesting it is an independent outcome of illness. The LupusQoL has been increasingly popular internationally and has been linguistically adapted for US English and further validated using traditional psychometrics in a US SLE population (178).

6.3.3.3.4.2 Rheumatoid Arthritis AIMS2-SF

The short form of the Arthritis Impact Measurement Scales 2 (AIMS2 –SF) (398) instrument was utilised to assess disease-specific HRQoL in RA. The original AIMS was developed by building on two previous health status measures (338) and the addition of items related to social role, specific daily activities and pain.

The AIMS2-SF comprises 26 of the 57 original items and refined using a Delphi technique. Items are spread across five component scales including physical (assessing physical functioning), symptom (assessing pain and stiffness), affect (assessing feelings of burden, low mood and nervousness), social interaction (assessing the amount of social interaction and sensitivity of others` to respondents` needs) and role (assessing inability or challenges with employment).

All items are scored on a 5-point frequency Likert-scale. Contrary to the other HRQoL scales, higher scores on all of the AIMS2-SF scales reflect poorer health status. Even though the content of the AIMS2-SF was not empirically developed using patient qualitative interviews like the LupusQoL it was chosen on the basis of its popularity and validity in RA research. AIMS2-SF has been reported to be a valid measure of functional status and sensitive to change as assessed by other disease activity parameters (542-544). Furthermore, in comparison with the other popular measure of disease-specific HRQoL in RA (337) the AIMS2-SF comprises a diverse set of items relating to differential types of impact (e.g. physical, social and role) which was more relevant to the uncertainty impact sub-domains revealed in the conceptual framework of this study (Figure 3.1) contrary to other RA-disease specific instruments which are qualitatively developed but are scored uni-dimensionally (398).

6.3.3.4 Other Patient Reported Variables

Patient beliefs which are related to a range of issues including medication and self-efficacy along with coping strategies and the amount and satisfaction with social support have been shown to contribute to patient outcomes in SLE and RA and were assessed.

6.3.3.4.1 Beliefs about Medication

Beliefs about medication that have been found to contribute to important patient outcomes such as treatment adherence (460) were studied. The Beliefs Medicines Questionnaire (BMQ) (22) was used in this study as medication beliefs may be important in both conditions under study. The BMQ comprises 18 items across two sub-scales developed the through refinement of a bigger item pool which was derived from general literature in a large sample of patients of six chronic illness groups (477). The BMQ-specific scale consists of two factors assessing necessity and concerns about an individual`s prescribed medication, whereas the BMQ-general scale consists of two factors, namely general harmfulness and overuse of medication. Items are scored on a 5-point agreement Likert scale ranging from 1=strongly disagree to 5=strongly agree. Summed total scores range from 5 to 25 for the BMQ-specific scale and from 6 to 30 and 5-25 for the BMQ-general scale. Higher scores on both scales indicate stronger beliefs in the concepts represented by the scales. Internal consistency for the specific scale is reported to range between 0.55 – 0.88 and 0.47 to 0.70 for the general scale (118, 460, 477), and test-retest reliability ranges from 0.60 to 0.78 over a 2 week period.

6.3.3.4.2 Self-efficacy

A number of self-efficacy instruments (545, 546) have been published and utilised with rheumatology samples. These measure belief in someone`s ability to perform a task. The General Perceived Self-Efficacy Scale (GSEC) was utilised in this study (547).The scale was developed by the author to reflect an optimistic self-belief that one can perform a novel or difficult task or cope with adversity in various domains (548, 549). There are ten items in this scale and each item refers to the ability to perform a task, and high scores imply an internal-stable attribution of the success of self-efficacy. Items are scored on a 4-point scale, where 1=not at all true, 2=hardly true, 3=moderately true and 4=exactly true, with higher scores indicating higher levels of self-efficacy.

A review of this instrument (550) reported the internal consistency coefficients for a variety of samples and countries, ranging from 0.75 to 0.91. Longitudinal studies reported variable stability coefficients ranging from 0.47 to 0.75, and further confirmed

the uni-dimensional factor structure in 28 countries using confirmatory factor analysis. Barlow et al (2005) further indicate the high internal consistency (0.88 – 0.91) of the GSEC in arthritis samples (551).

6.3.3.4.3 Coping

The brief Cope (552) 28-item self-report instrument of coping assesses a broad range of coping responses. This is an abbreviated version of the 60 item instrument (553) that was developed to reduce participant burden. Items of the Cope were developed theoretically on the basis of the Lazarus model of stress (24) and behavioural self-regulation model.

The instrument is divided into 14 sub-scales including self-distraction, active coping, denial, substance use, use of emotional support, use of instrumental support, behavioural disengagement, venting, positive reframing, planning, humour, acceptance, religion and self-blame. Participants are asked to report how frequently they engage in particular ways of coping. Items are scored on a 4-point frequency Likert scale ranging from 1=I haven't been doing this at all to 4=I've been doing this a lot. Scale scores range from 2-8, with higher scores indicating the greater use of that specific coping strategy.

The psychometric properties of brief COPE are modest, with internal consistency ranging between 0.5 and 0.9 (552) but good convergent and discriminant validity as assessed against dispositional variables of optimism, self-esteem and anxiety (553).

6.3.3.4.4 Social Support

The instrument utilised is a shortened four item version of the Short Form Social Support Questionnaire (554). Participants were asked to indicate the number of people in their social network that they are able to turn to for various types of support including sharing feelings, turning to in difficult times, practical help and spending time socially. The quantity responses were used as primers and were not included in the analysis. In response to each quantity, participants are asked to rate how satisfied they are with this type of support, with responses on a 6-point Likert-scale where 1=very satisfied to 6=very dissatisfied. Items were rescored and summed to produce a total score range from 4 to 24, with higher scores reflecting greater satisfaction with social support. The instrument has been adapted and used in the Health Services Research Group at City University.

6.3.4 Analysis

Parametric statistical techniques for comparing groups and exploring relationships among variables were utilised. Most rating scale literature utilises parametric statistical techniques (167). Even though parametric statistics should arguably only be used to analyse interval and not for ordinal data (191), researchers have argued that the choice of statistical tests should not be influenced by the nature of the scale used to collect data (555-557) as statistical tests assess a set of measurements and not the scales used to produce the instrument (558, 559). In addition, summed ordinal measurement approximates interval level measurement enough to justify the use of parametric tests (169). As described above, the instruments used in this chapter were ordinal apart from the PCQ, SF-12v2 and CRQ that provided transformed linear scores (0-100). Analyses were carried out using the IBM SPSS Statistics 21 software. Analysis for the first objective (Ii) was conducted on the total sample, whereas the remaining objectives were analysed in parallel in the two conditions using independent samples for SLE and RA.

6.3.4.1 Data cleaning

The data were checked by examining the ranges of all variables to ensure that they fell within the instruments` specified ranges, and any necessary errors were corrected. Internal consistency of the patient outcome variable scales was assessed using Cronbach`s alpha coefficient (526).

Missing data were calculated on item and scale level. Where data were missing randomly on a scale-level multiple imputation was used to replace missing values (560). Multiple imputation is an iterative procedure where multiple datasets are generated to replace the missing data with values on the basis of the remaining valid data. Tests and results are conducted and presented on the original and on each of the imputed datasets and a final combined “pooled” sample that averages the imputed datasets (561). Where specific patterns were retrieved and whole scales or subscales were missing, data on those scales were omitted from the analysis pairwise (for that specific case/person).

6.3.4.2 Construct Validity & Explorative Analysis

Univariate analyses were used for this exploration. Independent sample t-tests and one-way analysis of variance (ANOVAs) were used to compare patient uncertainty levels between binary and nominal groups respectively relative to objectives Ii and Iiii. The association between continuous variables (objectives Iii and Iiii) was assessed

using Pearson correlations. Following Cohen`s guidelines (1988, pp. 79-81), correlations in the range of 0.10 to 0.29 were considered small, 0.30 to 0.49 medium and >0.50 large (562).

6.3.4.3 The Contribution of Patient Uncertainty to Patient Outcomes

Single linear regression analysis was used to evaluate the extent to which patient uncertainty contributes to patient outcomes. Linear regression evaluates how much of the variance in a dependent outcome variable (in this case treatment adherence, mood and HRQoL) is accounted for by a single independent variable (i.e. patient uncertainty) (530). Multiple linear regressions (MLR) were subsequently used to evaluate the extent to which patient uncertainty and other variables contribute to patient outcomes. Similar to single linear regression, MLR evaluates how much of the variance in a dependent outcome variable is accounted for by a set of independent variables (530).

Linear regression does not require the predictor independent variables to be normally distributed, and predictors can be categorical as well as continuous (560). However, other assumptions need to be accounted for including normally distributed residuals, the lack of outliers and the lack of multicollinearity (i.e. an indication of strong linear association measured by Pearson correlations) between the independent variables (r=<0.7). Where independent variables were correlated above the 0.7 level, the one with the lower less correlation with the dependent variable was removed from the MLR model.

Preliminary univariate correlational analyses were performed between each dependent variable (DV) and potential contributors in order to identify which independent variables (IVs) to enter into the MLR. Univariate correlational analyses were performed between all IVs and DVs suggested by the literature and/or qualitative findings to have an association. Potential IVs included demographic characteristics, disease activity and all patient reported variables (including patient uncertainty, beliefs, self-efficacy, social support and coping). All variables displaying a small to large Pearson correlation (r> 0.1) were entered into the MRL. IVs were entered into the regression equation simultaneously using the “ENTER” method. The ENTER method was chosen as it evaluates the predictive power of each IV over and above the predictive power of the remaining IVs (530) and would therefore provide a comparison of patient uncertainty`s predictive power compared to other IVs.

There is no single sample size recommendation for multiple regression (563). It is generally recommended to take into account the number of independent variables in

each regression and aim to have a sample size of at least 50 + 8m (where m is the number of independent variables) (530, 564). Using the 50 + 8m sample size formula it was estimated that the SLE sample (n=165) could be used for a maximum of 14 IVs, whereas the RA sample (n=114) could be used for a maximum of 8 IVs without compromising the power of the analysis. If the number of IVs exceeded the above numbers (i.e. >14 for SLE and >8 for RA), a minimum correlation of 0.20 – 0.30 was used as a cut-off point to eliminate predictors that would be included in the MLR as IVs (530).

6.4 Results

Results are presented in reference to each of the research objectives. As the aim of this analysis was to explore patient uncertainty in SLE and RA, results are focused primarily on the interpretation of findings related to patient uncertainty. Findings related to the relationships between other patient variables are presented in tables but are only briefly described and interpreted.

6.4.1 Data cleaning

6.4.1.1 Missing data

The percentage of scale-level missing data is displayed on Tables 6.1.1 – 6.1.3. It was not possible to obtain a disease activity total score for 30.91% of the SLE sample. Information on participant age and disease duration was missing on 1.21 and 4.85% in the SLE and 6.14 and 12.28% of the RA sample (Table 6.1.1). Missing data on demographic characteristics ranged from 0.00 to 9.65% (Table 6.1.2). Missing data on the remaining patient outcome variables ranged from 0 to 64.85% (Table 6.1.3).

The elevated percentage of missing data in three of these sub-scales, including LupusQoL, Intimate Relationship and Body Image, and AIMS2-SF Role scales were due to their not-applicable response categories that are scored as missing-data. Scale-level missing data were input in all scales apart from the above three, as discovering where specific patterns were retrieved and random multiple input was not possible. Analyses involving these three scales were performed by omitting data pairwise, i.e. by omitting variables with non-random missing data.

The input “pooled” results are presented for all research questions. The significance and direction of results of the pooled dataset was consistent with the original and all five of the input datasets.

Table 6.1.1 Disease and Age Descriptive Data

	SLE			RA		
	Missing (%)	**range**	**Mean (SD)**	**Missing (%)**	**range**	**Mean (SD)**
Disease activity (BILAG)	**30.91**	0 - 18	4.25 (5.13)	**n/a**	n/a	n/a
Age	**1.21**	18 - 76	45.32 (14.34)	**6.1**	20 - 84	56.95 (12.52
Disease duration (yrs)	**4.85**	1 - 40	16.04 (10.8)	**12.3**	0.5 - 52	15.60 (12.37)

Table 6.1.2 Sample Characteristics

		SLE n (%)	**RA n (%)**
Gender			
	Female	158 (95.8)	87 (76.3)
	Male	7 (4.2)	27 (23.7)
	Missing	**-**	**-**
Ethnicity group			
	White	97 (58.8)	94 (82.5)
	Black	40 (24.2)	3 (2.6)
	Other	28 (17)	10 (8.8)
	Missing	**-**	**7 (6.1)**
Work group			
	Employed	81 (49.1)	50 (43.9)
	Unable/Unemployed	32 (19.4)	15 (13.2)
	Retired	29 (17.6)	37 (32.5)
	Other	23 (13.9)	5 (4.4)
	Missing	**-**	**7 (6.1)**
Living group			
	Living alone	36 (21.8)	18 (15.8)
	Living with partner	70 (42.4)	57 (50)
	Living with family	49 (29.7)	30 (26.3)
	Living other	10 (6.1)	4 (3.5)
	Missing	**-**	**5 (4.4)**
Education			
	No education	13 (7.9)	17 (14.9)
	Secondary education	59 (35.8)	41 (36)
	University education	85 (51.5)	45 (39.5)
	Missing	**8 (4.85)**	**11 (9.6)**

Table 6.1.3 Missing Data

	SLE Missing (%)	RA Missing (%)
PCQ symptoms & flares	0.60	0.00
PCQ medication	5.55	2.63
PCQ trust in doctor	0.60	2.63
PCQ self-management	1.21	11.40
PCQ impact	2.42	1.75
CQR compliance	13.33	13.2
HADs Anxiety	1.81	4.39
HADs Depression	1.21	2.64
SF12 PCS	1.21	0.00
SF12 MCS	1.21	0.00
Self-Efficacy	9.09	4.39
Social Support	4.24	2.63
BMQ General	3.03	16.67
BMQ Specific	3.64	15.80
Cope Active	2.42	21.05
Cope Planning	2.42	20.18
Cope Reframing	1.21	20.18
Cope Acceptance	1.81	20.18
Cope Humour	3.03	18.42
Cope Religion	2.42	20.18
Cope Emotional	3.6	19.30
Cope Instrumental	2.42	20.18
Cope Self-distraction	3.64	20.18
Cope Denial	2.42	20.18
Cope Venting	4.24	20.18
Cope Substance abuse	1.81	20.18
Cope Disengagement	3.04	20.18
Cope Self-blame	1.81	19.30
LupusQoL Physical Health	3.03	n/a
LupusQoL Planning	1.21	n/a
LupusQoL Pain	0.60	n/a
LupusQoL Intimate Relationships	26.67	n/a
LupusQoL Burden	0.60	n/a
LupusQoL Emotional Health	1.21	n/a
LupusQoL Body Image	64.85	n/a
LupusQoL Fatigue	1.81	n/a
AIMS2-SF Physical	n/a	2.64
AIMS2-SF Symptoms	n/a	0.88
AIMS2-SF Affect	n/a	2.64
AIMS2-SF Social Interaction	n/a	1.75
AIMS2-SF Role Limitations	n/a	58.78

6.4.1.2 Internal Consistency

Cronbach`s alpha scores are displayed on Table 6.1.4. Consistent with the total sample alphas (Table 5.24), the PCQ scales displayed consistently high internal consistency in both the SLE and RA samples as Cronbach`s alpha scores ranged between 0.82 and 0.93. Consistent with previous findings (537), the compliance questionnaire (CQR) displayed sub-optimal internal consistency in both samples (0.62 & 0.64). The remaining outcome variables including mood (HADs), generic HRQoL (SF-12v^2) and SLE-specific (LupusQoL) and RA-specific HRQoL (AIMS2-SF) displayed optimal internal consistency (>0.75), apart from the social interaction and role AIMS2-SF scales. As the role scale comprised only 2 items and displayed no internal consistency (alpha = 0.03) and a very high percentage of missing data (58.78), the scale was removed from any further analyses. Self-efficacy, social support, beliefs about medication (BMQ) and coping (brief Cope) produced satisfactory alphas in both samples except for some of the cope sub-scales (denial, venting, self-blame), which is consistent with previous findings (552) that displayed lower internal consistency in both SLE and RA.

6.4.2 Descriptive Data

6.4.2.1 Demographic and Disease Variables Descriptive Data

The characteristics of this sample were presented in section 5.5.2. A total of 165 SLE and 114 RA patients (total =279) completed the study`s questionnaire booklet. The SLE sample comprised 158 females and 7 males ranging between 18 and 76 years of age (mean=45.31) and a mean disease duration of 16.04 years (Table 6.1.1). The RA sample comprised 87 females and 27 males, ranging between 20 and 84 years of age (mean=56.95) and with a mean disease duration of 15.60 years (Table 6.1.1). SLE disease activity as quantified by the original BILAG global score ranged between 0 and 18, with an average of 4.25 indicating similar total disease activity scores with other UK studies (535, 565). Approximately 60% of the SLE participants were of white ethnicity and 25% of black, whereas the RA percentage of participants of white ethnicity was larger (82.5%). Additional demographic characteristics related to ethnicity, work, living and education status are displayed in Table 6.1.2.

Table 6.1.4 Cronbach`s Alpha

	SLE	RA
PCQ symptoms & flares	0.88	0.91
PCQ medication	0.88	0.90
PCQ trust in doctor	0.84	0.89
PCQ self-management	0.82	0.82
PCQ impact	0.93	0.87
CQR compliance	0.62	0.64
HADs Anxiety	0.90	0.85
HADs Depression	0.86	0.77
SF12 PCS	0.90	0.90
SF12 MCS	0.87	0.87
Self-efficacy	0.94	0.94
Social Support	0.91	0.92
BMQ General	0.78	0.70
BMQ Specific	0.85	0.83
Cope Active	0.83	0.72
Cope Planning	0.68	0.72
Cope Reframing	0.73	0.58
Cope Acceptance	0.67	0.53
Cope Humour	0.84	0.84
Cope Religion	0.84	0.90
Cope Emotional	0.64	0.62
Cope Instrumental	0.78	0.74
Cope Self-distraction	0.62	0.72
Cope Denial	0.64	0.68
Cope Venting	0.62	0.58
Cope Substance abuse	0.86	0.78
Cope Disengagement	0.76	0.59
Cope Self-blame	0.56	0.59
LupusQoL Physical Health	0.93	n/a
LupusQoL Planning	0.88	n/a
LupusQoL Pain	0.94	n/a
LupusQoL Intimate Relationships	0.96	n/a
LupusQoL Burden	0.89	n/a
LupusQoL Emotional Health	0.93	n/a
LupusQoL Body Image	0.84	n/a
LupusQoL Fatigue	0.82	n/a
AIMS2-SF Physical	n/a	0.88
AIMS2-SF Symptoms	n/a	0.80
AIMS2-SF Affect	n/a	0.84
AIMS2-SF Social Interaction	n/a	0.48
AIMS2-SF Role Limitations	n/a	0.03

6.4.2.2 Patient Uncertainty Descriptive Data

PCQ scales were transformed to a linearised scale of 0.00 – 100.00. Results are displayed in Table 6.2.1. Out of the five different scales, both SLE and RA participants displayed the lower level of uncertainty in the *self-management* scale, with mean scores above the scale mid-point. Compared to the RA sample, the SLE participants displayed relatively lower levels of uncertainty within *trust in doctor* and *medication* scales with mean scores >50, whilst reporting higher uncertainty in the *impact* and *symptoms and flares* scales with mean scores <50.

Table 6.2.1 Patient Certainty Questionnaire Descriptive Data

	SLE n=165			RA n=114			T-test n=279, df=277	
	Mean	**SD**	**range**	**Mean**	**SD**	**range**	**t**	**p-value**
Sympt. & Flares	47.71	11.27	0-100	54.25	13.46	0-100	-4.40	**0.00**
Medication	59.29	15.62	0-100	55.41	16.80	0-100	1.97	0.05
Trust in Doctor	59.03	13.06	0-100	58.58	16.40	0-100	0.25	0.81
Self-manag.	64.34	17.91	0-100	67.88	18.61	0-100	-1.59	0.11
Impact	49.67	19.47	0-100	44.51	20.05	0-100	2.14	**0.03**

6.4.2.3 Behavioural & Psychosocial Outcomes Descriptive Data

Mean treatment adherence in this sample was relatively lower than the mean adherence reported by other studies (65 – 85) (458, 460). The mean SLE (60.86) adherence score was lower than the RA (63.30), but this difference was not significant ($p = 0.06$).There was no significant difference between mood in the SLE and RA sample. Mean anxiety levels were relatively high, and the SLE mean (8.06) fell within the moderate range (8.00 – 10.00) and the RA mean (7.11) was just above the "normal range" (0.00 – 7.00) (436). Mean depression levels for both SLE (5.34) and RA (3.41) fell in the "normal" range (0.00 – 7.00).

Generic HRQoL mean scores in both SLE and RA fell below the SF-12v^2 scale mean (50.00). Physical (PCS) and mental (MCS) mean scores in SLE were 40.76 and 45.37 respectively, thus indicating relatively poor HRQoL, particularly in the PCQ domain. The mean PCS in the RA sample was even lower (35.61), whereas the MCS was average (50.37). In contrast to treatment adherence and mood there were significant differences of generic HRQoL scores in the two samples (Table 6.2.3) as the RA PCS mean score was significantly poorer than the SLE ($p<0.01$), whereas the SLE MCS mean score was significantly poorer in the SLE sample ($p<0.01$). These findings are consistent with previous literature (403, 404). Disease-specific HRQoL descriptive data are also displayed in Table 6.2.2.

Table 6.2.2 Behavioural & Psychosocial Outcomes Descriptive Data

	SLE n=165			RA n=114			T-test n=279, df=277	
	Mean	**SD**	**range**	**Mean**	**SD**	**range**	**t**	**p-value**
Adherence								
CQR	60.86	10.67	24.56 - 97.86	63.30	10.59	28.07 - 88.99	-1.91	0.06
Mood								
HADs Anxiety	8.06	4.97	0 - 21	7.11	4.27	0 - 20	1.70	0.90
HADs Depression	5.34	4.21	0 - 19	4.88	3.41	0 - 13	0.97	0.33
Generic HRQoL								
SF-12 PCS	40.76	12.12	13.76 - 66.19	35.61	10.96	12.27 - 57.67	3.63	0.00
SF-12 MCS	45.37	11.12	14.38 - 66.78	50.37	10.18	25.20 - 68.93	-3.82	0.00
SLE-specific HRQoL (LupusQoL)								
Physical Health	86.19	19.66	25.00-100.00	-	-	-	-	-
Emotional	91.16	16.06	29.00-100.00	-	-	-	-	-
Body Image	81.98	21.40	25.00-100.00	-	-	-	-	-
Pain	88.06	18.94	25.00-100.00	-	-	-	-	-
Planning	88.66	21.13	25.00-100.00	-	-	-	-	-
Fatigue	79.75	19.85	31.00-100.00	-	-	-	-	-
Intimate Relations* n=121	84.19	25.23	25.00-100.00	-	-	-	-	-
Burden* n=58	79.22	23.88	25.00-100.00	-	-	-	-	-
RA-specific HRQoL (AIMS2-SF)								
Physical	-	-	-	2.84	2.08	0.00 – 7.94	-	-
Symptoms	-	-	-	4.13	2.73	0.00 – 10.00	-	-
Affect	-	-	-	3.54	2.15	0.00 – 10.00	-	-
Social Interactions	-	-	-	5.11	1.69	1.88 – 8.13	-	-
Role* n=47	-	-	-	1.94	2.15	0.00 – 7.50	-	-

6.4.2.4 Other Patient Reported Variables Descriptive Data

Descriptive data of other the patient reported variables are displayed in Table 6.2.3. Both samples displayed relatively high social support, self-efficacy and specific beliefs about medication scores. Positive coping strategies including acceptance and active coping displayed the highest means in both samples, but self-distraction was also rated relatively high. Other negative coping strategies, notably denial, substance-abuse and disengagement were the lowest in both samples. None of the t-tests were significant, thus indicating that there were no significant differences on any of these variables between SLE and RA samples.

Table 6.3 Other Patient Reported Variables Descriptive Data

	SLE n=165			RA n=114			T-test n=279, df=277	
	Mean	**SD**	**range**	**Mean**	**SD**	**range**	**t**	**p-value**
Social Support:	19.85	4.78	4 - 24	19.87	4.95	4 - 24	-0.04	0.97
Self-efficacy:	30.67	6.69	4 - 40	31.21	-5.82	11 - 40	-0.71	0.48
Medication Beliefs:								
Specific	35.24	6.64	14 - 50	36.67	5.94	20 - 50	-1.83	0.07
General	21.44	6.08	8 - 37	20.24	6.25	8 - 36	1.54	0.13
Coping Strategies:								
Active	4.91	1.97	2 - 8	4.83	1.99	2 - 8	0.35	0.73
Planning	4.48	1.93	2 - 8	4.43	2.00	2 - 8	0.21	0.83
Reframing	4.56	1.99	2 - 8	4.62	2.27	2 - 8	-0.29	0.81
Acceptance	6.35	1.71	2 - 8	6.15	1.76	2 - 8	0.95	0.34
Humour	3.53	1.90	2 - 8	3.46	1.89	2 - 8	1.83	0.07
Religion	3.7	2.17	2 - 8	3.25	1.96	2 - 8	1.77	0.08
Emotional	4.45	1.81	2 - 8	4.38	2.05	2 - 8	0.28	0.78
Instrumental	3.99	1.82	2 - 8	4.13	1.99	2 - 8	-0.58	0.57
Self-distraction	4.71	2.00	2 - 8	4.63	2.24	2 - 8	0.31	0.76
Denial	2.64	1.26	2 - 8	2.69	1.28	2 - 8	-0.34	0.74
Venting	3.6	1.54	2 - 8	3.34	1.48	2 - 8	1.38	0.17
Substance-abuse	2.63	1.41	2 - 8	2.68	1.28	2 - 8	-0.30	0.76
Disengagement	2.7	1.34	2 - 8	2.74	1.31	2 - 8	-0.24	0.81
Self-blame	3.46	1.64	2 - 8	3.29	1.93	2 - 8	0.77	0.45

6.4.3 Is there a difference between the levels of patient uncertainty in SLE and RA?

Five independent sample t-tests were conducted to explore any differences between the levels of patient uncertainty across the five PCQ scales in SLE and RA (Table 6.2.1). The SLE and RA samples were not however matched on the basis of demographic variables (e.g. age, sex and disease duration). Significant differences were observed on two of the PCQ scales. The mean SLE score on the *symptoms and flares* scale (47.71) was significantly lower than the RA one (54.25) ($t=-4.403$, $p<0.01$), thus indicating that the SLE sample was significantly more uncertain with regards to symptoms interpretation and flare predictability. A significant difference in the opposite direction was observed on the *impact* scale. The SLE mean (49.67) was significantly higher than the RA one (44.51) ($t=2.14$, $p<0.05$), indicating that the SLE patients were significantly less uncertain with regards to the lack of any future impact of their condition on their lives. A border-line significant difference was observed on the *medication* scale as the SLE sample displayed a higher mean score (59.29) than the RA sample (55.41) ($t=1.972$, $p=0.05$). There was no significant difference between levels of uncertainty in the *trust in doctor* and *self-management* scales.

6.4.4 Is patient uncertainty associated with gender, age, disease-duration and illness severity?

6.4.4.1 SLE

There was no significant difference in the levels of uncertainty reported by females and males on any of the PCQ scales (Table 6.5.1). Older age was weakly correlated with lower levels of uncertainty in the *medication* (r=0.16), *trust in doctor* (r=0.13) and the *impact* (r=0.17) scales and higher level of uncertainty in the *symptoms and flares* (r=-0.14). Correlations between disease duration and patient uncertainty in all scales apart *symptoms and flares* were positive but weak (0.13 – 0.16) suggesting that longer disease duration was only weakly associated with lower levels of uncertainty.

The association of patient uncertainty and SLE disease activity was very weak (Table 6.4.2) with *the trust in doctor* (r=-0.12) and the *self-management* scale (r=0.19) suggesting that higher disease activity is weakly associated with higher uncertainty with regards to the *trust in doctor* and lower *self-managem*ent uncertainty Graphical representations of these associations are displayed in Appendices 6.1 – 6.3.

Table 6.4.1 PCQ Scales Association with Gender

	Female (n=158)		**Male (n = 7)**		**T-test n=165 (df = 163)**	
	Mean	**SD**	**Mean**	**SD**	**t**	**p - value**
SLE PCQ Scales						
Symptoms & Flares	47.66	11.523	48.57	8.324	0.21	0.84
Medication	58.84	15.170	63.43	25.304	0.48	0.63
Trust in Doctor	59.07	14.315	58.71	8.098	-0.07	0.95
Self-management	64.30	18.463	60.57	11.674	-0.53	0.59
Impact	49.65	19.775	48.57	15.555	-0.14	0.89
RA PCQ Scales	**Female (n=87)**		**Male (n = 27)**		**T-test n=114 (df = 112)**	
	Mean	**SD**	**Mean**	**SD**	**t**	**p - value**
Symptoms & Flares	55.14	14.45	51.41	9.32	1.26	0.21
Medication	55.05	17.71	56	14.42	-.26	0.80
Trust in Doctor	57.12	17.14	62.51	12.72	-1.51	0.13
Self-management	67.59	19.06	68.81	17.39	-.30	0.77
Impact	43.39	20.93	47.74	17.81	-.99	0.32

6.4.4.2 RA

Similar to SLE there was no significant difference in the levels of uncertainty reported by females and males on any of the PCQ scales (Table 6.4.1). Older age was weakly associated with lower levels of uncertainty in the *trust in doctor* (r=0.20) and *self-management* scale (Table 6.4.2), and higher uncertainty in the impact scale (r=0.18) Age displayed nearly no association with the levels of uncertainty in the *symptoms and flares* (r = 0.01) and *medication* (r = 0.03) scales.

Longer disease duration was weakly associated with lower levels of uncertainty (Table 6.4.2) in the *symptoms and flares* (r=0.26), *medication* (r=0.23), *trust in doctor* (r=0.14) and *self-management* (r=0.21) scales and higher patient uncertainty in the *impact* scale (r=-0.17). Graphical representations of these associations are displayed in Appendices 6.4 – 6.5.

Table 6.4.2 PCQ Scales Association with Age Disease Duration and Activity

	Age	Disease Duration	Disease activity
SLE PCQ Scales			
Symptoms & Flares	-0.14	0.01	-0.07
Medication	0.16	0.14	0.01
Trust in Doctor	0.13	0.13	-0.12
Self-management	0.06	0.15	-0.19
Impact	0.17	0.16	-0.02
RA PCQ Scales			
Symptoms & Flares	0.01	0.26	-
Medication	0.03	0.23	-
Trust in Doctor	0.20	0.14	-
Self-management	0.21	0.21	-
Impact	-0.18	-0.17	-

Pearson correlations examined following Cohen`s guidelines; r: 0.10 to 0.29 were considered small, r: 0.30 to 0.49 medium and >0.50 large (562).

6.4.5 Is patient uncertainty associated with social support and any specific coping strategies?

6.4.5.1 SLE

Pearson correlations were computed to address this research objective (Table 6.5). *Symptoms and flares* patient uncertainty displayed minimal association with the coping strategies. Higher levels of uncertainty in the *medication* scale were weakly associated with more instrumental, coping, substance-abuse, disengagement and self-blame strategies (r = -0.10 to -0.18). Higher uncertainty in the *trust in doctor* scale was weakly associated with more substance-abuse (r = -0.18) and in the *self-management* scales with more denial strategies (r = -0.18). Lower uncertainty in relation to the lack of future *impact* was weakly associated with more self-blame (r = 0.19) and less active, planning, acceptance and religion strategies (r = -0.12 to -0.21). Higher levels of satisfaction with social support were weakly associated with lower levels of uncertainty in all scales (r = 0.11 – 0.25) apart from symptoms and flares.

Table 6.5 SLE: PCQ Scales Associations with Social Support and Coping

PCQ scales:	Symptoms & Flares	Medication	Trust in Doctor	Self-management	Impact
Social Support	0.04	0.11	0.19	0.14	0.25
Coping Strategies					
Active	0.00	-0.03	-0.13	0.15	-0.16
Planning	0.09	-0.06	-0.09	0.09	-0.21
Reframing	0.09	0.04	-0.01	0.11	-0.02
Acceptance	-0.00	-0.14	-0.09	0.08	-0.12
Humour	0.01	0.02	0.02	0.06	-0.06
Religion	0.05	-0.09	-0.07	-0.03	-0.14
Emotional	0.01	-0.13	-0.07	-0.03	-0.07
Instrumental	0.02	-0.16	-0.09	-0.01	-0.09
Self-distraction	0.11	-0.02	-0.06	-0.04	-0.11
Denial	-0.05	-0.05	-0.03	-0.18	0.14
Venting	0.05	-0.18	-0.07	-0.08	-0.13
Substance-abuse	0.01	-0.11	-0.18	-0.06	-0.11
Disengagement	0.01	-0.10	0.01	-0.06	-0.14
Self-blame	0.10	-0.11	-0.06	-0.08	0.19

Pearson correlations examined following Cohen`s guidelines; r: 0.10 to 0.29 were considered small, r: 0.30 to 0.49 medium and >0.50 large (562).

6.4.5.2 RA

Pearson correlations computed for this research question are presented in Table 6.6. Consistent with the SLE sample, patient uncertainty related to *symptoms and flares* was not associated with any coping strategy apart from a weak association with religion (r = -0.10) and disengagement (r = 0.16). Higher levels of uncertainty in the *medication* scales were moderately associated with the higher use of planning and religion (r = 0.30), and weakly associated with higher use of instrumental, self-distraction, denial and venting (r = -0.13 to -0.25) coping strategies. Increased use of instrumental, denial and substance abuse was weakly correlated with higher uncertainty in the *trust in doctor* scale (r = -0.14 to -0.20). Increased use of planning, emotional, instrumental and denial strategy was weakly correlated with higher uncertainty in the *self-management scale* (r = -0.15 to -0.22). Higher uncertainty in the *impact* scale was moderately correlated with higher use of venting (r = -0.42) and self-blame (r = -0.38) and weakly correlated with the use of more denial and self-distraction coping. Higher levels of satisfaction with social support were weakly associated with lower levels of uncertainty in all uncertainty scales (r = 0.10 to 0.31).

Table 6.6 RA PCQ Scales Association with Social Support and Coping

PCQ scales:	Symptoms & Flares	Medication	Trust in Doctor	Self-management	Impact
Social Support	0.18	0.25	0.33	0.10	0.31
Coping Strategies					
Active	-0.17	-0.16	-0.09	-0.09	-0.03
Planning	-0.16	-0.30	-0.10	-0.15	-0.09
Reframing	-0.03	-0.13	-0.11	0.04	0.02
Acceptance	-0.02	-0.07	-0.04	0.05	0.09
Humour	0.17	0.10	0.09	-0.00	0.04
Religion	-0.10	-0.29	0.09	-0.01	-0.09
Emotional	-0.09	-0.08	0.00	-0.15	0.04
Instrumental	-0.17	-0.25	-0.14	-0.18	-0.12
Self-distraction	-0.05	-0.13	-0.10	-0.04	-0.17
Denial	-0.09	-0.16	-0.20	-0.22	-0.23
Venting	-0.07	-0.13	-0.04	-0.11	-0.42
Substance-abuse	0.04	0.02	-0.14	-0.01	-0.17
Disengagement	0.16	-0.41	0.02	-0.08	-0.15
Self-blame	0.08	-0.17	-0.07	-0.13	-0.38

Pearson correlations examined following Cohen`s guidelines; r: 0.10 to 0.29 were considered small, r: 0.30 to 0.49 medium and >0.50 large (562).

6.4.6 The Association of Patient Uncertainty with Patient Outcomes

The association of each of the PCQ scales to patient outcomes including adherence, anxiety, depression and HRQoL was explored using single linear regressions. The significance of standardised beta coefficients and the R square scores were used to interpret the regression analysis. Standardised beta coefficients indicate how many standard deviations a dependent variable will change per standard deviation increase in an independent variable. The R^2 indicates the percentage of variance in the dependent variable explained by the regression model. The association of patient uncertainty relative to other variables to outcomes was explored using multiple linear regressions. Standardised beta coefficients were used to interpret these results.

6.4.7 Are higher levels of patient certainty associated with lower levels of treatment adherence?

Higher scores on all of the PCQ scales denote lower uncertainty, whereas higher scores on the CQR instrument denote higher levels of adherence.

SLE sample: Three of the PCQ scales were significantly associated with the levels of treatment adherence (Table 6.7). Higher levels of uncertainty in the *medication*, *trust in doctor* and *impact* scales were associated to lower adherence, explaining 4.90%, 10.90% and 3.20% of the adherence variance respectively.

RA sample: Higher levels of uncertainty in the *symptoms and flares*, *medication* and *trust in doctor* scales were associated with lower levels of treatment adherence, explaining 4.50%, 12.80% and 8.70% of the adherence variance respectively (Table 6.8).

Table 6.7 SLE PCQ Sub-sales Contribution to Patient Outcomes (Single Linear Regressions)

		CQR	HADs		SF-12					LupusQoL				
IVs:		**Compl.**	**Anxiety**	**Depres.**	**PCS**	**MCS**	**Physic Health**	**Plann.**	**Pain**	**Intim. Relat.**	**Burden**	**Emot. Health**	**Body Image**	**Fatigue**
Symptoms & Flares	**Beta**	0.156	0.010	0.000	-0.053	-0.099	-0.096	-0.067	**-0.163***	0.009	-0.043	-0.065	-0.042	-0.094
	R^2	0.024	0.000	0.000	0.003	0.010	0.009	0.004	0.026	0.000	0.002	0.004	0.002	0.009
Medication	**Beta**	**0.217***	**-0.183***	**-0.286****	**0.281****	**0.219****	**0.316****	**0.308****	**0.295****	0.148	**0.404****	**0.308****	0.248	**0.331****
	R^2	0.047	0.033	0.082	0.079	0.048	0.100	0.095	0.087	0.022	0.163	0.092	0.062	0.110
Trust in doctor	**Beta**	**0.331****	**-0.234****	**-0.359****	**0.209****	**0.206****	**0.261****	**0.225****	**0.247****	0.152	**0.170***	**0.223****	0.195	**0.236****
	R^2	0.109	0.055	0.129	0.044	0.043	0.071	0.051	0.061	0.023	0.029	0.050	0.038	0.056
Self-manag.	**Beta**	0.082	**-0.281****	**-0.214****	0.074	**0.156***	0.066	0.145	0.082	0.107	**0.169***	**0.207****	0.102	**0.169***
	R^2	0.007	0.079	0.046	0.006	0.024	0.004	0.021	0.007	0.011	0.029	0.043	0.010	0.029
Impact	**Beta**	**0.180***	**-0.381****	**-0.516****	**0.467****	**0.305****	**0.542****	**0.550****	**0.468****	**0.291****	**0.516****	**0.396****	**0.480****	**0.550****
	R^2	0.032	0.145	0.266	0.218	0.093	0.294	0.303	0.219	0.085	0.266	0.157	0.230	0.262

CQR Compliance Questionnaire Rheumatology; HADs Hospital Depression and Anxiety scale; PCS physical component scale (SF-36); MCS mental component scale (SF-36); PH Physical Health (LupusQoL); PL Planning (LupusQoL); PA Pain (LupusQoL); IR Intimate Relations (LupusQoL); BU Burden (LupusQoL); EH Emotional Health (LupusQoL); BI Body Image (LupusQoL); FA Fatigue (LupusQoL).

**** beta significant at p<0.05, ** beta significant at p<0.01***

Table 6.8 RA PCQ Sub-sales Contribution to Patient Outcomes (Single Linear Regressions)

		CQR	HADs		SF-12		AIMS2-SF			
		Compl.	Anxiety	Depres.	PCS	MCS	Physical	Symptoms	Affect	Social Interaction
IVs:										
Symptoms & Flares	**Beta**	0.213*	-0.070	0.025	-0.103	0.036	**0.194***	**0.128***	0.018	-0.115
	R^2	0.045	0.005	0.001	0.011	0.001	0.038	0.016	0.000	0.013
Medication	**Beta**	**0.358****	**-0.196***	-0.162	**0.209***	**0.169***	**-0.187***	**-0.362****	**-0.200***	-0.009
	R^2	0.128	0.038	0.026	0.044	0.028	0.035	0.131	0.040	0.000
Trust in doctor	**Beta**	**0.296****	-0.115	-0.092	**0.073***	0.052	0.016	-0.034	-0.097	**-0.301****
	R^2	0.087	0.013	0.008	0.005	0.003	0.000	0.001	0.009	0.091
Self-manag.	**Beta**	0.045	**-0.196***	**-0.236***	**0.092***	**0.200***	0.041	-0.171	-0.097	**-0.154***
	R^2	0.002	0.038	0.059	0.008	0.040	0.002	0.029	0.009	0.024
Impact	**Beta**	0.146	**-0.418****	**-0.565****	**0.509****	**0.344****	**-0.510****	**-0.297****	**-0.515****	**-0.230***
	R^2	0.021	0.175	0.319	0.259	0.118	0.260	0.088	0.265	0.053

CQR Compliance Questionnaire; HADs Hospital Depression and Anxiety scale; PCS physical component scale (SF-36); MCS mental component scale (SF-36

**** beta significant at p<0.05, ** beta significant at p<0.01***

6.4.7.1 Is this association significant relative to other demographic, illness and patient variables associated with treatment adherence in SLE?

The eight variables that displayed small to medium Pearson correlations with treatment adherence as assessed by the CQR questionnaire (Appendix 6.6) were entered into a multiple linear regression (MLR) model. The model was significant (F=5.36, p<0.01), explaining 30.10% of the adherence variance (Table 6.9). *Trust in doctor* was the uncertainty scale with a significant positive to adherence relative, indicating that lower PCQ scores (i.e. higher uncertainty) were associated with lower treatment adherence as was Black ethnicity and heightened general beliefs about medication.

Table 6.9 SLE: Multiple Linear Regression Model for Treatment Adherence

	Unstandardised Coefficients		**Standard. Coefficients**			**95% Confidence Interval for B**	
Model	**B**	**SE**	**Beta**	**t**	**sig.**	**lower bound**	**upper bound**
Constant	54.442	8.942		6.089	0.000	36.725	72.725
Ethnicity/Black	**-5.165**	**2.020**	**-.217**	**-2.557**	**0.012***	**-9.168**	**-1.163**
PCQ Medication	.075	.063	.109	1.186	0.238	-.050	.199
PCQ Trust in Doctor	**.178**	**.071**	**.244**	**2.492**	**0.014***	**.036**	**.319**
PCQ Impact	-.071	.058	-.132	-1.213	0.228	-.186	.045
HADs Depression	.149	.271	.061	.549	0.584	-.389	.686
Self-efficacy	.224	.164	.137	1.365	0.175	-.101	.548
Social support	.052	.188	.024	.275	0.784	-.321	.424
BMQ General	**-.430**	**.153**	**-.250**	**-2.808**	**0.006****	**-.734**	**-.127**
Cope Disengagement	-1.033	.714	-.131	-1.446	0.151	-2.447	.382
		R^2	0.301				
		F	**5.360****				

Dependent variable SLE treatment adherence
P value significant at <0.05, **P value significant at <0.01

6.4.7.2 Is this association significant relative to other demographic, illness and patient variables associated with treatment adherence in RA?

Only five variables displayed small to medium Pearson correlations with treatment adherence as assessed by the CQR questionnaire (Appendix 6.7). An MLR model of these five IVs was significant (F=6.60, p<0.01), explaining 23.40% of the adherence variance (Table 6.10). None of the PCQ scales displayed a significant association with treatment adherence on the multivariate level, however greater satisfaction with social support and heighted specific beliefs about medication were significantly associated with higher levels of treatment adherence.

Table 6.10 RA: Multiple Linear Regression Model for Treatment Adherence

	Unstandardised Coefficients		**Standard. Coefficients**			**95% Confidence Interval for B**	
Model	**B**	**SE**	**Beta**	**t**	**sig.**	**lower bound**	**upper bound**
Constant	24.454	8.074		3.029	0.003	8.451	40.458
PCQ sympt. & flares	.017	.082	.022	.202	0.840	-.146	.179
PCQ medication	.148	.060	.240	2.456	0.016	.029	.268
PCQ trust in doctor	.057	.070	.090	.810	0.420	-.082	.196
Social support	**.443**	**.194**	**.212**	**2.286**	**0.024***	**.059**	**.826**
BMQ Specific	**.486**	**.163**	**.260**	**2.977**	**0.004****	**.162**	**.809**
		R^2	0.234				
		F	**6.598****				

Dependent variable RA treatment adherence
P value significant at <0.05, **P value significant at <0.01

6.4.8 Are higher levels of patient uncertainty associated with higher levels of depression and anxiety?

Higher scores on all of the PCQ scales denote lower uncertainty, whereas higher scores on the HADs instrument denote higher levels of anxiety and depression

SLE sample: Higher levels of uncertainty in the *medication*, *trust in doctor*, *self-management* and *impact* scales were associated with higher levels of anxiety and depression, explaining a range of 3.30% to 14.50% of the variance in anxiety and 4.60 to 26.70% of the variance in depression (Table 6.7).

RA sample: Higher levels of uncertainty in the *medication*, *self-management* and *impact* scales were associated with higher anxiety levels, accounting for 3.80% to 17.50% of the anxiety variance. Higher levels of uncertainty in the *self-management* and *impact* scales were associated with higher depression levels and accounted for 5.90% and as much as 31.90% of the depression variance respectively.

6.4.8.1 Is this association significant relative to other demographic, illness and patient variables associated with anxiety and depression in SLE?

6.4.8.1.1 SLE Anxiety

A total of fifteen variables produced small to medium Pearson correlations with anxiety (Appendix 6.6). To safeguard sufficient power, the three variables with correlation <0.20 (PCQ *medication*, Cope-denial and disease activity) were eliminated and a final pool of 12 IVs was entered in the MLR model. The model was significant (F=17.19, p<0.01), explaining 61.20% of the anxiety variance (Table 6.12). *Self-management* was the only uncertainty scale with a significant negative association with anxiety, indicating that lower PCQ scores (i.e. higher uncertainty) related to higher levels of anxiety. Depression levels and heightened specific beliefs about medication were also significantly associated with higher anxiety scores.

Table 6.11 SLE: Multiple Linear Regression Model for of Anxiety

	Unstandardised Coefficients		Standard. Coefficients			95% Confidence Interval for B	
	B	**SE**	**Beta**	**t**	**Sig.**	**Lower Bound**	**Upper Bound**
(Constant)	-.280	3.364		-.083	.934	-6.936	6.375
PCQ Trust in Doctor	.011	.024	.033	.481	.632	-.036	.058
PCQ Self-manag.	**-.035**	**.016**	**-.125**	**-2.139**	**.034***	**-.067**	**-.003**
PCQ Impact	.020	.019	.078	1.052	.295	-.018	.058
HADs depression	**.770**	**.091**	**.652**	**8.431**	**.000****	**.589**	**.950**
Self-efficacy	-.067	.056	-.085	-1.198	.233	-.178	.044
Social support	.064	.065	.062	.994	.322	-.064	.192
BMQ Specific	**.115**	**.046**	**.154**	**2.502**	**.014***	**.024**	**.206**
BMQ General	-.003	.051	-.004	-.064	.949	-.103	.097
Cope Self-distraction	.282	.161	.115	1.752	.082	-.036	.601
Cope Venting	-.092	.240	-.029	-.385	.701	-.566	.382
Cope Disengagement	-.276	.264	-.073	-1.045	.298	-.798	.246
Cope Self-blame	.395	.228	.130	1.729	.086	-.057	.847
		R^2	**0.612**				
		F	**17.190****				

Dependent variable SLE HADs Anxiety
****P value significant at <0.05, **P value significant at <0.01***

6.4.8.1.2. SLE Depression

A total of fifteen variables produced small to large Pearson correlations with depression (Appendix 6.6). To safeguard sufficient power the three variables with correlation <0.20 (Cope planning and Cope religion) were eliminated and a final pool of 13 IVs was entered in the MLR model. The model was significant (F=22.39, p<0.01), explaining 69.50% of the depression variance (Table 6.12). *Impact* was the only uncertainty scale with a significant negative association with depression, indicating that lower PCQ scores (i.e. higher uncertainty) related to higher levels of depression. Anxiety levels and denial were positively associated with higher levels of depression, whereas self-efficacy contributed negatively to depression levels.

Table 6.12 SLE: Multiple Linear Regression Model for Depression

	Unstandard. Coefficients		Standard. Coefficients			95% Confidence Interval for B	
	B	SE	Beta	t	Sig.	Lower Bound	Upper Bound
(Constant)	7.892	2.556		3.087	.002	2.834	12.950
PCQ Medication	-.024	.017	-.086	-1.447	.150	-.057	.009
PCQ Trust in Doctor	-.032	.018	-.106	-1.726	.087	-.068	.005
PCQ Self-management	.025	.013	.105	1.880	.062	-.001	.051
PCQ Impact	**-.032**	**.015**	**-.146**	**-2.129**	**.035***	**-.061**	**-.002**
HADs anxiety	**.454**	**.053**	**.536**	**8.565**	**.000****	**.349**	**.558**
Self-efficacy	**-.097**	**.042**	**-.145**	**-2.290**	**.024***	**-.181**	**-.013**
Social support	-.075	.049	-.085	-1.527	.129	-.172	.022
BMQ Specific	-.022	.036	-.034	-.598	.551	-.093	.050
BMQ General	.007	.039	.010	.183	.855	-.071	.085
Cope Denial	**.461**	**.193**	**.135**	**2.386**	**.019***	**.079**	**.843**
Cope Venting	-.038	.171	-.014	-.224	.823	-.377	.301
Cope Disengagement	.368	.205	.115	1.797	.075	-.037	.774
Cope Self-blame	.015	.175	.006	.088	.930	-.330	.361
		R^2	**0.695**				
		F	**22.388****				

Dependent variable SLE HADs Depression
P value significant at <0.05, **P value significant at <0.01

6.4.8.2 Is this association significant relative to other demographic, illness and patient variables associated with anxiety and depression in RA?

6.4.8.2.1 RA Anxiety

Nine variables displayed small to large Pearson correlations with anxiety (Appendix 6.7). PCQ *self-management* produced a low correlation (<0.20) and was eliminated from the final pool of 8 IVs entered in the MLR model. The model was significant (F=14.75, p<0.01), explaining 52.90% of the anxiety variance (Table 6.13). None of the PCQ scales remained significant on a multivariate level. Depression levels were significantly associated with anxiety compared to other IVs, whereas greater satisfaction with social support was associated with lower anxiety scores.

Table 6.13 RA: Multiple Linear Regression Model for Anxiety

	Unstandard. Coefficients		Standard. Coefficients			95% Confidence Interval for B	
	B	SE	Beta	t	Sig.	Lower Bound	Upper Bound
(Constant)	6.045	3.892		1.553	.123	-1.672	13.763
PCQ Impact	.008	.019	.037	.418	.677	-.030	.046
HADs depression	**.619**	**.125**	**.492**	**4.973**	**.000****	**.372**	**.866**
Self-efficacy	-.095	.070	-.124	-1.360	.177	-.234	.044
Social support	**-.150**	**.064**	**-.173**	**-2.350**	**.021***	**-.276**	**-.023**
BMQ Specific	.042	.060	.054	.705	.482	-.076	.161
BMQ General	.052	.058	.064	.896	.372	-.063	.166
Cope Venting	-.026	.246	-.009	-.107	.915	-.514	.462
Cope Self-blame	.312	.224	.116	1.391	.167	-.133	.756
		R^2	**0.529**				
		F	**14.749****				

Dependent variable RA HADs Anxiety
****P value significant at <0.05, **P value significant at <0.01***

6.4.8.2.2 RA Depression

A total of eleven variables displayed small to large Pearson correlations with depression (Appendix 6.7). To safeguard sufficient power the four variables with correlation <0.30 (PCQ *self-management*, BMQ general, denial and disengagement) were eliminated and a final pool of 7 IVs was entered in the MLR model. The model was significant (F=25.41, p<0.01), explaining 60.20% of the depression variance (Table 6.14). *Impact* was the only uncertainty scale with a significant negative association with depression, indicating that lower PCQ scores (i.e. higher uncertainty) associated with higher levels of depression. Anxiety levels and denial were significantly associated with depression compared to other IVs but positively, whereas self-efficacy was associated with depression negatively.

Table 6.14 RA: Multiple Linear Regression Model for Depression

	Unstandard. Coefficients		**Standard. Coefficients**			**95% Confidence Interval for B**	
	B	**SE**	**Beta**	**t**	**Sig.**	**Lower Bound**	**Upper Bound**
(Constant)	7.564	2.536		2.982	.004	2.535	12.592
PCQ Impact	**-.035**	**.013**	**-.206**	**-2.674**	**.009****	**-.061**	**-.009**
HADs anxiety	**.315**	**.061**	**.397**	**5.146**	**.000****	**.194**	**.436**
Self-efficacy	**-.167**	**.047**	**-.273**	**-3.578**	**.001****	**-.260**	**-.074**
Social support	-.003	.046	-.004	-.066	.948	-.094	.088
BMQ Specific	.026	.042	.042	.614	.540	-.058	.109
Cope Denial	.066	.170	.027	.386	.701	-.272	.403
Cope Self-blame	.235	.156	.110	1.503	.136	-.075	.545
		R^2	**0.602**				
		F	**25.411****				

Dependent variable RA HADs Depression
****P value significant at <0.05, **P value significant at <0.01***

6.4.9 Are higher levels of patient uncertainty associated with poorer HRQoL (generic)?

Higher scores on all of the PCQ scales denote lower uncertainty, whereas higher scores on the SF-12v^2 instrument denote better HRQoL.

SLE sample: Higher levels of uncertainty in the *medication*, *trust in doctor* and *impact* scales were associated with lower levels of HRQoL on the physical component subscale, explaining 7.90, 4.40 and 21.80% of the PCS variance respectively. Similarly, higher uncertainty in all of the PCQ scales apart from the *symptoms and flares* were negatively associated with the mental component subscale, explaining a range of 2.40% to 9.30% of the MCS variance (Table 6.7).

RA sample: Higher levels of uncertainty in the *medication*, *trust in doctor*, *self-management* and *impact* scales were associated with lower levels of HRQoL on the physical component subscale, explaining 4.40%, 0.50%, 0.80% and 25.90% of the PCS variance respectively. Similarly, higher uncertainty in the *medication* and *self-management* scores were associated negatively with the mental component sub-scale scores, explaining 2.80% and 40% of the MCS variance, whereas the *impact* scale accounted for 11.80% of the variance (Table 6.8).

6.4.9.1 Is this association significant relative to other demographic, illness and patient variables associated with HRQoL in SLE?

6.4.9.1.1 SLE SF-12v^2 Physical Component Subscale (PCS)

Twelve variables displaying small to medium Pearson correlations with a physical component subscale (PCS) (Appendix 6.6) were entered into a multiple linear regression (MLR) model. The HADs anxiety scale was excluded due to high multi-colinearity with the HADs depression scale. The model was significant (F=10.94, p<0.01), explaining 48.10% of the adherence variance (Table 6.15). *Impact* was the only uncertainty scale with a significant positive association with PCS, indicating that lower PCQ scores (i.e. higher uncertainty) were associated with lower levels of HRQoL within the physical component. Older age was also significantly associated with lower PCS scores and poorer HRQoL.

Table 6.15 SLE: Multiple Linear Regression Model for HRQoL – SF-12 Physical Component Scale (PCS)

	Unstandard. Coefficients		Standard. Coefficients			95% Confidence Interval for B	
	B	SE	Beta	t	Sig.	Lower Bound	Upper Bound
(Constant)	56.829	9.645		5.892	.000	37.749	75.910
Age	**-.374**	**.057**	**-.446**	**-6.571**	**.000****	**-.486**	**-.261**
PCQ Medication	.101	.060	.126	1.682	.095	-.018	.219
PCQ Trust in Doctor	-.029	.067	-.034	-.438	.662	-.162	.103
PCQ Impact	**.254**	**.059**	**.405**	**4.319**	**.000****	**.137**	**.370**
HADs Depression	-.351	.252	-.122	-1.390	.167	-.849	.148
Self-efficacy	-.266	.161	-.139	-1.654	.100	-.585	.052
Social support	.243	.175	.096	1.388	.167	-.103	.590
BMQ Specific	-.170	.129	-.094	-1.316	.191	-.425	.085
BMQ General	-.049	.148	-.025	-.334	.739	-.341	.243
Cope Planning	-.662	.474	-.106	-1.398	.165	-1.599	.275
Cope Religion	-.237	.403	-.043	-.588	.558	-1.035	.561
		R^2	**0.481**				
		F	**10.935****				

Dependent variable SLE SF-12 PCS
****P value significant at <0.05, **P value significant at <0.01***

6.4.9.2 SLE SF-12 Mental Component Subscale (MCS)

A total of sixteen variables produced small to large Pearson correlations with the mental component subscale (MCS) (Appendix 6.6). To safeguard sufficient statistical power the three variables with the weakest correlations (PCQ *self-management*, BMQ general, denial and disease activity) were deleted, as was the HADs depression scale to eliminate multicolinearity. A final pool of 12 IVs was entered in the MLR model which was significant (F=16.37, p<0.01), explaining 60.40% of the MCS variance (Table 6.16). None of the PCQ scales displayed a significant association with MCS on a multivariate level. Anxiety was associated negatively, whereas self-efficacy and satisfaction in social support were associated positively compared to the remaining IVs.

Table 6.16 SLE: Multiple Linear Regression Model for HRQoL – SF-12 Mental Component Scale (MCS)

	Unstandard. Coefficients		**Standard. Coefficients**			**95% Confidence Interval for B**	
	B	**SE**	**Beta**	**t**	**Sig.**	**Lower Bound**	**Upper Bound**
(Constant)	42.015	7.611		5.520	.000	26.957	57.073
PCQ Medication	.084	.048	.114	1.756	.081	-.011	.180
PCQ Trust in Doctor	.005	.055	.006	.086	.932	-.103	.113
PCQ Impact	-.056	.045	-.097	-1.248	.214	-.144	.033
HADs Anxiety	**-1.279**	**.159**	**-.570**	**-8.042**	**.000****	**-1.594**	**-.964**
Self-efficacy	**.285**	**.125**	**.161**	**2.280**	**.024***	**.038**	**.532**
Social support	**.342**	**.146**	**.146**	**2.348**	**.020***	**.054**	**.630**
BMQ Specific	.013	.108	.008	.117	.907	-.202	.227
BMQ General	.030	.118	.016	.254	.800	-.204	.264
Cope Self-distraction	-.034	.350	-.006	-.096	.924	-.726	.659
Cope Denial	-.945	.570	-.105	-1.658	.100	-2.073	.183
Cope Disengagement	-.553	.606	-.065	-.913	.363	-1.751	.645
Cope Self-blame	-.388	.491	-.057	-.789	.432	-1.359	.584
		R^2	**0.604**				
		F	**16.370****				

Dependent variable SLE SF-12 MCS
****P value significant at <0.05, **P value significant at <0.01***

6.4.9.2 Is this association significant compared to other demographic, illness and patient variables associated with HRQoL in RA?

6.4.9.2.1 RA SF-12 Physical Component Subscale (PCS)

A total of eighteen variables produced small to large Pearson correlations with the physical component subscale (PCS) (Appendix 6.7). To safeguard sufficient power, variables with correlations below 0.20 were eliminated, as was the HADs depression scale that displayed multicolinearity with the HADs anxiety scale. A total of 7 IVs were entered in the MLR model that was significant (F=6.60, p<0.01), accounting for 30.40% of the PCS variance (Table 6.17). *Impact* was the only uncertainty scale with a significant positive association with PCS, indicating that lower PCQ scores (i.e. higher uncertainty) were associated with lower levels of HRQoL within the physical component. None of the other independent variables were significantly associated with PCS on a multivariate level.

Table 6.17 RA: Multiple Linear Regression Model for HRQoL – SF-12 Physical Component Scale (PCS)

	Unstandard. Coefficients		Standard. Coefficients			95% Confidence Interval for B	
	B	**SE**	**Beta**	**t**	**Sig.**	**Lower Bound**	**Upper Bound**
(Constant)	30.839	11.191		2.756	.007	8.652	53.026
PCQ Impact	**.217**	**.058**	**.393**	**3.740**	**.000****	**.102**	**.332**
HADs Anxiety	.180	.270	.070	.666	.507	-.356	.716
Self-efficacy	.214	.206	.108	1.039	.301	-.194	.622
Social support	.033	.203	.015	.164	.870	-.369	.435
BMQ Specific	-.272	.186	-.136	-1.464	.146	-.639	.096
Cope Venting	-.467	.750	-.059	-.622	.535	-1.954	1.020
Cope Self-blame	-.547	.689	-.079	-.793	.429	-1.913	.820
		R^2	**0.304**				
		F	**6.601****				

Dependent variable RA SF-12 PCS
****P value significant at <0.05, **P value significant at <0.01***

6.4.9.2.2. RA SF-12 Mental Component Subscale (MCS)

A total of thirteen variables displayed small to large Pearson correlations with the mental component subscale (MCS) (Appendix 6.7). To safeguard sufficient power, variables with correlations below 0.20 were eliminated, as was the HADs depression scale that displayed multicolinearity with the HADs anxiety scale. A total of 7 IVs were entered in the MLR model which was significant (F=21.05, p<0.01), accounting for 58.20% of the MCS variance (Table 6.18). None of the PCQ scales were significantly associated with MCS on a multivariate level, as the only variable that was independently associated with MCS scores was anxiety.

Table 6.18 RA: Multiple Linear Regression Model for HRQoL – SF-12 Mental Component Scale (MCS)

	Unstandard. Coefficients		**Standard. Coefficients**			**95% Confidence Interval for B**	
	B	**SE**	**Beta**	**t**	**Sig.**	**Lower Bound**	**Upper Bound**
(Constant)	59.814	8.073		7.409	.000	43.808	75.821
PCQ Impact	-.052	.042	-.102	-1.248	.215	-.135	.031
HADs Anxiety	**-1.302**	**.195**	**-.545**	**-6.678**	**.000****	**-1.688**	**-.915**
Self-efficacy	.232	.149	.127	1.565	.121	-.062	.527
Social support	.243	.146	.117	1.659	.100	-.047	.533
BMQ Specific	-.114	.134	-.062	-.854	.395	-.380	.151
Cope Venting	-.792	.541	-.108	-1.464	.146	-1.865	.280
Cope Self-blame	-.954	.497	-.149	-1.919	.058	-1.940	.032
		R^2	**0.582**				
		F	**21.053****				

Dependent variable RA SF-12 MCS
****P value significant at <0.05, **P value significant at <0.01***

6.4.10 Are higher levels of patient uncertainty associated with poorer HRQoL (disease specific)?

Higher scores on all of the PCQ scales denote lower uncertainty, whereas higher scores on the LupusQoL denote better HRQoL.

6.4.10.1 Disease Specific HRQoL: SLE LupusQoL

Higher levels of uncertainty in the medication, *trust in doctor* and *impact* scales were associated with lower levels of HRQoL (Table 6.7) on the physical health, planning and pain domains contributing to a range of 10.00%, 7.10% and 29.40% of the physical health, 9.50%, 5.10% and 30.30% of the planning and 8.70%, 6.10% and 21.90% of the pain variance respectively. On the other hand higher levels of uncertainty in *symptoms and flares* scale were associated with higher levels of HRQoL explaining 2.60% of the pain variance.

Higher levels of uncertainty in all of the PCQ scales apart from the *symptoms and flares* were positively associated with the burden, emotional and fatigue domains, explaining a range of 2.90% to 26.60%; 4.30% to 15.70%, and 2.90% to 26.20% of their respective variance. *Impact* was the only uncertainty scale that was significantly associated with the intimate relations and body image domains of HRQoL and was only accounting for 8.50% and 23.00% of their respective variances.

6.4.10.1.1 LupusQoL Physical Health

A total of eighteen variables displayed small to large Pearson correlations with the physical health (PH) domain (Appendix 6.6). To safeguard sufficient power, six variables with correlations below 0.20 were eliminated, as was the HADs anxiety scale that displayed multicolinearity with the HADs depression scale. A total of 12 IVs were entered in the MLR model that was significant (F=10.79, p<0.01), accounting for 50.10% of the PH variance (Table 6.19). *Impact* was the only uncertainty scale with a significant positive contribution to PH, indicating that lower PCQ scores (i.e. higher uncertainty) were associated with lower levels of HRQoL in relation to PH. Additionally, age, depression and the reframing coping strategy were negatively associated with PH scores.

Table 6.19 SLE: Multiple Linear Regression Model for HRQoL – LupusQoL Physical Health

	Unstandard. Coefficients		**Standard. Coefficients**			**95% Confidence Interval for B**	
	B	**SE**	**Beta**	**t**	**Sig.**	**Lower Bound**	**Upper Bound**
(Constant)	34.154	6.524		5.235	.000	21.246	47.063
Age	**-.154**	**.038**	**-.275**	**-4.047**	**.000****	**-.229**	**-.079**
PCQ Medication	.067	.039	.126	1.710	.090	-.011	.145
PCQ Trust in Doctor	-.020	.045	-.035	-.449	.654	-.109	.068
PCQ Impact	**.157**	**.037**	**.377**	**4.238**	**.000****	**.084**	**.231**
HADs Depression	**-.359**	**.175**	**-.188**	**-2.053**	**.042***	**-.706**	**-.013**
Self-efficacy	-.036	.104	-.028	-.348	.728	-.242	.169
Social support	.205	.119	.122	1.724	.087	-.030	.440
BMQ Specific	-.094	.085	-.078	-1.104	.272	-.263	.075
BMQ General	-.039	.096	-.029	-.408	.684	-.228	.150
Cope Reframing	**-.677**	**.272**	**-.169**	**-2.491**	**.014***	**-1.215**	**-.139**
Cope Denial	-.375	.453	-.058	-.826	.410	-1.271	.522
Cope Self-blame	-.331	.358	-.067	-.925	.357	-1.040	.377
		R^2	**0.501**				
		F	**10.792****				

Dependent variable SLE LupusQoL Physical Health Domain
****P value significant at <0.05, **P value significant at <0.01***

6.4.10.1.2 Emotional Health:

A total of seventeen variables displayed small to large Pearson correlations with the emotional health (EH) domain (Appendix 6.6). The instrumental coping strategy displaying a correlation <0.20 was eliminated, as was the HADs anxiety scale that displayed multicolinearity with the HADs depression scale. A total of 15 IVs were entered in the MLR model that was significant (F=17.65, p<0.01), accounting for 67.80% of the EH variance (Table 6.20). *Impact* was the only uncertainty scale with a significant positive contribution to EH, indicating that lower PCQ scores (i.e. higher uncertainty) were associated with lower levels of HRQoL in relation to EH. Additionally, black ethnicity, depression and the self-blame coping strategy were negatively, whereas self-efficacy positively associated with EH scores.

Table 6.20 SLE: Multiple Linear Regression Model for HRQoL – LupusQoL Emotional Health

	Unstandard. Coefficients		Standard. Coefficients			95% Confidence Interval for B	
	B	**SE**	**Beta**	**t**	**Sig.**	**Lower Bound**	**Upper Bound**
(Constant)	34.808	3.465		10.045	.000	27.951	41.665
Ethnicity: Black	-2.044	.712	-.166	-2.870	**.005****	-3.453	-.634
PCQ Medication	.051	.022	.146	2.326	**.022***	.008	.095
PCQ Self-manag.	-.027	.024	-.071	-1.107	.271	-.075	.021
PCQ Trust in doctor	-.012	.017	-.040	-.687	.493	-.045	.022
PCQ Impact	-.038	.020	-.139	-1.892	.061	-.078	.002
HADs Depression	**-.676**	**.093**	**-.536**	**-7.276**	**.000****	**-.860**	**-.492**
Self-efficacy	**.186**	**.057**	**.220**	**3.247**	**.001****	**.072**	**.299**
Social support	-.105	.066	-.095	-1.595	.113	-.236	.025
BMQ Specific	-.115	.046	-.145	-2.489	.014	-.207	-.024
BMQ General	-.118	.052	-.133	-2.277	.024	-.220	-.015
Cope Self-distraction	-.114	.163	-.043	-.701	.485	-.436	.208
Cope Denial	34.808	3.465	-.043	-.689	.492	-.723	.349
Cope Venting	-2.044	.712	-.077	-1.095	.276	-.741	.213
Cope Disengagement	.051	.022	.127	1.884	.062	-.026	1.053
Cope Self-blame	**-.027**	**.024**	**-.197**	**-2.805**	**.006****	**-1.088**	**-.188**
		R^2	**0.678**				
		F	**17.651****				

Dependent variable SLE LupusQoL Emotional Health Domain
****P value significant at <0.05, **P value significant at <0.01***

6.4.10.1.3 Body Image

Eleven variables displayed small to large Pearson correlations with the body image (BI) domain (Appendix 6.6). After eliminating the HADs anxiety scale to control for multicolinearity with the HADs depression scale, the remaining ten variables were entered into an MLR. The model was significant (F=4.26, p<0.01), accounting for 51.60% of the BI variance (Table 6.21). None of the PCQ scales were associated with BI significantly on a multivariate level. The only variable independently associated with BI on a multivariate level was depression

Table 6.21 SLE: Multiple Linear Regression Model for HRQoL – LupusQoL Body Image

	Unstandard. Coefficients		Standard. Coefficients			95% Confidence Interval for B	
	B	SE	Beta	t	Sig.	Lower Bound	Upper Bound
(Constant)	25.561	6.920		3.694	.001	11.575	39.547
PCQ Medication	.006	.046	.016	.123	.903	-.088	.099
PCQ Impact	.036	.044	.126	.807	.424	-.054	.125
HADs Depression	**-.547**	**.200**	**-.423**	**-2.735**	**.009****	**-.952**	**-.143**
Self-efficacy	.029	.127	.034	.229	.820	-.228	.287
BMQ Specific	-.040	.101	-.049	-.400	.691	-.244	.163
BMQ General	-.127	.108	-.140	-1.171	.249	-.346	.092
Cope Planning	-.579	.420	-.205	-1.378	.176	-1.428	.270
Cope Instrumental	-.088	.427	-.029	-.206	.838	-.950	.774
Cope Disengagement	-.121	.560	-.029	-.215	.831	-1.253	1.012
Cope Self-blame	-.235	.452	-.071	-.520	.606	-1.149	.679
		R^2	**0.516**				
		F	**4.264****				

Dependent variable SLE LupusQoL Body Image Domain
****P value significant at <0.05, **P value significant at <0.01***

6.4.10.1.4 Pain

Fourteen variables displayed small to large Pearson correlations with the pain (PA) domain (Appendix 6.6). After eliminating the HADs anxiety scale to control for multicolinearity with the HADs depression scale the remaining thirteen variables were entered into an MLR. The model was significant (F=7.39, p<0.01), accounting for 42.90% of the PA variance Table 6.22). *Symptoms and flares* was the only uncertainty scale with a significant negative association with PA, indicating that lower PCQ scores (i.e. higher uncertainty) were associated with higher levels of HRQoL in relation to PA. Depression was also negatively associated with PA.

Table 6.22 SLE: Multiple Linear Regression Model for HRQoL – LupusQoL Pain

	Unstandard. Coefficients		Standardized Coefficients			95% Confidence Interval for B	
	B	**SE**	**Beta**	**t**	**Sig.**	**Lower Bound**	**Upper Bound**
(Constant)	13.073	2.605		5.018	.000	7.918	18.228
PCQ Sympt. & Flares	**-.053**	**.020**	**-.196**	**-2.653**	**.009****	**-.092**	**-.013**
PCQ Medication	.021	.016	.107	1.357	.177	-.010	.053
PCQ Trust in Doctor	-.003	.019	-.014	-.160	.873	-.040	.034
PCQ Impact	.018	.015	.117	1.213	.227	-.012	.048
HADs Depression	**-.239**	**.070**	**-.333**	**-3.423**	**.001****	**-.378**	**-.101**
Self-efficacy	.061	.044	.127	1.401	.163	-.025	.148
Social support	.059	.048	.093	1.232	.220	-.036	.154
BMQ Specific	-.066	.035	-.145	-1.896	.060	-.134	.003
BMQ General	-.019	.039	-.038	-.490	.625	-.096	.058
Cope Self-distraction	-.176	.113	-.118	-1.557	.122	-.400	.048
Cope Denial	-.163	.190	-.067	-.857	.393	-.538	.213
Cope Disengagement	.223	.200	.097	1.114	.267	-.173	.620
Cope Self-blame	.133	.160	.072	.834	.406	-.183	.449
		R^2	**0.429**				
		F	**7.392****				

Dependent variable SLE LupusQoL Pain Domain
****P value significant at <0.05, **P value significant at <0.01***

6.4.10.1.5 Planning

A total of seventeen variables displayed small to large Pearson correlations with the planning (PL) domain (Appendix 6.6). Three variables displaying a correlation <0.20 were eliminated, as was the HADs anxiety scale that displayed multicolinearity with the HADs depression scale. A total of 12 IVs were entered into the MLR model that was significant (F=10.22, p<0.01), accounting for 48.70% of the PL variance (Table 6.23). *Impact* was the only uncertainty scale with a significant positive association with PL, indicating that lower PCQ scores (i.e. higher uncertainty) were associated with lower levels of HRQoL in relation to PL. In the opposite direction, depression was negatively associated with PL.

Table 6.23 SLE: Multiple Linear Regression Model for HRQoL – LupusQoL Planning

	Unstandard. Coefficients		Standardized Coefficients			95% Confidence Interval for B	
	B	SE	Beta	t	Sig.	Lower Bound	Upper Bound
(Constant)	13.531	2.801		4.831	.000	7.989	19.072
PCQ Medication	.022	.017	.097	1.306	.194	-.011	.056
PCQ Trust in Doctor	-.033	.019	-.137	-1.720	.088	-.072	.005
PCQ Impact	**.047**	**.017**	**.262**	**2.831**	**.005****	**.014**	**.080**
HADs Depression	**-.254**	**.075**	**-.309**	**-3.389**	**.001****	**-.402**	**-.106**
Self-efficacy	.037	.047	.067	.788	.432	-.056	.129
Social support	.076	.052	.104	1.452	.149	-.027	.178
BMQ Specific	-.059	.037	-.114	-1.585	.115	-.133	.015
BMQ General	-.045	.042	-.078	-1.078	.283	-.128	.038
Cope Planning	-.229	.132	-.128	-1.726	.087	-.491	.033
Cope Denial	-.214	.204	-.076	-1.047	.297	-.618	.190
Cope Disengagement	.116	.215	.044	.542	.589	-.308	.541
Cope Self-blame	-.066	.169	-.031	-.389	.698	-.400	.269
		R^2	**0.487**				
		F	**10.220****				

Dependent variable SLE LupusQoL Planning Domain
****P value significant at <0.05, **P value significant at <0.01***

6.4.10.1.6 Fatigue

A total of seventeen variables displayed small to large Pearson correlations with the fatigue (FA) domain (Appendix 6.6). Seven variables displaying a correlation <0.2 were eliminated, as was the HADs anxiety scale that displayed multicolinearity with the HADs depression scale. A total of 9 IVs were entered into the MLR model that was significant (F=9.85, p<0.01), accounting for 48.70% of the FA variance (Table 6.24). *Impact* was the only uncertainty scale with a significant positive association with FA, indicating that lower PCQ scores (i.e. higher uncertainty) related to lower levels of HRQoL in relation to PH. In the opposite direction, depression scores and BMQ specific beliefs about medication were negatively associated with FA scores.

Table 6.24 SLE: Multiple Linear Regression Model for HRQoL – LupusQoL Fatigue

	Unstandard. Coefficients		**Standard. Coefficients**			**95% Confidence Interval for B**	
	B	**SE**	**Beta**	**t**	**Sig.**	**Lower Bound**	**Upper Bound**
(Constant)	17.478	3.008		5.810	.000	11.527	23.429
PCQ Medication	.024	.020	.097	1.228	.222	-.015	.063
PCQ Trust in doctor	-.017	.022	-.064	-.766	.445	-.061	.027
PCQ Impact	**.057**	**.018**	**.293**	**3.103**	**.002****	**.021**	**.093**
HADs Depression	**-.201**	**.083**	**-.225**	**-2.413**	**.017****	**-.365**	**-.036**
Self-efficacy	-.026	.051	-.044	-.518	.605	-.127	.074
BMQ Specific	**-.084**	**.042**	**-.150**	**-1.994**	**.048***	**-.168**	**-.001**
BMQ General	-.047	.047	-.076	-1.018	.311	-.139	.045
Cope Venting	-.209	.199	-.087	-1.054	.294	-.602	.184
Cope Self-blame	-.276	.197	-.121	-1.401	.163	-.667	.114
		R^2	**0.402**				
		F	**9.848****				

Dependent variable SLE LupusQoL Fatigue Domain
****P value significant at <0.05, **P value significant at <0.01***

6.4.10.1.7 Intimate Relations

Twelve variables displayed small to large Pearson correlations with the intimate relations (IR) domain (Appendix 6.6). After eliminating the HADs anxiety scale that displayed multicolinearity with the HADs depression scale, the remaining 11 IVs were entered into the MLR model that was significant (F=6.64, p<0.01), accounting for 42.20% of the IR variance (Table 6.25). None of the PCQ scales were significantly associated with IR a multivariate level. Age and depression both were negatively associated with IR scores on a multivariate level.

Table 6.25 SLE: Multiple Linear Regression Model for HRQoL – LupusQoL Intimate Relations

	Unstandard. Coefficients		Standard. Coefficients			95% Confidence Interval for B	
	B	**SE**	**Beta**	**t**	**Sig.**	**Lower Bound**	**Upper Bound**
(Constant)	12.331	2.422		5.090	.000	7.525	17.137
Age	**-.044**	**.015**	**-.242**	**-2.951**	**.004****	**-.074**	**-.014**
PCQ Impact	.000	.014	-.004	-.035	.972	-.027	.027
HADs Depression	**-.200**	**.069**	**-.321**	**-2.886**	**.005****	**-.338**	**-.063**
Self-efficacy	.064	.041	.153	1.580	.117	-.016	.145
Social support	.002	.047	.003	.036	.972	-.092	.095
BMQ Specific	-.053	.034	-.135	-1.573	.119	-.120	.014
BMQ General	-.034	.037	-.078	-.931	.354	-.107	.039
Cope Denial	-.169	.185	-.080	-.913	.364	-.536	.198
Cope Substance abuse	-.258	.157	-.137	-1.648	.102	-.569	.053
Cope Disengagement	.130	.201	.065	.647	.519	-.269	.529
Cope Self-blame	-.117	.151	-.073	-.776	.440	-.416	.182
		R^2	**0.422**				
		F	**6.640****				

Dependent variable SLE LupusQoL Intimate Relations Domain
****P value significant at <0.05, **P value significant at <0.01***

6.4.10.1.8 Burden

A total of seventeen variables displayed small to large Pearson correlations with the burden (BU) domain (Appendix 6.6). Nine variables displaying a correlation <0.2 were eliminated, as was the HADs depression scale that displayed multicolinearity with the HADs anxiety scale. A total of 10 IVs were entered into the MLR model that was significant (F=11.85, p<0.01), accounting for 43.50% of the BU variance (Table 6.26). Two of the uncertainty scales, *medication* and *impact*, were positively associated with BU, indicating that lower PCQ scores (i.e. higher uncertainty) related to lower HRQoL in relation to BU. In the opposite direction BMQ specific beliefs about medication were negatively associated with BU scores.

Table 6.26 SLE: Multiple Linear Regression Model for HRQoL – LupusQoL Burden

	Unstandard. Coefficients		**Standard. Coefficients**			**95% Confidence Interval for B**	
	B	**SE**	**Beta**	**t**	**Sig.**	**Lower Bound**	**Upper Bound**
(Constant)	13.906	2.487		5.592	.000	8.987	18.826
PCQ Medication	**.047**	**.017**	**.203**	**2.757**	**.007****	**.013**	**.081**
PCQ Impact	**.034**	**.016**	**.186**	**2.134**	**.035***	**.002**	**.065**
HADs Anxiety	-.094	.057	-.133	-1.647	.102	-.207	.019
Self-efficacy	.024	.046	.043	.525	.601	-.067	.115
BMQ Specific	**-.153**	**.038**	**-.291**	**-4.073**	**.000****	**-.227**	**-.079**
BMQ General	-.039	.039	-.067	-.996	.321	-.117	.039
Cope Planning	-.127	.143	-.070	-.885	.378	-.410	.157
Cope Self-distraction	-.097	.140	-.056	-.689	.492	-.375	.181
Cope Venting	-.125	.194	-.055	-.647	.519	-.509	.258
Cope Self-blame	-.161	.175	-.075	-.919	.360	-.508	.186
		R^2	**0.435**				
		F	**11.846****				

Dependent variable SLE LupusQoL Burden Domain
****P value significant at <0.05, **P value significant at <0.01***

6.4.10.2 Disease Specific HRQoL: RA AIMS2-SF

Higher scores on all of the PCQ scales denote lower uncertainty, whereas higher scores on the AIMS2-SF instrument denote poorer HRQoL.

Higher uncertainty in the *symptoms and flares* scales was significantly associated with lower scores on the AIMS2-SF (Table 6.8) physical functioning domain (indicating better HRQoL) and explained 3.80% of its variance. In contrast, higher uncertainty in the *medication* and *impact* scales was significantly associated with higher scores on the physical functioning domain, i.e. lower levels of HRQoL, and explained 3.50% and 26.00% of its variance respectively. Similarly, *symptoms and flares*, *medication* and *impact* explained 1.60%, 13.10% and 29.70% of the symptoms variance. Higher uncertainty in the *medication* and *impact* scales related to higher levels of HRQoL on the affect domain, explaining 4.00% and 26.50% of the variance respectively. Finally, higher uncertainty in the *trust in doctor*, *self-management* and *impact* scales related to lower levels of HRQoL on the social interaction domain, explaining 9.10%, 2.40% and 5.30% of the variance respectively.

6.4.10.2.1 AIMS2-SF Physical

Thirteen variables displayed small to large Pearson correlations with the physical domain (Appendix 6.7). After eliminating the HADs anxiety scale that displayed multicolinearity with the HADs depression scale, the remaining 12 IVs were entered into the MLR model that was significant (F=10.04, p<0.01), accounting for 54.40% of the physical domain variance (Table 6.27). Two of the PCQ scales, *symptoms and flares* and *impact*, were independently associated with the physical domain but in the opposite direction. *Symptoms and flares* uncertainty was positively associated, indicating that lower PCQ scores (i.e. higher uncertainty) related to lower AIMS2-SF scores and higher levels of physical HRQoL, whereas *impact* uncertainty was negatively associated, thus indicating that lower PCQ scores (i.e. higher uncertainty) related to higher AIMS2-SF scores and poorer HRQoL. Age and depression were also positively associated with AIMS2-SF scores and poorer physical HRQoL on a multivariate level.

Table 6.27 RA: Multiple Linear Regression Model for HRQoL – AIMS2-SF Physical

	Unstandard. Coefficients		**Standard. Coefficients**			**95% Confidence Interval for B**	
	B	**SE**	**Beta**	**t**	**Sig.**	**Lower Bound**	**Upper Bound**
(Constant)	-12.385	7.650		-1.619	.109	-27.560	2.791
Age	**.119**	**.056**	**.156**	**2.126**	**.0360***	**.008**	**.230**
Disease duration	.021	.069	.026	.301	.764	-.117	.158
PCQ Sympt. & flares	**.222**	**.061**	**.301**	**3.646**	**.000****	**.101**	**.343**
PCQ Medication	-.084	.051	-.140	-1.626	.107	-.186	.018
PCQ Impact	**-.161**	**.050**	**-.322**	**-3.203**	**.002****	**-.261**	**-.061**
HADs Depression	**1.083**	**.294**	**.371**	**3.683**	**.000****	**.500**	**1.667**
Self-efficacy	.232	.166	.130	1.397	.165	-.098	.562
Cope Self-distraction	.382	.381	.080	1.005	.317	-.373	1.137
Cope Denial	.674	.681	.080	.990	.324	-.676	2.025
Cope Venting	.404	.589	.057	.685	.495	-.765	1.572
Cope Disengagement	.714	.712	.088	1.003	.318	-.698	2.126
Cope Self-blame	-.311	.610	-.050	-.511	.611	-1.521	.898
		R^2	**0.544**				
		F	**10.038****				

Dependent variable RA AIMS2-SF Physical Domain
P value significant at <0.05, **P value significant at <0.01

6.4.10.2.2 AIMS2-SF Symptoms

Nine variables displayed small to medium Pearson correlations with the physical domain (Appendix 6.7). After eliminating the HADs anxiety scale that displayed multicolinearity with the HADs depression scale, the remaining 8 IVs were entered into the MLR model that was significant (F=7.60, p<0.01), accounting for 31.90% of the symptoms domain variance (Table 6.28). *Medication* was associated significantly, indicating that lower PCQ scores (i.e. higher uncertainty) related to higher AIMS2-SF scores, denoting poorer HRQoL in relation to symptoms. In the opposite direction, depression and the instrumental and disengagement strategies were positively associated with the symptoms domain scores (i.e. poorer HRQoL).

Table 6.28 RA: Multiple Linear Regression Model for HRQoL – AIMS2-SF Symptoms

	Unstandard. Coefficients		Standard. Coefficients			95% Confidence Interval for B	
	B	SE	Beta	t	Sig.	Lower Bound	Upper Bound
(Constant)	2.263	1.689		1.340	.183	-1.086	5.612
PCQ Medication	**-.058**	**.017**	**-.294**	**-3.378**	**.001****	**-.092**	**-.024**
PCQ Impact	.014	.017	.087	.821	.414	-.020	.049
HADs Depression	**.280**	**.095**	**.291**	**2.958**	**.004****	**.092**	**.468**
Cope Instrumental	**.304**	**.145**	**.176**	**2.096**	**.038***	**.016**	**.592**
Cope Denial	.192	.246	.069	.779	.438	-.296	.679
Cope Venting	-.038	.220	-.016	-.174	.862	-.474	.397
Cope Disengagement	**.532**	**.250**	**.199**	**2.125**	**.036***	**.036**	**1.029**
Cope Self-blame	.223	.220	.108	1.013	.314	-.213	.659
		R^2	**0.319**				
		F	**7.602****				

Dependent variable RA AIMS2-SF Symptoms Domain
****P value significant at <0.05, **P value significant at <0.01***

6.4.10.2.3 AIMS2-SF Affect

Ten variables displayed small to large Pearson correlations with the affect domain (Appendix 6.7). To safeguard sufficient statistical power, the denial coping strategies displaying the weakest correlation r=0.21 were eliminated, as was the HADs depression scale that displayed multicolinearity with the HADs anxiety scale. The remaining 8 IVs were entered into the MLR model that was significant (F=23.79, p<0.01), accounting for 64.40% of the symptoms domain variance (Table 6.29). None of the PCQ scales were associated with the affect domains scores significantly on a multivariate level. Anxiety and the self-blame scores were positively associated with the affect domain (i.e. to poorer HRQoL).

Table 6.29 RA: Multiple Linear Regression Model for HRQoL – AIMS2-SF Affect

	Unstandard. Coefficients		Standard. Coefficients			95% Confidence Interval for B	
	B	SE	Beta	t	Sig.	Lower Bound	Upper Bound
(Constant)	7.681	3.170		2.423	.017	1.395	13.967
PCQ Impact	-.022	.016	-.100	-1.324	.188	-.054	.011
HADs Anxiety	**.488**	**.076**	**.488**	**6.445**	**.000****	**.338**	**.639**
Self-efficacy	-.082	.058	-.106	-1.410	.162	-.197	.033
Social support	-.103	.057	-.119	-1.815	.072	-.216	.010
BMQ specific	-.046	.052	-.060	-.891	.375	-.149	.057
Cope Venting	.337	.210	.110	1.601	.112	-.080	.753
Cope Disengagement	.103	.241	.029	.425	.672	-.376	.582
Cope Self-blame	**.561**	**.219**	**.209**	**2.564**	**.012***	**.127**	**.995**
R^2		**R^2**	**0.644**				
F		**F**	**23.790****				

Dependent variable RA AIMS2-SF Affect Domain
****P value significant at <0.05, **P value significant at <0.01***

6.4.10.2.4 AIMS2-SF Social interaction

Eight variables displayed small to medium Pearson correlations with the physical domain (Appendix 6.7). After eliminating the HADs anxiety scale that displayed multicolinearity with the HADs depression scale, the remaining 7 IVs were entered into the MLR model that was significant (F=6.23, p<0.01), accounting for 29.10% of the social interaction domain variance (Table 6.30). *Trust in doctor* was the only uncertainty scale with a significant negative association, indicating that lower PCQ scores (i.e. higher uncertainty) related to higher AIMS2-SF scores and poorer HRQoL in relation to social interaction. In the opposite direction, depression was positively associated with the social interaction domain (i.e. to better HRQoL).

Table 6.30 RA: Multiple Linear Regression Model for HRQoL – AIMS2-SF Social Interaction

	Unstandard. Coefficients		Standard. Coefficients			95% Confidence Interval for B	
	B	**SE**	**Beta**	**t**	**Sig.**	**Lower Bound**	**Upper Bound**
(Constant)	11.949	2.384		5.013	.000	7.223	16.675
PCQ Trust in doctor	**-.051**	**.016**	**-.301**	**-3.101**	**.002****	**-.083**	**-.018**
PCQ Impact	.027	.015	.197	1.784	.077	-.003	.057
HADs Depression	**.313**	**.097**	**.388**	**3.226**	**.002****	**.121**	**.505**
Self-efficacy	-.041	.053	-.084	-.783	.435	-.146	.063
Social support	-.050	.052	-.090	-.964	.337	-.152	.053
Cope Acceptance	-.260	.133	-.166	-1.957	.053	-.523	.003
Cope Denial	.106	.203	.046	.520	.604	-.297	.508
		R^2	**0.291**				
		F	**6.229****				

Dependent variable RA AIMS2-SF Social Interaction Domain
****P value significant at <0.05, **P value significant at <0.01***

6.5 Conclusions

This analysis constitutes the first quantitative exploration of patient uncertainty in SLE and RA using a disease-specific instrument. The newly developed PCQ scales were utilised in order to conduct a construct validity assessment and a preliminary exploration of the contribution of patient uncertainty to treatment adherence, mood and HRQoL in SLE and RA. The PCQ instrument was used to assess levels of uncertainty in relation to five domains; *symptom* interpretation and *flare* prediction, *medication* effectiveness and necessity, *trust in doctor*, knowledge of *self-management* and the expectation of *impact*. The exploratory research objectives were guided by the thesis` qualitative findings and up to date literature.

These findings provided some interesting findings and indications for future research, even though they provided mixed support to the study`s hypotheses. However, it is important to acknowledge that findings in this chapter were specific to each of the five domains of patient uncertainty. In contrast, the hypotheses were general and related to patient uncertainty as an overall concept. The separation between the different patient uncertainty domains could therefore account for the differential findings to some extent.

6.5.1 Construct Validity Conclusions

The role of the illness trajectory in the expressed levels of patient uncertainty was firstly explored. The two patient groups appeared to experience comparable levels of uncertainty in relation to three of the five domains, but differences were observed in the *symptoms and flares* and *impact* domains. Patients with SLE reported higher levels of uncertainty in relation to symptom interpretation and flare prediction. This finding was in accordance with the preceding qualitative study findings, as HCPs indicated the increased complexity of SLE and patient interviews displayed heightened uncertainty in relation to illness characteristics amongst the patients with SLE. Contrary to the qualitative indications, the RA sample appeared to be more uncertain in the *impact* domain; however this, difference was less substantial ($p<0.05$). It is however important to note that these analyses did not control for participants` age, sex or disease duration that could have also contributed to these differential findings between the SLE and RA samples in addition to the illness trajectory.

Findings related to demographic variables as sources of patient uncertainty provided mixed support to the study`s hypotheses as derived from the qualitative data. In

agreement with HCPs suggestions, gender did not appear to influence the levels of uncertainty reported by patients. Contrary to the HCPs suggestions, patient age was also not strongly associated with uncertainty in any of the five domains across either patient group. In line with the HCPs` suggestions older patients appeared to be less uncertain in relation to their *medication* and *impact* in the SLE group and in relation to their *self-management* in RA, but nevertheless these associations were weak.

Similarly, the exploration of disease characteristics as potential sources of patient uncertainty also provided mixed support for the study`s hypotheses. HCPs provided contradicting arguments in relation to whether greater disease severity is associated with greater patient uncertainty. Findings indicated that greater disease activity was only marginally associated with greater *self-management* uncertainty in SLE, whereas the remaining uncertainty domains displayed no association with disease activity. This finding involved current disease activity (within 4 weeks of assessment of patient uncertainty) and not cumulative damage or previous levels of disease activity, and this could have potentially influenced the levels of uncertainty experienced by patients.

Findings were not consistent in the two patient groups in relation to the association of longer disease duration with lower levels of uncertainty. Contrary to expectations, disease duration displayed no significant association with any of the patient uncertainty domains in SLE, however in the RA sample patients with longer disease duration appeared to be less uncertain in relation to the symptom interpretation and flare prediction, the necessity and effectiveness of their *medication* and their *self-management*.

Findings did not provide strong evidence for the association of satisfaction with social support and coping strategies with patient uncertainty. Patients reporting lower levels of uncertainty within the *medication*, *trust in doctor* and *impact* domains also reported greater satisfaction with social support in the RA sample, but this relationship was weaker in the SLE sample. *Symptoms and flares* and *self-management* uncertainty consistently showed no association with the satisfaction with social support in either condition. The causal mechanism of the significant associations cannot be determined within these analyses and could only be interpreted as being indicative of medium associations.

Both the HCPs and previous theories (24, 74) suggested the importance of the role of coping in the expression and management of patient uncertainty. The SLE sample barely displayed any significant association with any of the coping strategies and

patient uncertainty. Some links were displayed in the RA sample. Reporting greater use of planning and religion as a coping strategy was associated with greater levels of uncertainty in relation to *medication* effectiveness and necessity in RA, whereas greater use of venting and self-blame as a coping strategy was associated with greater uncertainty in relation to *impact*. Similar to the social support analyses, these findings can only be interpreted as indicative of an association as no causal relationship between coping and uncertainty can be determined due to the cross-sectional study design and the potential dynamic association between such variables.

6.5.2 The Association of Patient Uncertainty with Patient Outcomes Conclusions

The second part of this chapter`s analysis related to the association of the five patient uncertainty domains with treatment adherence, mood and HRQoL, expecting them to have a negative relationship. All domains of uncertainty apart from the *symptoms and flares* appeared to be associated with patient outcomes in the expected direction, or in other words higher levels of uncertainty related to negative outcomes.

Multiple significant findings were reported when investigating the association of single patient uncertainty domains to individual outcomes, particularly in relation to the *impact* domain. When the association of patient uncertainty was compared with other patient reported variables (e.g. beliefs, mood, social support and coping), and demographic and disease characteristics that have been found to predict such outcomes, results still showed some significant associations for some of the patient uncertainty domains .

Even though *medication* and *trust in doctor* uncertainty were associated with patient adherence in both SLE and RA on a univariate level, only the *trust in doctor* domain in the SLE sample was significantly associated to adherence in comparison to other variables. This finding suggested that being more uncertain in relation to trusting one`s doctor relates to lower treatment adherence. This finding is in line with previous literature suggesting that beliefs about one`s condition and dissatisfaction with health-care can contribute to adherence (384, 459-462).

Considering the qualitative findings and previous literature it was expected that patient uncertainty would be associated with anxiety levels (see section 3.3.4.2). Nevertheless, findings were modest as greater uncertainty in relation to managing one`s condition (i.e. *self-management*) was the only patient uncertainty domain associated with greater anxiety levels in SLE. None of the patient uncertainty domains were associated with anxiety levels in RA when analysed relative to other variables, however patient uncertainty was significantly associated with depression in both conditions as patients

who were more uncertain in relation to *impact* reported greater depressive symptoms. Importantly, these findings are consistent with the literature supporting the idea that anxiety is associated with the challenge of adjusting to a new condition (343, 449), whereas depression is associated with the overall burden of an illness (343, 447-449).

Predictably, being more uncertain in relation to the *impact* of one`s condition was associated with poorer generic HRQoL in relation to physical aspects in both conditions. Considering that *impact* uncertainty related to issues including planning, functionality and mobility, the association with physical HRQoL is conceptually consistent. Nevertheless, patient uncertainty consistently failed in displaying any significant relationship with the mental aspects of generic HRQoL in either SLE or RA.

In line with the investigation of generic HRQoL, greater *impact* uncertainty was associated with poorer disease-specific HRQoL in relation to physical, fatigue, planning and burden aspects in SLE. Patient uncertainty in relation to *medication* was also associated with poorer HRQoL in relation to burden and emotional health in SLE and the symptoms in RA, with the latter suggesting that greater uncertainty in relation to *medication* effectiveness and necessity relates to the reporting of more symptoms. Finally, greater uncertainty in relation to the *trust in doctor* was associated with poorer HRQoL in relation to social interactions in RA.

Contrary to the analysis expectations, patient uncertainty in relation to *symptoms and flares* was positively associated with aspects of disease specific HRQoL in both SLE and RA. Being more uncertain in relation to symptom interpretation and flare prediction related to better disease specific HRQoL in relation to pain in SLE and the physical domain in RA. In other words, lower uncertainty (i.e. greater certainty) in this domain related to poorer HRQoL. This unexpected finding is open to a range of different interpretations.

Considering the HCP `s suggestion that patients with the most severe disease are less uncertain it could be postulated that greater uncertainty designates less disease severity and hence better HRQoL. However, higher patient uncertainty was associated with to better HRQoL over and above disease activity in the SLE sample, which is contrary to this suggestion. This contradicting finding could be taken to suggest that not all domains of patient uncertainty are necessarily aversive, as in this case *symptoms and flares* patient uncertainty was positively associated with physical aspects of disease specific HRQoL.

6.6 Chapter 6 Summary

This Chapter presented an initial exploratory quantitative exploration of patient uncertainty in patients with SLE and RA by utilising the newly developed PCQ instrument (Chapter 5). The analysis aimed to assess the construct validity of patient uncertainty in each of the two conditions and to preliminary explore the association of patient uncertainty with important patient outcomes. Results were compared with the preliminary qualitative hypotheses presented in Chapter 3 and interpreted in relation to the patient uncertainty concept. Illness trajectory was associated with some, but not all, domains of patient uncertainty, whereas demographic variables and disease activity displayed a very minor influence on the degree of patient uncertainty reported. These findings designated the multi-dimensional nature of patient uncertainty and the individuality of the five uncertainty domains. Furthermore, these analyses display the association of different patient uncertainty domains with to patient outcomes (such as treatment adherence, mood and HRQoL) as assessed by commonly used instruments in both SLE and RA. The implications of these findings will be discussed in more detail in Chapter 7.

Chapter 7: General Discussion

7.1 Chapter 7 Overview

This thesis explored patient uncertainty regarding systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), with the objective of developing and evaluating a new self-report instrument to measure patient uncertainty. The existing patient uncertainty literature concerning chronic conditions was reviewed and the various approaches to the development and evaluation of instruments were considered. Mixed methods were applied in the three phases of data collection, which led to the exploration and quantification of patient uncertainty regarding SLE and RA. Interviews with patients and health care professionals (HCPs) were conducted in order to conceptualise patient uncertainty, as well as to generate and to qualitatively evaluate items affecting the new patient uncertainty instrument. Two stages of psychometric evaluation were employed via two independent field tests, which led to the revision and refinement of the new instrument. Data collected in the second field test were further used to provide a preliminary exploration of patient uncertainty regarding SLE and RA. This chapter provides an overview of the thesis findings in relation to the literature and discusses limitations, as well as the implications for future research.

7.2 Overview of Findings

A review of the literature on chronic illness revealed that patient uncertainty is a key and potentially aversive aspect of the illness experience (25-27), particularly in complex and unpredictable conditions like SLE and RA. Nevertheless, patient uncertainty regarding SLE or RA had never previously been comprehensively assessed (28-33). The literature is dominated by the uncertainty in illness theory (UIT), a generic descriptive theory (74, 80) initially developed to address uncertainty in hospitalised and acute conditions, and which was later reconceptualised (RUIT) to address enduring uncertainty regarding chronic illness. The literature review indicated that patient uncertainty is a complex and poorly understood construct, conceptualised in a different ways both between disciplines and in chronic conditions (40, 82). Qualitative explorations further indicated variability between the aspects of patient uncertainty experienced in different chronic conditions (34, 53-56). These findings emphasise the need for illness-specific assessment of uncertainty, as the existing instruments are generic and fail to capture issues important for specific conditions.

Taking into account the current best practice guidelines of exploring a new construct (139, 143, 182), a comprehensive approach towards conceptualising and quantifying patient uncertainty regarding SLE and RA was employed. Considering the limitations of traditional psychometrics and the additional benefits of modern psychometric techniques such as Rasch Measurement Theory (RMT), the new instrument was developed and evaluated in line with the RMT.

An overview of the thesis` findings is presented below. The structure of the overview echoes the four chapters (chapter 3 to 6) that presented studies across the three data collection phases of this thesis and is purposively kept brief, as it is partly repetitive of the results and conclusion sections of these chapters.

7.2.1 Conceptual Development & Item Generation

The first aim of this thesis was to develop a conceptual framework of patient uncertainty regarding SLE and RA by using a qualitative exploration, consisting of interviews with patients and health care professionals (HCPs). A five-domain conceptual framework of patient uncertainty was inductively developed on the basis of quotations extracted from interviews with patients and which reflected the different issues regarding uncertainty experienced by patients within these domains. The domains included *symptoms and prognosis*, *medical* and *self-management*, *impact* and *social functioning* and were applicable to both patients with SLE and those with RA, although some differences were observed at a sub-domain level between the two conditions.

Specifically, the patients with SLE appeared to experience a more diverse set of patient uncertainty sub-domains in relation to issues concerning illness flares, illness unpredictability and having children. There were also differences in the breadth of quotations within these five domains, and subsequent sub-domains were not consistent between domains, as the *self-management* and *social functioning* domains appeared to be narrower when compared to the remaining domains. The HCPs` understanding of patient uncertainty was in line with domains revealed in the patient interviews which, however, provided more detailed sub-domains of patient uncertainty. The HCP interview findings further suggested potential sources and potential aversive consequences of patient uncertainty.

In line with previous cognitive theories portraying uncertainty as an inherent part of life (2, 24), the findings of this thesis portrayed patient uncertainty as an implicit fact of

living with a chronic condition and revealed the different issues of uncertainty experienced by patients with SLE and RA. Patients did not choose to use the term "uncertainty"; however, uncertainty was revealed as a subjective perception relative to a variety of issues, either directly or indirectly related to the one's condition. These issues were inductively categorised, resulting in a five-domain framework. The manifestation of patient uncertainty is complex, as it comprises different states, including a lack of knowledge or understanding, difficulty in interpretation or judgement, unpredictability and the expectation of potential consequences or risks related to the different domains. Patients often exhibited a sense of anxiety.

This work is the first comprehensive exploration of patient uncertainty in rheumatology. It expands previous research by the addition of new domains, not all of which are included in previous theories. These involve *impact,* comprising issues of family planning, functionality and future planning and *social functioning,* relating to issues of disclosing diagnosis, support and reactions from social circles. On a sub-domain level, this exploration revealed new issues of patient uncertainty, including illness progression reflecting multi-organ involvement and the unpredictability of flares, which were not included at this level of specificity in previous conceptualisations. The sub-domains related to medication toxicity and ineffectiveness further reflected the challenges of treatment specific to these conditions. In addition, as emphasised by the HCPs, *impact* is a salient domain of patient uncertainty, indicating that family planning is of particular concern to the patients with SLE; whereas, future mobility and functionality to the patients with RA. These issues that were subsequently confirmed by the patient interviews and included in the conceptual framework as sub-domains have not been included in previous theories and further highlight the value of disease-specific exploration.

Following the qualitative interview findings, items for the new instrument were generated on the basis of patients' remarks and were categorised according to five scales, reflecting the structure of the conceptual framework. Items were constructed following conventional principles (512) and used as many of the patients` own words as possible. A diverse set of 82 items reflecting the various manifestations of patient uncertainty was generated and was subsequently scored on the same 4-point Likert response scale, assessing different extents of uncertainty. The response scale was scored such that higher scores reflected less uncertainty (i.e. greater certainty), while lower scores reflected greater uncertainty in all five scales. The instrument was subsequently named the Patient Certainty Questionnaire (PCQ).

Prior to the quantitative field testing of the PCQ, cognitive debriefing interviews were conducted to qualitatively pre-test the relevance, acceptability and difficulty of interpreting the newly developed items. The results of the pre-tests were generally favourable, with suggestions for a few minor modifications that were made to enhance the comprehensiveness and relevance of certain items, although this did not alter the structure of the PCQ. The resulting first draft of the PCQ comprised 83 items across five scales, including *symptoms and prognosis* (27 items), *medical management* (26 items), *self-management* (5 items), *impact* (18 items) and *social functioning* (7 items).

7.2.2 Psychometric Evaluation (1st Field Test)

A multi-centre field test of 383 participants was conducted to evaluate and revise the first draft of the PCQ. Multiple tests were conducted to examine whether the preliminary five PCQ scales satisfied the criteria of RMT in terms of assessing the adequacy of the scale in relation to sample targeting, the measurement continuum and the measurement of the sample. A review of these results led to the revision and re-evaluation of the scales in the second draft of the PCQ.

Evaluation of the first draft of the PCQ led to the reduction of the number of items from 83 to 61 and changes to the scale structure. The *social functioning* scale was eliminated, as items did not perform adequately as a quantitative scale and the *medical management* scale was divided into two distinct scales, named *medication* and *trust in doctor*. Hence, the second draft of the PCQ did not entirely reflect the underlying conceptual framework structure, but the measurement properties improved when re-assessed against the RMT criteria.

In the first field test, it was not possible to evaluate the draft *medication* and *impact* scales, as revisions led to item additions and integration that resulted in unavailable data. The second draft of the PCQ instrument consisted of five scales, including *symptoms and flares* (16 items), *medication* (11 items, including 5 new items), *trust in doctor* (8 items), *self-management* (6 items) and *impact* (10 items), as well as an additional 10 single items.

7.2.3 Psychometric Evaluation (2nd Field Test)

A second field test with 279 participants was conducted in order to evaluate the second draft of the PCQ. The same RMT psychometric tests used in the first field test, were utilised again to evaluate the scales. Moreover, the extent to which raw scores

approached the interval measurement was examined and the total score of each scale was transformed into linearised logit measurements and 0 – 100 scores.

The second draft of the PCQ performed consistently well, replicating the first field test analyses and revisions. RMT analysis led to additional revisions to the *symptoms and flares* scale, involving the elimination of two items that hindered the scale's performance, as well as the elimination of the 10 single items. The final draft of the PCQ consisted of 49 items across five scales, namely *symptoms and flares* (14 items), *medication* (11 items), *trust in doctor* (8 items), *self-management* (6 items) and *impact* (10 items).

Sample to scale targeting was satisfactory in all scales apart from *self-management,* where the item location range was sub-optimal and could not be improved by additional items based on the breadth of the qualitative data. In other words, the range of uncertainty measured by the scales matched the range of uncertainty in the sample well in all scales, apart from *self-management*, where the range of uncertainty measured was limited when compared to the breadth of uncertainty measured in the sample.

The performance of all five measurement continuums (scales) was also satisfactory and the item ordering was largely similar to that of the first field test, thus displaying that item difficulty was consistent across both field tests. Response categories generally performed in line with the RMT criteria, apart from one *self-management* item that consistently displayed disordering in both field tests, indicating that the "somewhat uncertain" response category was problematic. Two items, one from the *trust in doctor* and another from the *impact* scale, indicated an underestimation of the trait. This means that persons with more ability (i.e. lower uncertainty) scored higher uncertainty than expected and persons with lower ability (i.e. higher uncertainty) scored lower uncertainty than predicted by the Rasch model. The remaining 47 items displayed optimal goodness of fit, in line with the RMT.

Two pairs of items on from the *symptoms and flares* category and another from the *trust in doctor* scale displayed a high residual correlation, which was again consistent with the first field test, as did another two pairs of items from the *medication scale*, indicating dependency between these pairs of items and therefore a bias in measurement. This issue could possibly be resolved by the integration of item pairs in subsequent instrument revisions. Item performance was generally stable across the two patient groups, as well as in the seven different age and disease duration groups.

All five scales produced high person separation indexes, indicating low levels of error and the scales` ability to separate the sample effectively. However, the validity of sample measurement was sub-optimal in all five scales, as the percentage of people scoring higher and lower than expected in relation to uncertainty was above that of the RMT criteria. The relationship of raw scores to linear measurement was assessed, indicating a sub-optimal relationship as the raw scores did not reflect interval measurement in any of the scales. This, however, was an expected finding and the S-shaped relationships observed were satisfactory and further highlights the advantages of RMT analysis that it offers the transformed interval scoring.

Overall, the RMT analysis results indicated that the measurement properties of these scales were satisfactory, despite minor deviations from the RMT expectations, as these were anticipated due to the stringent mathematical criteria involved in RMT (517). Therefore, this work contributes to “health measurement” in rheumatology with the addition of a new comprehensive scientifically rigorous instrument.

7.2.4 Initial Quantitative Exploration of Patient Uncertainty in SLE and RA

During the second field test, additional data were collected to allow for the first exploration of patient uncertainty regarding SLE and RA using the newly developed PCQ instrument. The exploration included an extended construct validity assessment and an examination of the association of patient uncertainty with treatment adherence, mood and health-related quality of life in each of the two conditions.

The HCPs` interview and the literature review findings were used to generate the hypotheses and to guide the analysis, which remained largely exploratory. The hypotheses were open to all domains of patient uncertainty, as no previous findings were explicit to specific domains, but rather to overall patient uncertainty. The analyses examined the relationship of uncertainty with commonly assessed outcomes and hypothesised that higher levels of uncertainty would be negatively associated with patient outcomes (i.e. lower treatment adherence, higher levels of depression and anxiety and poorer HRQoL). These analyses were conducted independently for each condition.

The association of illness and demographic variables as potential sources of patient uncertainty was explored. The levels of uncertainty expressed by patients were comparable between the SLE and RA samples in the domains of *medication, trust in doctor* and *self-management*. Patients with SLE, however, appeared to be significantly more uncertain in relation to symptom interpretation and flare prediction, whereas

patients with RA showed marginally greater uncertainty in relation to illness impact. These findings therefore indicated that the illness trajectory was primarily associated with patient uncertainty levels only within the *symptoms and flares* scales, confirming the suggestions made by the HCPs regarding the increased complexity of SLE.

Exploring the association of patient uncertainty with disease characteristics, including disease duration and current disease activity, provided mixed results in the study hypotheses. SLE disease activity showed no significant association with any of the PCQ scales, whereas disease duration displayed a differential association to uncertainty in the two patient groups. Contrary to expectations, no significant association was reported in the SLE sample, while in RA sample, those patients with a longer disease duration appeared to be less uncertain in relation to their symptom interpretation and flare prediction, to the necessity and effectiveness of medication and with regard to their self-management.

Contrary to the HCPs` suggestions, demographic characteristics, including gender, age and ethnicity, did not manifest a strong association with any of the PCQ scales. Findings did not provide any strong evidence for the association of social support and coping strategies with the expression of patient uncertainty, although there were some exceptions in the RA sample.

The association of patient uncertainty with patient outcomes, including treatment adherence, mood and HRQoL, was further explored. Considering previous literature suggesting that patient beliefs can contribute to outcomes and the qualitative findings of this study, it was expected that higher levels of patient uncertainty would be negatively associated with outcomes. Significant findings supported this expected relationship in all patient uncertainty domains, apart from the *symptoms and flares* domain, within which lower uncertainty appeared to have a negative relationship with aspects of disease-specific HRQoL.

The association of patient uncertainty with outcomes was not consistent either across the five scales or between the two conditions, as individual scales accounted for small to moderate version of the outcomes` variance when assessed on a univariate cross-sectional basis. However, when compared to other variables associated with outcomes, fewer patient uncertainty domains maintained a significant association with outcomes. A brief summary of these domains is provided below.

Higher levels of uncertainty in the *trust in doctor* scale related to lower treatment adherence in the SLE sample. Higher levels of uncertainty in the *self-management* scale related to higher anxiety levels in SLE sample, whereas higher uncertainty in the

impact scale were linked with higher depression levels in both the SLE and in the RA samples. In line with the study's expectations, higher uncertainty in the *impact* scale was associated with poorer HRQoL in relation to physical aspects in both conditions. Similarly, higher uncertainty in the *impact*, *medication* and *trust in doctor* scales were negatively associated with aspects of disease-specific HRQoL in both SLE and RA samples.

Contradictory findings were reported in relation to the *symptoms and flares* scale, where higher levels of uncertainty were positively associated with aspects of disease-specific HRQoL in both conditions; specifically, pain in the SLE sample and the physical domain in the RA sample. This finding is open to a range of interpretations, as it could represent an artefact of greater disease severity which, according to the HCPs` suggestions, could lead to lower uncertainty in relation to *symptoms and flares,* or it could reflect the fact that lower uncertainty in this scale could reflect greater certainty with regard to an unfavourable illness outcome.

All of the above findings suggest the multi-dimensionality of the patient uncertainty concept, as the five scales displayed differential associations with and contributions to other variables, both within and between the two conditions. The interpretation of study findings is limited by the cross-sectional design and the associational analyses which cannot be used to make any conclusion regarding causal mechanisms. Nevertheless, the first exploration of patient uncertainty using the PCQ provided some interesting findings in relation to the sources of patient uncertainty and their potential role association with patient outcomes, suggesting possible directions for future research.

7.3 Study Limitations

Study limitations will be discussed in relation to the qualitative phase, the psychometric evaluation phases, including both field tests, and the initial quantitative exploration of patient uncertainty.

7.3.1 Conceptual Development and Item Generation

Even though qualitative methodology is the *gold standard* technique of developing a conceptual framework and subsequently generating items for a new instrument, it is subject to some inherent challenges that should be considered when interpreting qualitative data. These challenges involve the sampling and analysis frame that relate to the qualitative investigation of this thesis.

First and foremost, a researcher`s subjectivity (510, 511) challenges qualitative research, as it affects both the methodology and the interpretation of a study. For

example, the fact that the topic list that was used to guide the patient interviews was closely related to the resulting patient uncertainty quotations, as well as the procedure of coding remarks as “uncertain”, could be criticised as being potential sources of interpretation bias. This was a point of concern for this study, as analysis involved a construct that is of an abstract and subjective nature, further challenging the scientific rigour of the analysis. However, care was taken to minimise this, in line with research guidelines.

The topics were only used as probes within open-ended questions. In addition, the topic list was created on the basis of HCPs and previous literature findings; therefore, it could be argued that the close proximity to the patient data indicates that patient data merely replicated the HCPs` findings. In addition, the iterative review of results within the multidisciplinary research team, not just by the candidate who conducted the interviews, also served to minimise the researcher` s interpretation bias.

In an additional attempt to minimise bias in the analysis of results, 25% of the transcripts were re-coded by an independent researcher, who was not part of the research team and who had no knowledge of the HCPs or of the findings from the literature review. This re-coding resulted in the same five overarching patient uncertainty domains. Ideally, all of the transcripts should have been re-coded by more than one independent researcher; however, this was not logistically possible.

Secondly, similar to all qualitative research, findings are not automatically generalisable to the entire SLE and RA populations, but are rather primarily representative of the recruited samples (566). In this case, patients with SLE and RA were recruited from a teaching hospital (University College London Hospital, UCLH). They were patients who attended regular appointments at the rheumatology clinics of UCLH, and some of them were generally familiar with taking part in research studies. However, the samples recruited were diverse in relation to age, disease duration and ethnicity.

In addition to the inherent challenges of qualitative methods, it is acknowledged that the study could have been further improved by modifications to the study design and analyses. The HCP interviews were conducted as a preliminary step and were a complementary aspect of this research. They were brief and structured, which limited the breadth and depth of the results produced. However, considering the breadth of the HCP interview findings, it could be argued that this could have been conducted more extensively in order to obtain a more comprehensive understanding of the HCPs` view on patient uncertainty.

It is further acknowledged that the qualitative analysis was restricted to conceptualising the uncertainty experienced by the patients and did not address certainty. In other words, remarks related to absolute certainty were not coded, nor were they further utilised in the qualitative analysis. This was a deliberate decision taken by the multidisciplinary research team to ensure that data analysis closely matched the research objective, which was to develop a conceptual framework of patient uncertainty. Even though the findings were restricted to patient uncertainty, this decision was in line with the guidelines for qualitative research (566), which highlight the need for clearly and specifically formulated research questions.

Finally, the study could have been improved if the cognitive debriefing interviews had been conducted in an independent sample; however, this was not logistically possible. The participants who were initially interviewed for the conceptual development and item generation were re-invited to complete the pre-testing, which could have potentially offered a favourable bias towards the qualitative assessment of these items.

7.3.2 Psychometric Evaluation (Field Tests)

The psychometric evaluation was limited with regard to the execution of the study protocol, as well as to issues of logistic feasibility in terms of the study design. Although the study protocol called for two independent samples for each of the field tests, this was not executed consistently by the external sites in the second field test, where the participants accounted for 35% of the sample. External sites were not in a position to provide information on participants who completed both field tests. Thus, it has to be acknowledged that there was some overlap of participants within 35% of the sample in the second field test.

Considering the general “rule of thumb” recommending 5 to 10 participants per scale item, samples sizes in both field tests were sufficient as, in the first field test 383 participants were recruited compared to the minimum of 270, and in the second field test there were 279, compared to the minimum of 160 minimum. The average response rates of 60.9% and 63.4% in the first and second field tests exceeded the reported 60% average response rate in medical and nursing surveys (567, 568).

Nevertheless, the post-hoc investigation of reasons for non-responses revealed that improvements to the study design could have improved this response rate. Specifically, incorrect contact details for participants, limited reading ability in English and the

participants' health status (for example, frailty) were listed as reasons for non-response. This issue could have been tackled with improved judgement of participant eligibility, as this was primarily based on electronic hospital records, which were not always updated or representative of the participants` ability to take part in the study. In addition, the fact that recruitment was largely conducted through the post and because reminder letters were not always sent out at external sites, even though they were part of the study protocol, could have affected the response rate, as face to face recruitment (568) and participant reminders (515, 567) have been linked with higher rates of response.

Another limitation of the psychometric evaluation is that final version of two of the PCQ scales (*medication* and *impact*) were only evaluated in a single study (the second field test), whereas, the remaining scales were evaluated in two field tests. Subsequent testing is required to confirm the extent to which these scales satisfy the RMT criteria. In addition, the *self-management* scale, which displayed sub-optimal targeting, as well as items in other scales with sub-optimal performance in trait estimation and residual correlations, would benefit from subsequent revisions, testing and possibly from additional qualitative assessment. Precision of measurement as denoted by the information function curve was sub-optimal in most of the PCQ scales and should be further explored.

Lastly, it is worth considering the generalisability of the PCQ instrument for psychometric evaluation. The majority of the study samples were recruited from London hospitals, even though additional participants were recruited from the Midlands and from the north of England. It could be argued that the PCQ needs to be evaluated more extensively in areas outside of London and other centres in the world in order to confirm the suitability for patients with SLE and RA in other parts of the UK and from other cultures.

7.3.3 Initial Quantitative Exploration of Patient Uncertainty in SLE and RA

The quantitative exploration of uncertainty in patients with SLE and RA was limited by the study design, including the cross-sectional and associational analysis and the instruments used.

The scientific rigour of any study involving patient outcomes is directly influenced by the quality of the instruments used to measure such outcomes (141). To this extent, Chapter 1 presented the justification of the thesis methodology in developing and evaluating the PCQ (see section 1.3). The newly developed PCQ instrument used to

quantify patient uncertainty was developed and validated using *gold standard* guidelines and, to a large extent, satisfied the psychometric criteria of the scientifically rigorous psychometric paradigm of RMT (Chapters 4 – 5). In addition, it is acknowledged that in some instances alternative instruments could have been chosen, e.g. an alternative disease-specific HRQoL instrument for RA.

However, it was not possible to thoroughly evaluate the psychometric development and validation of the remaining instruments that are used to quantify patient outcomes variables. The psychometric properties of the remaining instruments and the extent to which they measured the intended constructs successfully cannot be guaranteed. Nevertheless, it was considered important to utilise the newly developed PCQ in an exploratory study, together with other instruments that are commonly used in SLE and RA research, in order to develop an understanding of the role of the different domains of patient uncertainty. It is, however, acknowledged that the scientific rigour of the remaining instruments used in these analyses was not systematically assessed.

The cross-sectional design of the study further limited analyses and interpretation of the findings. As outlined in Chapter 2, the association between many patient outcomes is dynamic and often bi-directional causal pathways operate between them (300, 379-381, 453). Cross-sectional analyses could therefore potentially serve to amplify causal links between patient outcomes (300, 347, 379, 440, 491). For example, if dynamic links exist between different patient uncertainty domains and components of HRQoL, a cross-sectional analysis cannot clarify the direction of such a relationship because the observed associations could reflect an overlap of such variables, and not necessarily a causal relationship.

The disadvantages of the cross-sectional design could have been addressed by the use of moderation analysis. Moderation analysis would have examined whether patient uncertainty moderates the relationship between disease and treatment variables and patient outcomes i.e. affects the strength and/or direction of the relationship between the predictor disease variables and outcomes (569). However, the lack of information regarding treatment and the limited information on disease activity did not permit such analyses to take place. The study protocol was devised with the objective of developing and evaluation the new instrument and hence did not include the collection of treatment related variables and disease history. Even though collecting disease activity data was part of the protocol, it proved to be impossible to obtain this in practice for the RA sample; and difficult for the SLE sample for which disease activity data were collected

for only two thirds of the sample.

These findings were further biased by the choice of analysis used in terms of specifying HRQoL as an outcome and patient uncertainty as an independent variable related to that outcome. However, all analyses were guided by theoretical frameworks (15, 17, 150, 155), as well as by findings from the literature review and by the qualitative HCPs findings (see section 2.4).

Finally, it is acknowledged that the interpretation of the study findings was restricted to issues related to patient uncertainty and were not expanded to interpretations and implications related to the remaining patient outcomes. This was deliberate, as further interpretation would lack a theoretical and literature background and would extend beyond the aims of this study and of this thesis, as these were restricted to the preliminarily exploration of the association patient uncertainty with outcomes.

7.4 Thesis Implications

The findings of this thesis offer a range of implications in relation to the concept and role of patient uncertainty in SLE and RA, the potential use of the PCQ and the benefits of the methodology used.

7.4.1 Implications for Patient Uncertainty as a Concept

The qualitative exploration portrayed patient uncertainty as a concept with multiple domains and further indicated how these domains could be associated with characteristics specific to an illness. These findings offer certain implications and could inform patient uncertainty literature across a range of different chronic conditions. Firstly, the findings displayed the insufficiency of the Uncertainty in Illness Theory (UIT) (74). The UIT` s prescriptive definition of patient uncertainty, namely “the inability to determine the meaning of illness-related events”, is widely used in the literature but does not encompass the spectrum of patient uncertainty issues discovered in this thesis or in other qualitative explorations. Moreover, the UIT is limited to defining one state of uncertainty and does not capture all of the different aspects of patient uncertainty.

Contrary to this prescriptive definition, the findings of this thesis indicate that patient uncertainty is a perception that takes many forms and is not only the inability to determine the meaning of illness-related events. These included the lack of knowledge or understanding, difficulty in interpretation or judgement, unpredictability, expectation of potential consequences or risks related with the illnesses characteristics, prognosis,

management and impact. The discovery of new patient uncertainty domains that were not included in any of the previous conceptualisations further highlights the importance of detailed and systematic exploration of the concept, which according to the findings of this thesis, requires disease-specific assessment.

It can therefore be concluded that patient uncertainty, similar to general uncertainty, should be approached as an inherent fact of life and an inherent fact of living with a chronic condition like SLE and RA. Patient uncertainty involves cognition that simply reflects a lack of certainty in relation to a range of issues that are either directly or indirectly related to the disease.

Considering the differences between the characteristics, demands and impact of various conditions, these findings further imply that a comprehensive exploration of the patient uncertainty domains needs to be disease-specific. Although uncertainty is universal, the domains of uncertainty can differ between conditions, as they simply reflect the different issues of uncertainty experienced by patients. In conclusion, the conceptual framework implies the inadequacy of the existing theories to comprehensively capture the patient uncertainty concept and further highlights the need for disease-specific assessment of the patient uncertainty concept.

The findings of this thesis further imply that patient uncertainty is a cognition associated with the manner in which a patient reacts to and feels about his/her condition. Theories have previously indicated the role of cognitions, such as illness perceptions (17, 18, 570, 571) or self-efficacy (15) on health outcomes and disease adjustment and management(572). The findings of this thesis imply that patient uncertainty should also be addressed as an important cognition when addressing the patients` perspective of a condition. The initial quantitative exploration of patient uncertainty, using the newly developed PCQ instrument, offers further implications with regard to the particular role of patients' uncertainty domains in SLE and RA patient outcomes.

The literature review presented in Chapter 1 concluded that uncertainty is considered an aversive perception (2, 3, 24, 25, 29, 573) which, according to general theories of cognition, poses a challenge to life in general (2, 3, 24, 574) and to patient adjustment in chronic illness in particular (25, 29, 573). The quantitative findings of this thesis imply that patient uncertainty is an aversive outcome in four of the five domains measured by the PCQ instrument. In contrast to the thesis hypotheses and previous literature, the findings implied that greater patient uncertainty with regard to *symptoms and flares* is not necessarily an aversive perception.

A closer inspection of the content of this domain offers a potential explanation for this contradicting finding. As opposed to the remaining four domains in which lower uncertainty reflected greater certainty of a positive outcome, for example greater certainty of medication effectiveness and necessity, greater certainty in trusting one` s doctor, greater certainty with regard to self-management knowledge and greater certainty of the lack of any illness impacting on the patient` s lives, lower uncertainty in the *symptoms and flares* scale did not necessarily reflect greater certainty of a positive outcome. Being less uncertain with regards to symptom interpretation and flare prediction could ultimately reflect lower uncertainty of a negative outcome, such as being more certain that one` s condition will flare-up in the future.

In other words, lower uncertainty in relation to *symptoms and flares* could reflect greater certainty of an unfavourable illness course and thus higher uncertainty could be less distressing than lower uncertainty. This finding challenges the notion that uncertainty is consistently an aversive concept and highlights the importance of considering the subject or specific issues regarding which a patient expresses uncertainty.

Findings designated the multi-dimensional nature of the patient uncertainty which was firstly suggested in the qualitative study and subsequently demonstrated in the quantitative exploration. The five different uncertainty domains displayed differential associations with illness trajectory, demographic and other patient outcomes, thus supporting the individuality of these dimensions. Furthermore, when assessing the contribution of patient uncertainty domains to patient outcomes the domains did not contribute to outcomes in parallel either within or between the two conditions, and in most cases only one of the domains contributed to a specific outcome. Therefore these findings suggested both the differential contribution of patient uncertainty domains to outcomes and the variable influence of patient uncertainty on patient outcomes in SLE and RA.

7.4.2 Implications for Patient Uncertainty in SLE and RA

As discussed in the introduction to this thesis, patient-centred care and, more specifically, patient outcomes have been the focus of the National Health System's (NHS) vision agenda (163) as a means of improving care. In the past two decades, literature on SLE and RA has increasingly focused on the patients` perspective, accessing the physical, mental and social aspects of such diagnoses (343). The

findings of this thesis add to the understanding of patients with SLE and RA, offering insight into the domains of patient uncertainty and their potential role in patient management.

The findings indicate that both patients with SLE and those with RA experience uncertainty in a variety of domains. The conceptual framework comprised some of the domains that have previously been reported in other studies, such as symptom recognition, illness progression and predictability and long-term planning, as well as introducing domains that had not previously been explicitly assessed in patients with SLE and RA. The conceptual framework also highlighted the limitations of previous conceptualisations in terms of capturing the breadth of the patient uncertainty concept in cases of SLE and RA. (20). Subsequently, the findings demonstrate that the PCQ is a useful instrument for assessing patient uncertainty in SLE and RA, as it adequately measures issues that are important to these patients and which were not addressed by previous instruments.

The findings offer further implications for the potential role of patient uncertainty in SLE and RA management. In line with previous literature portraying uncertainty as an aversive perception (42-44), the qualitative findings of this thesis suggested that patient uncertainty is sometimes linked with negative outcomes. Qualitative studies have previously linked beliefs about medicines and dissatisfaction with health care with treatment adherence in patients with SLE and RA (120, 459, 461, 462). The findings of this thesis indicate that patients with SLE who are more uncertain about trusting their doctor adhere less to their treatment regime. In other words, these findings suggest an additional cognition that could play a role in SLE adherence management.

The findings also indicate patient uncertainty is associated to some extent with mood, in different ways between the two conditions. Previous research suggested that beliefs about one` s condition demonstrate a dynamic relationship with mood (448) and specifically suggested that depression is linked to the overall burden of a condition (448). By contrast, anxiety has been linked to the challenges of living and adjusting to a disease (343, 449). The findings of this thesis indicate that patients with SLE who are more uncertain about managing their condition experience higher levels of uncertainty, whereas patients with either SLE and RA who express greater uncertainty regarding the impact of their condition on their lives experienced higher levels of depressive symptoms. Therefore, in line with the suggested links between cognition and mood, this study has introduced two domains of patient uncertainty which are linked with anxiety and depression.

The findings further imply that patient uncertainty is also somewhat related to HRQoL levels, particularly the physical aspects of both generic and disease-specific HRQoL. Even though patients with SLE or RA reported low levels of HRQoL (49, 400), these did not display any strong links with disease severity but rather revealed strong associations with mood, coping and beliefs (302, 403, 404, 410, 425). These findings demonstrate that some domains of patient uncertainty are related with lower levels of HRQoL, particularly with regard to the physical aspects.

The findings indicate that patients reporting higher levels of impact uncertainty also tended to report poorer HRQoL as impact was the PCQ scale with the strongest univariate associations with the assessed outcomes and particularly HRQoL. This was true for both generic and disease-specific in both SLE and RA. Patients who are more uncertain in relation to medication effectiveness and necessity report a greater HRQoL burden in SLE cases and in HRQoL symptoms in people with RA. Contrary to the remaining domains of patient uncertainty, uncertainty regarding *symptoms and flares* contributed positively to physical aspects of disease-specific HRQoL. As explained above, this is an interesting finding that is open to interpretation, as it can constitute an artefact of disease severity or can simply reflect the differential content of the *symptoms and flares* scale.

The thesis demonstrates that patient uncertainty is a relevant concept for rheumatic patients and offers the first comprehensive conceptualisation and self-report instrument specific to SLE and RA. These findings are in line with both the general and rheumatic bio-psychosocial model of illness (150, 155), as they imply that cognition like patient uncertainty is linked to psychosocial, physical and behavioural outcomes in patients with SLE of RA. Exploring the role of cognitions such as patient uncertainty in patient outcomes is particularly relevant to SLE and to RA, as physical, psychosocial and behavioural outcomes have not been solely or consistently linked with clinical variables (see section 2.4). These findings cannot be used to conclude a causal or moderating role of patient uncertainty in patient outcomes, but they do offer the basis for future analyses that will explore these.

7.4.3 Methodological Implications

The methodology discussed and used in this thesis offers useful implications for all types of self-report variables and instruments. As research and practice increasingly focus on the measurement of patient outcomes , it is crucial that more attention is paid to the development and evaluation of the instruments used to assess such outcomes (139, 141, 162). Sub-optimal instruments can ultimately undermine the findings of any research, as the adequacy of any form of measurement relies directly on the adequacy of the instrument used to measure it (141, 142). The mixed methods methodology used in this thesis to quantify patient uncertainty displays the benefits of a disease-specific, bottom-up approach to developing a new self-report instrument.

Following best practice guidelines (139, 143, 182) for developing a conceptual framework, the findings provided a comprehensive and relevant conceptualisation of patient uncertainty regarding SLE and RA when compared to previous literature. This included several domains and sub-domains of patient uncertainty that were not covered by previous definitions and instruments of patient uncertainty. Thus, the findings of this thesis highlighted the insufficiency of existing conceptualisations to account for patient uncertainty in SLE and RA and, subsequently, the inadequacy of existing generic instruments to quantify all aspects of patient uncertainty in SLE and RA cases.

In addition to the conceptual framework and instrument development methodology, the complementary psychometric approach employed to evaluate the PCQ also offers useful insight into the benefits and scientific rigour of modern psychometric techniques. Using the Rasch Measurement Theory (RMT), the PCQ scales were evaluated against a testable model and their performance was tested on person and item location, response scale ordering against stringent criteria (517) and offered interval level measurement. Another advantage of the RMT is that the RUMM software accounts for missing data by the computation of class intervals on an item and not a person basis.

These characteristics of the RMT demonstrate its superiority compared to traditional psychometric techniques that rely largely on correlational analyses and which are sample dependent (142).This thesis has therefore provided a useful framework for exploring new concepts and for developing future patient instruments which can be used to inform “health measurement” across any patient group.

7.5 Recommendations for Future Research

With regard to recommendations for future research, it must be acknowledged that the newly developed PCQ instrument would benefit from additional psychometric evaluation. The RMT results indicated various sub-optimal findings that could be improved. Firstly, subsequent evaluation should seek to reconsider the items that underestimated the trait or that displayed dependency, and should consider their deletion or integration. Secondly, the *self-management* scale needs to be addressed and ways of extending its breadth of items and subsequent range of uncertainty should be targeted. It is possible that supplementary qualitative data, perhaps in a focus group format, could help to address this issue.

In addition, future research could aim to assess alternative response scales for the PCQ scales. The four-point "certainty" Likert scale was empirically validated both qualitatively and quantitatively in the cognitive debriefing interviews and field testing. However, it would be interesting to explore whether alternative and more conventional response categories such as an "agreement" scale would lead to different results. In other words, assess whether respondents are more inclined to choose a negative response category on a "certainty", rather than on an "agreement" scale.

The psychometric evaluation of the PCQ instrument was conducted primarily in London hospitals, whereas the participants used in the item generation were solely recruited from one London hospital. Additional validation would therefore be recommended in order to determine the suitability and performance of the instrument in other parts of the UK, as well as in other cultures. As the PCQ instrument was developed and evaluated in two rheumatic conditions, further research could aim to assess the applicability and performance in other rheumatic conditions, such as psoriatic arthritis or ankylosing spondylitis, given the similarities in disease course and treatment to SLE and RA, and could possibly also be used in other chronic conditions.

In contrast with other available uncertainty instruments, this thesis utilised comprehensive methodology comprising a conceptual framework approach and inductive item generation, as well as the use of extensive modern psychometric analyses for the development and validation of the instrument scales. Future research could therefore use such methodology as a template for the exploration and quantification of patient uncertainty in other chronic conditions and in any other patient outcomes.

Future research should aim to assess patient uncertainty in longitudinal designs, whilst collecting more elaborative disease and treatment related data that would permit the conduct of more sophisticated statistical techniques that can assess the causal and moderation roles of uncertainty. Such explorations would allow for a more detailed examination of the role of illness characteristics in the expression of patient uncertainty and permit further conclusions to be made regarding the sources of uncertainty, as well as the strength and/or direction of the relationships of patient uncertainty with other outcomes.

In addition, future research should serve to examine the *symptoms and flares* domain that did not display the expected associations in this thesis more fully, and attempt to explain the notionally contradictory nature of this specific uncertainty domain. Future research should also aim to investigate whether higher levels of uncertainty in this domain do not have a negative association with other outcomes as they do in other domains, or whether the contradictory findings reflect an artefact of overriding disease severity that could be associated with lower uncertainty in this domain. To establish this, more thorough disease severity data should be collected, including information on previous disease activity or cumulative disease damage, which could be associated with the contradictory findings reported in this thesis.

Apart from disease severity, other variables indicated as potential sources of patient uncertainty, including age and disease duration, should be further explored using applicable methodological designs that would allow for the collection of longitudinal data in order to explore their roles in patient uncertainty. Subsequent longitudinal studies with more sophisticated statistical techniques would also serve to explore the contribution of patient uncertainty to outcomes such as treatment adherence, mood and HRQoL, and would serve to clarify the causal direction of their relationship, as cross-sectional explorations like the one presented in this thesis could serve to amplify such relationships and to limit interpretation of findings.

The association of coping, social support and patient uncertainty was not as strong as was suggested by the literature and by the qualitative findings; however, the scientific rigour of the instruments used to assess these variables is questionable. It would be worthwhile to explore these relationships in the future, particularly by means of instruments with improved psychometric properties.

Future research should consider the timing of patient uncertainty by using the PCQ instrument to measure uncertainty in newly diagnosed SLE and RA patients. This

would enable the exploration of whether there are any differences in the levels of patient uncertainty at the onset of disease. Another distinct patient group in which patient uncertainty could be considered is adolescents suffering from SLE or RA. Using the PCQ instrument in this patient group would require some preparatory work to ensure the instrument`s relevance, applicability and performance.

In the longer term, if the role of patient uncertainty in SLE and RA patient outcomes is established, research should address ways of managing patient uncertainty in order to improve such outcomes. Efforts to reduce uncertainty should be tailored to each specific domain. This would be necessary because the domains of patient uncertainty reflect different subjective perceptions, for example interpretation, knowledge, expectations and trust, as well as displaying differential associations with other variables. Future research should therefore aim to explore whether patient uncertainty levels are amenable to change and, if so, how this change could be achieved.

Gaining a better understanding of the sources of patient uncertainty would be a pre-requisite for managing patient uncertainty levels. Several self-management interventions in chronic illness have drawn from the bio-psychosocial model and other social cognition theories to improve the moderating variables of chronic illness, such as illness perceptions, self-efficacy and coping (147, 343). Such interventions include techniques tailored to the nature and the sources of each target variable. It is necessary, therefore, to gain a better understanding of the sources of patient uncertainty in each of the domains.

Whether interventions can help to manage patient uncertainty and whether this will have any subsequent effect on patient outcomes could be the focus of future research in the longer term. For example, whether decreasing levels of uncertainty in relation to the trust patients have in their doctors would improve treatment adherence in the SLE sample. In addition, whether decreasing levels of *medication* and *impact* uncertainty would improve depression levels in RA and HRQoL in both conditions could be the focus of future interventions aimed at improving patient management.

Considering the contradictory findings related to the *symptoms and flares* domain of patient uncertainty, this should be addressed independently from the remaining domains in relation to its contribution to patient outcomes. If subsequent research confirms that lower levels of uncertainty in the *symptoms and flares* domain are associated with lower levels of HRQoL, the mechanism behind this should be further

researched, as discussed above. Evidently, interventions aiming to decrease uncertainty to improve outcomes should not target this domain.

7.5.1 Future Use of the PCQ

The PCQ is a validated instrument that can be used in any research study aiming to explore the patient perspective within SLE and RA and as described above within other rheumatic conditions with similar disease course and features following cross-validation. As noted earlier the PCQ measures, a subjective multi-dimensional patient cognition which has been associated to some extent with treatment adherence, mood and HRQoL in SLE and RA (not consistently between the two conditions or across the five domains). The PCQ can therefore be used by research looking at the non-clinical predictors and contributors of such outcomes in SLE or RA. As far as clinical trials and intervention research is concerned, the PCQ is not intended for use as a patient reported outcome as it does not measure an “outcome” of disease. If however, subsequent research confirms the role of patient uncertainty in causing and/or moderating disease outcomes such as HRQoL, PCQ will constitute a useful instrument for use in such research to address aspects of the patient response.

7.6 Chapter 7 Summary

This thesis was motivated by the potential relevance of the poorly researched concept of patient uncertainty regarding SLE and RA. The literature review revealed the key role of patient uncertainty in the illness experience, particularly in chronic and unpredictable conditions like SLE and RA. Diverse findings indicated the presence of patient uncertainty in these conditions. Nevertheless, the existing literature lacked a comprehensive conceptualisation of patient uncertainty in rheumatology and, subsequently, an appropriate instrument to quantify it.

The thesis makes three contributions. Firstly, qualitative explorations demonstrate the relevance of patient uncertainty regarding SLE and RA and further offer the first comprehensive conceptual framework for patient uncertainty in these rheumatic conditions, including five different domains.

Secondly, the thesis offers a new instrument, the PCQ that quantifies patient uncertainty. In line with best practice guidelines (139, 143, 144) rheumatology outcome-recommendations (179, 532), the PCQ is an instrument developed and evaluated using comprehensive methodology, with a large amount of patient input, and specific to SLE and RA. Therefore, the thesis contributes a scientifically rigorous instrument to SLE and RA health measurement.

Thirdly, the thesis offers a preliminary indication of how different domains of patient uncertainty are associated with behavioural and psychosocial outcomes in SLE and RA, suggesting areas for future research. Finally, the methodology used in this thesis serves as a useful template for the rigorous development and validation of self-report instruments.

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