The Experience and Impact of Fatigue in Patients with Systemic Lupus Erythematosus, and their Partners: A qualitative study

A thesis submitted in fulfillment of the requirements for the degree of Master of Science in Health Psychology

Author:
Linda Hoek (s1148788)
University of Twente, Enschede
Faculty of Behavioral Sciences
Department Psychology, Health & Technology

Supervisors:
Dr. Christina Bode
Nadine Köhle, MSc.

Faculty of Behavioral, Management and Social Sciences
Department Psychology, Health & Technology

Enschede, January 2015

UNIVERSITY OF TWENTE.

Abstract

Background: Severe fatigue is one of the most disabling symptoms of systemic auto-immune diseases and has a major impact on quality of life of patients. How patients' fatigue is experienced by partners and how it affects the quality of life as a couple has yet been underexplored. Therefore, the aim of this study was to explore the experience and impact of severe fatigue in patients and partners, facing a systemic auto-immune disease, as individuals and as couples.

Methods: Data for this study were collected using a qualitative, cross-sectional design. Eligibility criteria required patients to be diagnosed with Systemic Lupus Erythematosus (SLE) or related diseases, experience fatigue on a daily or regular basis and couples to communicate in Dutch. This study contained nine adult heterosexual couples, whom were separately interviewed about their experience with patients' severe fatigue and the impact on quality of life, using a semi-structured interview scheme. After obtaining all transcriptions, inductive and deductive coding was used to identify categories and data-patterns.

Results: Severe fatigue did not only have a major impact on quality of life of patients, but also on their partners' life. Among other aspects of quality of life, fatigue had the largest impact on cognitive functioning, activities of daily living and employment status in patients. For partners, patients' fatigue caused above all the most impact on daily activities and the partner relationship. Clear differences between partners' quality of life were found. In couples, communication, acceptance and knowledge of the disease were reported as important outcomes for relational satisfaction.

Conclusion: Severe SLE-related fatigue was more disabling for patients than for partners, while the impact was comparable in couples for some domains. Communication, acceptance and knowledge of the illness were important outcomes for relational satisfaction within couples. Exploring the interpretation of efficient communication should be subject of future research in order to successfully develop self-management interventions for couples facing SLE-related fatigue.

Samenvatting

Achtergrond: Eén van de meest invaliderende kenmerken van Systemische Lupus Erythematodes (SLE) is ernstige vermoeidheid. Deze ernstige vermoeidheid heeft een grote impact op de kwaliteit van leven van SLE-patiënten. Hoe de vermoeidheid van SLE-patiënten wordt ervaren door partners en hoe het van invloed is op hun kwaliteit van leven, is tot nog toe niet onderzocht. In dit onderzoek is gekeken naar hoe ernstige vermoeidheid wordt ervaren en welke impact het heeft op het leven van SLE-patiënten en hun partners, als individuen en als koppels.

Methode: De data voor deze studie zijn verzameld door gebruik te maken van een kwalitatieve, cross-sectionele onderzoeksopzet. Patiënten in de studie dienden gediagnosticeerd te zijn met SLE of gerelateerde aandoeningen, regelmatig vermoeidheidsklachten te ervaren en alle participanten dienden de Nederlandse taal te beheersen. Dit onderzoek werd gehouden onder negen heteroseksuele koppels, waarbij elke participant individueel werd geïnterviewd over de ervaring van SLE-gerelateerde vermoeidheid (of die van hun partner) en de impact hiervan op hun kwaliteit van leven. Hiervoor is er een semigestructureerd interviewschema aangehouden. Na het transcriberen van alle interviews, is de data inductief en deductief geanalyseerd om categorieën en patronen te kunnen identificeren.

Resultaten: Ernstige vermoeidheid bleek niet alleen een grote impact te hebben op de kwaliteit van leven van SLE-patiënten, maar ook op de kwaliteit van leven van hun partners. Vermoeidheid had voor SLE-patiënten de grootste impact op cognitief functioneren, dagelijkse activiteiten en werk. De gevolgen van de vermoeidheid van de patiënt speelden voor de partner voornamelijk een rol bij de partnerrelatie en dagelijkse activiteiten, naast andere domeinen van kwaliteit van leven. Onder partners waren er duidelijk verschillen in welke impact vermoeidheid van de patiënt had op hun kwaliteit van leven. Wanneer gekeken werd naar koppels, kwamen communicatie, acceptatie en kennis van de aandoening naar voren als belangrijke uitkomsten voor tevredenheid met hun relatie.

Conclusie: Ernstige SLE-gerelateerde vermoeidheid was meer invaliderend voor patiënten dan voor partners, hoewel er vergelijkingen zijn binnen bepaalde domeinen van kwaliteit van leven. Communicatie, acceptatie en kennis van de aandoening waren belangrijke uitkomsten voor relationele tevredenheid binnen koppels. Verdieping in de interpretatie van efficiënte communicatie binnen koppels zou onderwerp moeten zijn voor vervolgonderzoek om succesvol een zelfmanagement interventie te kunnen ontwikkelen voor koppels die moeten leven met de gevolgen van SLE-gerelateerde vermoeidheid.

1. Introduction

Systemic auto-immune diseases are rare diseases that affect less than eight thousand patients in The Netherlands. These diseases cause the patient's body to form antibodies attacking multiple organs such as the skin, joints, muscles and other internal organs or systems (Giffords, 2003; LupusNederland, 2014; Nederlandse Vereniging voor Lupus, APS, Sclerodermie en MCTD (NVLE); Reumafonds, 2014). Examples of these diseases are systemic lupus erythematosus (SLE), antiphospholipid syndrome (APS) and mixed connective tissue disease (MCTD). Symptoms of these diseases may vary between and within patients (Giffords, 2003), for instance, patients may not all have the same symptoms or severity of symptoms and within patients, flares or relapses and remissions can occur abruptly. These often occur unexpectedly and without a clear cause.

SLE is the most frequent among previous mentioned systemic auto-immune diseases, counting 7500 patients diagnosed by the ARA-criteria in The Netherlands (NVLE). These ARA-criteria are listed symptoms of the disease and for diagnosis of SLE, at least four out of the eleven symptoms must be present. Examples of these criteria are photosensitivity, neurological disorders, hematological disorders and the most recognizable, butterfly-formed facial malar rash. The lack of accurate tests for lupus and the complexity of the disease often causes delay of diagnosis (Hatfield-Timajchy, 2007). SLE is mainly present in women, whereas 90% of all patients are female and the disease develops between the age of twenty and forty (Reumafonds, 2014). As previously mentioned, SLE can affect the whole bodily system including damage to the skin, abdominal organs, brain, blood and other systems. It is a chronic disease with alternating mild periods and flares that occasionally lead to hospitalization, and cannot be cured up till now. By using medication, certain symptoms of the disease can be suppressed. Even though SLE is most medically severe, other milder forms of lupus are skin lupus and drug induced lupus erythematosus.

APS is characterized by hypercoagulability which can lead to thromboses and pregnancy morbidities (Muscal & Brey, 2010; NVLE). This systemic auto-immune disease, also known as the Hughes syndrome, occurs in half of the cases simultaneously with other systemic auto-immune diseases. For example, it is present in 30% of patients with SLE. As in most auto-immune diseases, APS is mostly present in females, 60% of the cases and develops between the age of twenty and forty. Symptoms of the disease are, amongst others, arterial leg thromboses, pulmonary embolism, brain damage, extreme fatigue and malfunctioning of kidneys and liver. No specific treatment can cure this disease, but most patients use anticoagulants to prevent thromboses.

MCTD is considered as a disease with mixed symptoms of other auto-immune diseases (NVLE). For the most part it contains symptoms from illnesses as SLE, scleroderma and polymyositis. Development of the disease starts between the age of 20 and 50, with 90% of the patients being

female. Amongst a list of symptoms that can occur in patients with MCTD, examples are arthritis, muscular disorders, pulmonary malfunctioning and pericarditis. Even more than in other systemic auto-immune diseases, individual adjusted treatment is very important even though there is no cure for this disease up till now (Tani et al., 2014).

Raynaud phenomenon and Sjögren syndrome are mostly secondary symptoms that occur together with other systemic auto-immune diseases. The Raynaud phenomenon is characterized by the sudden appearance of white discoloration of fingers and/or toes (NVLE), caused by cold (weather) conditions, humidity or emotions. The Sjögren syndrome is a chronic inflammation of the salivary- and lachrymal glands, but inflammation can also occur in other organs according to the Nederlandse Vereniging Sjögren Patiënten (NVSP, 2014).

Besides fluctuating primary physical symptoms, up to 90% of patients with systemic auto-immune diseases experience fatigue (Ahn & Ramsey-Goldman, 2012; Gallop, Nixon, Swinburn, Sterling, Naegeli & Silk, 2012; Sterling et al., 2014). According to the ad hoc committee on systemic lupus erythematosus response criteria for fatigue (2007), fatigue is a complicated symptom to be defined in SLE and other related auto-immune diseases. Research on other chronic diseases, such as stroke, shows that fatigue can be divided into normal and pathological fatigue. Normal fatigue is referred to as a state in which a person is exhausted due to overexertion, for example by exercising. The definition of pathological fatigue, which is the subject of this thesis, is: “a feeling of physical tiredness and lack of energy that was described as pathologic, abnormal, excessive, chronic, persistent or problematic” (De Groot, Philips & Eskes, 2003, p. 1715). Despite the lack of a clear definition of fatigue in systemic auto-immune diseases, it is thought to be associated with several factors. Reduced physical activity, medical treatment, psychosocial factors, e.g. anxiety, depression and pain, diet, e.g. lack of vitamin D, and comorbidities, e.g. obesity and fibromyalgia have been shown to relate to fatigue (Balsamo & Santos-Neto, 2011; Somers, Kurakula, Criscione-Schreiber, Keefe & Clowse, 2012; Wang, Gladman, Ibañez & Urowitz, 2012). However, opposite results from other researchers did not find support for these relationships (e.g. Kozora, Ellison, Waxmonsky, Wamboldt & Patterson, 2005).

Since fatigue is often present on a daily basis, it has a considerable impact on the quality of life of patients with SLE and related auto-immune diseases. Quality of life can be defined as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns (WHO, according to Lechner, Mesters & Bolman, 2006, p. 58). It is a subjective evaluation of life and the character of quality of life relative to the context. According to Lechner et al. (2006) quality of life can be evaluated at a psychological, physical and social level. Besides general quality of life, Gallop et al. (2012) have studied the health related quality of life in patients with SLE and found seven domains in

health related quality of life which were affected by SLE: emotions, social impact/family/leisure time, cognitive impact, appearance, work and independency.

Even though reduced quality of life in patients with a systemic auto-immune disease that experience fatigue is in general scarcely investigated, research on quality of life of their partners has never been conducted. Thus far, Giffords (2003) found that SLE in general has a big impact on direct family of SLE-patients:

> Though the person with the chronic illness is the one who must experience the restrictions, the physical changes, the apprehension and anxieties, it also affects those who care about the person. The people who care about the person with lupus or other chronic illnesses may also face an adjustment process. Family, friends and colleagues also experience feelings of denial, anger, fear, frustration, etcetera. (p. 66)

Even though there is little known about the quality of life of partners from SLE patients and related diseases, research in other chronic diseases such as breast- and prostate cancer shows that the disease has a major impact on the quality of life of partners (Carlson, Bultz, Speca, St. Pierre, 2000; Harden et al., 2013; Kim & Given, 2008; Kuenzler, Hodgkinson, Zindel, Bargetz & Znoj, 2011; Pitceathlya & Maguirea, 2003; Wadhwa et al., 2013; Wagner, Bigatti & Storniolo, 2006), especially on mental health, general health and vitality. Adaptations to work, feeling the need to support the partner but still have to learn a lot about the disease, anger towards the situation, feelings of fear for the future and financial aspects (Hilton, Crawford & Tarko, 2000) are frequently occurring problems in lives of cancer patients' spouses. In addition, adapting to practical matters such as providing transport, monitoring symptoms and an augmentation of household chores makes a partner always taking account for his ill partner (Wagner et al., 2006). Research on fatigue in chronic diseases, e.g. cardiovascular disease, asthma, cancer, diabetes mellitus, shows that it affects personal life and social relations of partners from patients (Baanders & Heijmans, 2007). Partners have a smaller amount of time, are less flexible in personal life and experience a disruption of social relationships and interaction. The lives of partners can therefore be just as disturbed as the lives of a patient living with fatigue, still, it has never been explored in partners from patients with a systemic auto-immune disease. Results from research on other chronic diseases (Baanders & Heijmans, 2007) indicate that there is a need for further investigation of this specific area, especially since patients with a chronic disease rely on their partner's emotional and practical support (McCaughan et al., 2013).

Furthermore, besides the individual experiences of patient and partner it is highly interesting to investigate how fatigue interferes within the lives of couples. From previous research, it is apparent that coping with a chronic disease becomes a task of married life (e.g., Brooks, King & Wearden, 2014). Especially when one partner is suffering from a life-changing disease, the role of a spouse is a crucial determinant in illness perceptions of the patient (Coyne & Fiske, 1992; Goodwin,

2000). Besides, a partner has to deal with own well-being and on the other hand the care for the patient (Coyne & Fiske, 1992). In view of the fact that a spouse is majorly involved in facing a chronic disease and that severe fatigue is a symptom that is often present at a daily basis, it is highly relevant to explore the experiences and interference of fatigue in couples. So far, however, no previous research on fatigue in couples facing a systemic auto-immune disease has been conducted. Therefore, this study focuses on the experience and impact of fatigue on the quality of life in patients with a systemic auto-immune disease and their partners, and explores the interference of fatigue within couples.

Research Questions

This study contains three research questions, which have been depicted in figure 1.

1. How do patients with a systemic auto-immune disease* experience fatigue and how does it affect the experienced quality of life?
2. How do partners from patients with a systemic auto-immune disease* experience the partner's fatigue and how does it affect their experienced quality of life?
3. To what extend can the experienced quality of life, which is affected by fatigue in patients with a systemic auto-immune disease*, be compared between patients and partners and how does fatigue interfere within the lives of patients and partners as a couple?

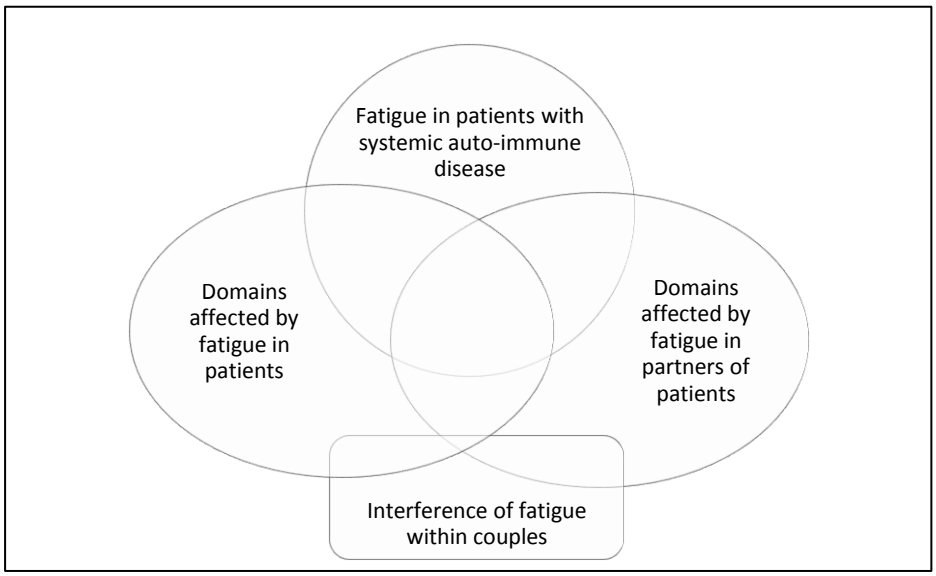

Figure 1. Visual representation of research questions

* Such as SLE, antiphospholipid syndrome (APS), mixed connective tissue disease (MCTD) and/or the Sjögren Syndrome

2. Methods

To gain insights into the experience of fatigue and the impact on quality of life of patients and partners, this study followed a (semi-)explorative and descriptive character. An observational, cross-sectional qualitative research design was used. Data was collected in a natural setting, making sure that conditions were not manipulated (Crosby, DiClemente & Salazar, 2006).

Sampling and Participants

The Ethics Committee of the Faculty of Behavioral Sciences at the University of Twente gave its approval before recruiting participants. To protect participants in research in The Netherlands, the law on medical-scientific research (Wet Medisch-wetenschappelijk Onderzoek, WMO) was established in 1998. Since participants in this study were not subjected to any form of action, nor were they required to follow certain behavioral rules, the study was not found to be WMO-obligated. Nine patients and their partners were recruited by convenience sampling, with the support of the Dutch patient organization for people with SLE, APS, scleroderma and MCTD, the NVLE. At the World Lupus Day-congress, on the 10th of may 2014, patients and partners were informed about this study by poster, by giving them brochures, see appendix A, and by approaching them directly. Patients and partners could voluntarily register for this study by filling in a form where they could write down their name, email address, phone number, residence, their illness, age and they were asked if they had a partner who would be willing to join the study. Patients and partners could also subscribe afterwards per mail or telephone. After subscribing, patients were checked for meeting the following inclusion criteria:

- Participants are diagnosed by a medical specialist with one of the following diseases: SLE, APS, MCTD and/or the Sjögren Syndrome, or their partner is.
- Participants experience fatigue on a regular basis, or their partner has to.
- Participants are aged eighteen years or more
- Participants are able to communicate in Dutch

Eligible participants were then contacted within two weeks to make an appointment for the interview. Interviewing nine patients with a systemic auto-immune disease and their partners was found to be sufficient, based on other study samples (Årestedt, Persson & Benzein, 2014; Crosby et al., 2006; Eghlileb et al., 2007; Guest, Bunce & Johnson, 2006; Jumisko, Lexell & Söderberg, 2007; Sutanto et al., 2013). This study included eight female patients and one male patient. This is a convenient reflection of the population of people having a systemic auto-immune disease, since 90% of these patients is female (Giffords, 2003; LupusNederland, 2014; NVLE; Reumafonds, 2014).

Procedure and Interview

Participants were interviewed individually at a location of their choice, which could be at their homes or at the University of Twente. They were interviewed by one of the two interviewers that were involved in this study. Before starting the interview, participants were debriefed about the study, the processing of data and that the data was reported anonymously as well as treated confidentially. Participants subsequently were asked to sign a consent form, stating the participant signs to be informed about the study, understands the expectations and was aware of the collection and analysis of the anonymous data. Participants could also withdraw their participation at any moment during the interview.

The experience and impact of fatigue was investigated by using a semi-structured interview. Questions in this self-developed interview were in Dutch and were almost similar for patients as was for their partners, as can be seen in the interview protocol (Appendix B). Patients started by filling in the FSS, which is described in the next subchapter, and were generally asked about the onset of the disease and when they first noticed the occurrence of fatigue. In order to prevent biased answers, the interview continued purposely with open questions. The first part, exploring the experience of fatigue, contained three open questions for patients, for example, 'Can you describe the feeling of fatigue?'. The second part of the interview, exploring the impact of fatigue on quality of life, also began with an open question: 'Can you describe how fatigue influences your life'?, but had had a more structured framework with topics to discuss when they were not spontaneously mentioned. Topics were then introduced by questions such as 'How does (your partners') fatigue have an influence on your social relationships?'. Other topics were personality, cognitive functioning, emotional functioning, activities of daily living, employment status and voluntary work. Interviews with patients ranged in duration from half an hour to one hour and if needed, a short break between the first and second part was held.

Partners also initiated by filling in the adjusted FSS, which is described in the next subchapter, and were generally asked about whether they were in a relationship from the onset of the disease and if fatigue was present from the start of their relationship. The first part contained one open question: 'What does your partner's fatigue mean to you?'. The second part also began with one open question: 'Can you tell me how your partner's fatigue influences your life?'. Topics to discuss, if not spontaneously mentioned, were emotional impact, personality, cognitive impact, daily activities, leisure time/social life/family, employment status and voluntary work. Interviews with partners ranged in duration from fifteen minutes to forty-five minutes. All participants in this study could afterwards denote their interest in having a summary of the study in either by hardcopy or by mail.

Fatigue Severity Scale

The Fatigue Severity Scale (FSS) is a widely used questionnaire to measure fatigue in patients with SLE. The questionnaire was intended to measure fatigue in patients with SLE and Multiple Sclerose (Krupp, LaRocca, Muir-Nash & Steinberg, 1989), but is also used for measuring fatigue in patients with brain injury, cancer, chronic fatigue syndrome, hepatitis C, Parkinson's disease and patients sleep disorders or insomnia (Lerdal, Wahl, Rustoen, Hanestad and Moum, 2005). The FSS measures the impact of fatigue on specific types of functioning within the last two weeks (Ad hoc committee on systemic lupus erythematosus response criteria for fatigue, 2007). It contains nine questions about fatigue as in where individuals choose a number between one, strongly disagree, and seven, strongly agree. The FSS contains questions about fatigue and motivation, physical activity and the daily problems fatigue may cause. A question example from the FSS was:

'Fatigue interferes with my physical functioning'

Completely disagree 1 2 3 4 5 6 7 Completely agree

In this study, scores of all nine questions were summed up per participant and the total number was divided into nine. Even though some studies used a cut-off score of 3 (e.g., Omdal, Waterloo, Koldingsnes, Husby, & Mellgren, 2003), meaning being fatigued, most studies used a FSS-score above 4 to indicate severe fatigue (Lerdal et al., 2005). According to the Ad hoc committee on systemic lupus erythematosus response criteria for fatigue (2007), the Cronbach's alpha of the English version of the FSS is 0.89. There was no information about the reliability and validity of the Dutch version of the FSS. Partners filled in an adjusted FSS-form, as can be seen in the interview protocol (Appendix B)**,** to get insights in partners' believe on the severity of patients' fatigue.

Data analysis

All interviews were audio-recorded and transcribed verbatim. The analysis contained three steps to code the data: open coding, axial coding and selective coding (Crosby et al., 2006; Mertens, 1998). Data-analysis was conducted by using bottom-up and top-down coding. The researcher started by reading all transcripts in order to identify relevant text fragments. These fragments were meaningful parts of the text, containing words and phrases focusing on the aim of this study. Each fragment was given a code, but could also obtain several codes. After analyzing four interviews, nearly almost all codes were identified. *Atlas.Ti* (Muhr, 1991) was then used to conduct content analysis, using queries based on codes, word clusters, words and phrases, with the use of *Atlas.Ti*. After obtaining all codes per group (patients and partners), a code scheme with examples of codes was developed (Appendix C) in where all codes were put under a collective category. Examples of categories are 'daily

activities', 'future plans' and 'cognitive functioning'. Constant comparison of the data for resemblances and differences was applied in order to find supportive and disconfirming evidence (Brod, Tesler & Christensen, 2009). All transcripts were individually analyzed to focus on finding answers to the first two research questions. For comparing couples, however, interviews had to be considered as dyadic units in order to recognize similarities, differences and interactions (Brooks et al., 2014). Comparison could be applied by analyzing all reported aspects dealing with consequences to fatigue as a couple. Main themes in where fatigue had an impact on couples' lives were denoted and described for each couple.

Inter-rater reliability

In order to decrease potential differences and error, this study evaluated its qualitative data by a peer reviewed inter-rater reliability test (Cohen & Crabtree, 2008; Moret, Reuzel, Van der Wilt & Grin, 2007). After the development of the concept code scheme and analyzing the interviews, an independent researcher has individually coded one randomly chosen interview by using *Atlas.Ti*. When comparing the coded interviews from both researchers, dissimilarities have been discussed. Dissimilarities were mostly found by means of giving a code to certain fragments whereas the other researcher did not give a code to this fragment. For example:

> *"No, all of our friends are aware of it and take it into account, we either go together or we're going separately. When I say 'I have to help with something', you know, a job for someone, than I will go by myself, but in general it works well like this (PR4)"*

The first researcher coded this fragment as 'social environment - no consequences and contact', whereas the second researcher did not code this fragment. Some codes were deliberately adjusted whereupon an inter-rater reliability could be determined. All remaining differences regarding to coding were summed up and divided by the total number of fragments, this number was deducted from one resulting in a reliability ratio of 0.83 (1-(5/30)). According to Streiner and Norman (1991), ratios above 0.75 are sufficient, therefore the concept version of the code scheme became, with little adjustments, the final version (Appendix C).

3. Results

This chapter represents the results that derived from patients' and partners' interviews. The results will be divided into three paragraphs: patients, partners and couples. The first two paragraphs commence with a general description of demographic characteristics, including an accompanying table, followed by descriptions of the experience and impact of patients' fatigue. Both paragraphs will end with a paragraph summary. The third paragraph describes the results of the interference of fatigue in couples' lives per couple, starting with the general findings and ending with a paragraph summary. Results correspond to the research questions.

3.1 Patients

3.1.1 General findings patients

Table 1a presents the demographic characteristics of all patients in this study. Most patients were diagnosed with SLE, sometimes combined with other auto-immune diseases, one patient was diagnosed with APS and one patient suffered from MCTD. Since almost all patients scored above 4 on the FSS, indicating severe fatigue, most were not employed. Patients were mostly either married for more than 30 years or less than 10 years.

3.1.2 The experience of fatigue

When patients were asked to describe the feeling of fatigue, they spontaneously explained fatigue in wide-ranging terms of physical and psychological complaints, frequency, emotional aspects and daily living. What should be stated is that all patients were able to differentiate between normal fatigue and pathological fatigue. Participants assured that pathological fatigue, started from or around the onset of the disease, was significantly different than normal fatigue.

> *"Yes, it is totally different. Because, the fatigue I had before I became ill, often was a logical consequence to a certain action. I responded to that in a sensitive way and then I would recover. For example, if you were going out and then got early into bed, you would recover. Or if you were exercising (PT6)"*

Severe fatigue as a symptom

The majority of patients described fatigue as reduced physical energy in terms of 'not having strength', 'the need to sleep or to lie down', 'worked hard', 'a tired body', 'a heavy body', 'everything turned into syrup'.

Table 1a. Patient Demographic Characteristics (*N*=9)

Participant (Nr.)	*Disease*	*Gender (M/F)*	*Age (years)*	*Education level*[1] *(Low/Middle/High)*	*Employment status*	*Voluntary work (Yes/No)*	*Together with partner*[2] *(years)*	*Children*	*FSS-Score (max. 7)*
PT1	SLE	F	50	High	Disabled	No	B	3	6
PT2	SLE	F	57	Middle	Disabled	No	D	2	6
PT3	SLE	F	63	Low	Part-time employed	No	E	2	5,4
PT4	APS	F	70	Middle	Retired	Yes	E	1	5,2
PT5	SLE	F	66	Low	Retired	No	E	2	5,3
PT6	SLE	F	37	High	Disabled	No	B	2	5,7
PT7	SLE/Sjögren/ Hashimoto's disease	M	51	Low	Disabled	No	A	2	5,2
PT8	MCTD	F	66	Low	Retired	No	E	3	3,9
PT9	SLE/Sjögren/ Hashimoto's disease/ Fibromyalgia/COPD	F	51	Low	Partially disabled	No	A	2	5,4

[1] Low: No education, primary school or lower vocational education
Middle: High school and middle vocational education
High: High vocational education and university

[2] A= 0-10; B=11-20; C=21-30; D=31-40; E=>41

"Yes, a feeling of exhaustion. Sometimes it felt like a poisoning of my muscles, or my nerves. I can't… or the feeling like everything turned into syrup (PT6)"

Fatigue was also described in terms of reduced mental energy, similar to 'a numb feeling' or 'having no more drive'.

"I even have got, because I paint, but I didn't even resumed doing that, which is about, I think, at least a year, nine months ago that I have painted for the last time or something, yes, even haven't had the energy to pick it all up and to put it down here, because then I have to tidy it up again and if I want to go to sleep, I don't even have the energy you know? (PT1)"

Some patients reported fatigue as associated with being ill. They complained about 'having a headache', 'getting ill' and 'having a fever'.

"And I often compare it with having a fever. You don't have fever, but you do have that feeling of fever. You have a fever, what can you do? Well, nothing. So that is the best way to describe it, the feeling of having a fever (PT7)"

Frequency of severe fatigue

Overall, being fatigued varied between patients, but most of them agreed on being less fatigued in the morning. Fatigue was almost always present at a base level, but previous activity was mentioned as instigator of feeling more fatigued. Some patients mentioned a daily fatigue cycle, a pattern in which they function best in the mornings and function worse in afternoons and evenings, despite of a sleeping break in the afternoon. Only one patient clearly described the feeling of fatigue in the morning, independent of sleeping quality.

"Today I noticed it at twelve o'clock and that is right because I got up at eight o'clock so that must be right. Approximately at eight o'clock downstairs, at twelve o'clock I quickly went to the store with my daughter and then we were at the, in the car and then I started yawning, I'm so tired, you know, then I yawn and yawn and then I think, oh dear, there it is again (PT1)"

"No, sometimes it's when getting up and you think, hmm, you know? You feel ok like this, and that will continue all morning and by one o'clock or so, I start thinking no, it is not going to be like I expected (PT2)"

All patients could differentiate between ‘good’ and ‘bad’ days, concerning fatigue.

> *“The difference between bad and good? Yes, well, then I’m just, just a human that, yes, nice, then I can just do it all. Then I’m just feeling good about myself. And I cannot stand it when I, if I am tired, when I suddenly get blindsided by it, like not now (PT3)”*

There is a variability between and within patients in how they experience fatigue. Some patients feel fatigued all the time, whereas others have periods without fatigue. And even the feeling of fatigue changed within patients.

> *“And it’s also different. One day you’re even more tired, it is different but you are generally tired, tired of doing nothing (PT2)”*

> *“No, oh no, certainly there are periods that everything goes really well. And yes, that is also a wonderful feeling, yes (PT3)”*

Emotional aspects

A number of participants reported spontaneously, or after asking about emotions, negative feelings of ‘frustration’, ‘anger’, ‘sadness’, ‘disappointment’, ‘difficult’ and ‘depressing’ as a consequence to fatigue. An ‘Unpleasant feeling’, ‘feeling the need to cry’, ‘annoying’, ‘being uptight’ came parallel to the experience of fatigue.

> *“Troublesome, annoying, depressing, paralyzing. Yes. Tremendously limiting. Unpredictable (PT6)”*

> *“That frustrates me at times. That it just takes away a part of your life. As I see it anyway. Yes, I’m just oversleeping my life and I don’t like that. I just want, just be in the middle of life and experience it (PT1)”*

Most participants felt frustrated about being disabled in doing activities they used to do or wanted to do, as they were having an inner struggle.

> *“No, I really feel, I don’t want it. I resist it but I feel like I have to give in to it, myself (PT4)”*

Besides inner frustration and negative emotions towards themselves, some participants reported feelings of frustration or disappointment towards their social environment.

> *"Disappointment towards your environment if you're always there and you have to say like I really can't take it anymore. That is, I feel so burdened towards the other because saying no is really hard for me and then it's, yeah you will gather yourself together just to be the other person and that is just so, just so in conflict with yourself (PT3)"*

Daily living

When asking about what fatigue means to patients, especially problems with the inability of doing household chores and having daily leisure time were reported. Only one participant did not have problems with daily life. The majority of the participants described that they experienced fatigue as all the limitations it brings along in daily life.

> *"[My husband and I] were reading a theory the other day of an American who talked about the Spoon-theory. Saying that lupus patients only have a few spoons a day and that, for example, getting up and eating breakfast, you have already used one or two spoons. And that is indeed really … sometimes I've already used all, say, when taking a shower. Very confronted that all actions cost energy. It never comes naturally (PT6)"*

A frequent mentioned way to cope with daily fatigue was by anticipating and making choices in order to get through the day or making the best out of it.

> *"Yes, exactly, everything you'll [referring to interviewer] find normal doing, you do everything without thinking about it, but I have to think about it. Can I do it today, how do I feel? What do I have to do tomorrow? Do I have something to do tomorrow? If so, I can't do it today or cancel what I was planning for tomorrow. You always have to fit it in (PT2)"*

3.1.3 Impact of severe fatigue on patients' quality of life

In addition to spontaneous descriptions of fatigue, patients were also asked to describe in what way fatigue influences their lives. Although most patients spontaneously answered having problems during daily activities, the influence of fatigue in other domains for the most part had to be probed. Especially problems with cognitive functioning and the emotional impact were not often mentioned spontaneously, but were present in almost all participants after asking. The following domains were

identified: personality, cognitive functioning, emotional functioning, social environment, activities of daily living, employment and voluntary work, as can be seen in Figure 2a.

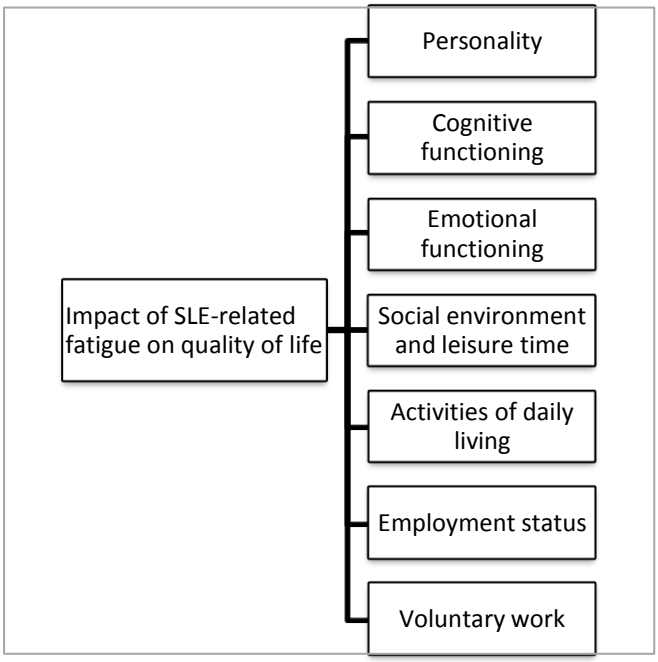

Figure 2a. Visual reproduction of impact of patients' fatigue on quality of life

Impact on personality

The first interview was decisive in mentioning changes in personality due to the fatigue, the subject 'personality' then was included in the interview as a probe subject. Most participants were aware that fatigue has negative consequences on their personality.

> *"But everything became a little less due to that fatigue. Everything became weary. To me it is, the sparks are gone. I used to be like yeah, making fun with my daughter at the café … but I can't find the energy (PT1)"*

Three patients said that they were not aware of consequences on personality themselves. However, two of them made clear that their social environment, mostly their partner, noticed slight changes, e.g. being more uptight or reduced spontaneity.

> *"Yes, I became a lot more contentious, I believe, towards other people. But that's only what I heard from other people, I do not notice it myself, that's what I hear from him [partner] (PT4)"*

Cognitive functioning

As stated before, patients did not spontaneously report cognitive malfunctioning. After specifically asking, patients reported negative consequences on their cognitive functioning as a result of fatigue. Especially in group conversations, loss of concentration is problematic in a way that patients cannot longer participate sufficiently in a social setting, like joining a birthday party.

> *"I do hear words, but no conversation anymore. I can't concentrate at all, I can't follow a conversation and it's mostly like: 'We need to go home, because I can't follow it anymore'. Too busy. It's not busy at all of course, because it's just a normal birthday party where people are talking, … but then I just have to go. I just can't keep going with it, only for a little while. Concentrating in a conversation, for me, that causes effort (PT7)"*

For the most part, all patients had wide-ranging examples of impaired cognitive functioning, particularly the inability to remember or to recall memories. Only one patient who reported that there caused no consequences to cognitive functioning.

Emotional functioning

Fatigue is causing a personal emotional impact on the lives of patients. Predominant feelings of frustration, as a result of not being able to finish or plan activities, were quoted. Not being able to do activities that they used to do or would like to do caused an inner struggle. Like mentioned before, feelings of 'frustration', 'anger', 'sadness', 'unpleasant feeling', 'feeling the need to cry', 'being uptight', 'disappointed', 'annoying', 'difficult' and 'depressing' were repeated when opening the subject for a second time.

> *"It became more and more a part of our daily living, instead of it overwhelming me. It's so bad, if I got back on my bike and then I couldn't even stand up anymore. I got upset by it. Still, it still is depressing (PT6)"*

Feelings of guilt towards their social environment were regularly given, one patient mentioned it repeatedly throughout the whole interview.

> *"Yes, I find it really frustrating for my husband as well of course. It's uh, we really enjoyed going on a vacation, but in the past few years we haven't gone at all. Because you can't count on yourself anymore (PT5)"*

Social environment and leisure time

A common view amongst interviewees was that they had problems with family and friends regarding to keeping contact. Patients who did not have any problems in this domain said that family and friends understood the situation. Some patients did not allow fatigue to cause problems, by not altering their social contacts, even though they had to give up activities the next day.

> *"Yes, yes, I want to be there. Yes, I'm not that kind of person that says 'I'm sick and I'm going to call and cancel them or I really can't right now because, yeah, my disease'. Pff, certainly not, that's not me (PT3)"*

Another solution or consequence to the problem of fatigue given by patients was to plan activities during the moments they had the littlest burden of fatigue.

> *"What we have agreed on now, because I said I got more fatigued during the day, that I, more often meet for lunch with people and not, you know, for a drink at six and continue that evening (PT4)"*

Other patients, on the contrary, did experience relational problems with family and friends due to fatigue. They felt a mutual misunderstanding, for example, planning activities ahead of time is a big problem for patients and feel misunderstood when explaining this to friends or family. Patients felt upset about the incomprehension of family and friends. Patients were also less socially involved. On the one hand, patients did not keep in touch with friends and family due to constant misunderstanding, on the other hand, family and friends did not invite them any longer.

> *"Yes, explained it ten times. Well, yes, but anyway, I can't help it. And well, those kinds of things, you know? Those, those fun things. You can't do it all anymore and mostly those are the things you do with your friends, your sister or anybody else. So at a certain point they'll stop asking you (PT2)"*

Half of the patients had relational problems with their partners and others did not have any problems. Two patients spontaneously reported being less sexual active, however, this was not marked as a problem. Five patients reported their partners had more tasks to take over, partners complaining about less common activities and therefore having more arguments.

> *"That's, I ask a lot, you know, you personally don't think 'oh, how as it?' and that bothers him*

a lot, he can't understand that I can't do that (PT4)"

Two patients quoted having no relational problems with their partner and even felt there was a positive consequence on their relationship. They felt that fatigue, as well as the disease, brought them closer together by having full understanding of the situation. Concerning leisure time, half of the patients said leisure time was being reduced. Going to concerts, sightseeing a big place, going to a museum, going shopping are long-lasting and exhausting activities in which patients could not engage any longer. Especially retired patients were frustrated about once having plans when retiring, but could not live up to them anymore.

"Yes, it's disappointingly of course. You finally do have time, you are retired, and you have time to go out and then you can't do it anymore (PT5)"

Activities of daily living

Fatigue has extensive consequences on daily living. All patients gave examples of fatigue having an impact on their daily chores such as cleaning, gardening and cooking. When discussing this, one patient said that fatigue was not influencing her activities of daily living. During the interview, however, examples of giving up household chores were given. All patients had to consider complaints of fatigue in to making a daily schedule and some had to divide their chores throughout the day in what once was taking an hour. Making adjustments to fatigue was a frequent mentioned theme throughout the interviews. Two patients did not feel like doing chores anymore. One patient had a cleaning help, but most patients were giving up household chores to their partner.

"Yes, if that doesn't work, I'll leave it. I'll leave it. My wife knows. Then we'll talk about it and I'll say: 'I'm thinking about not doing it'. I make a list of things that I might be able to do and then I'll just check how I can arrange my time and then I'll watch if I can do it or not. And if not, I'll mark it off my list and I'll just carry on. But my wife knows, if she comes home, it didn't work out today (PT7)"

"Yes, you have to plan everything for the day in any case. It's not like I hop downstairs every morning and making myself ready for ironing and after that vacuuming or whatever. That, it's not like that anyway. It's like, vacuuming is quite an activity on its own, there's no more energy left and ironing, it's like ironing two things and then I'll leave it and then I have to sit down for a while (PT2)"

Employment status

As can be seen in Table 1A, none of the patients was fully employed. Most not-retired patients felt that fatigue affected their capability to work. It was mostly the lack of energy that underlies the ability to work. Moreover, some patients suffered from reduced cognitive ability due to fatigue and therefore could not perform adequately at work. Four patients were disabled after a period of gradually giving up work activities. Some of these patients mentioned the importance of saving energy to function well at home and subsequently had to give up work.

> *"Yes, just because I know I can't do that much. And if I want to do something, I also want to enjoy life and otherwise I can't. If I started working again, I'll be sleeping at home for the rest of the day, being tired, not being focused, then I indeed put all my effort in the performance at work and yes. I don't have enough [energy] and that will be in the expense of me and my family (PT1)"*

> *"The fact that I had to accept that I was not able to function normally at work anymore. Because I, I just can't, anymore. So, it did a lot to me. Getting ill, that's one. That's annoying, but that's that. The fact that you can't work anymore, that's the worst (PT7)"*

Only one participant changed work activities after being declared partially disabled and one patient was employed on a part-time basis.

> *"Yes, I think so, I think it is interesting, I still learn every single day. Well, next year I hope to become 65 years old and then I'm going to quit. Which I can look forward to as well. But work to me is still important. I am a perfectionist and, well, saying no is a reoccurring theme. I'll put through with it and can be a little more contentious towards others, even thinking to myself that others think I'm whining and yes, I can be contentious at that point (PT3)"*

Voluntary work

For some patients, the interest in performing voluntary work was present. In fact, one participant was a volunteer at the library. Participating as a volunteer was important for maintaining social contact.

> *"Yes, I like that and then I'll be, yeah we're living here, yeah, nice neighbors, but not that much of a social life, so because of that [voluntary work] I'm getting more of [social life] which I like (PT3)"*

And even despite the fact that other patients were interested in voluntary work, one patient stopped because of being fatigued and two patients did not sign up for it because of the demands they cannot live up to due to fatigue.

> *"Because of that I think. That's because I quit it. It might have gone well. But people can't count on me and that bothers me a lot. I can't count on myself and, look, I can't keep my promises and appointments (PT5)"*

3.1.4 Paragraph summary

Patients with a systemic auto-immune disease experienced severe fatigue mostly as the lack of physical energy and having a heavy body. Fatigue was often present at a daily base and most patients were more fatigued at the end of the day, sometimes depending on previous activity. Patients felt that fatigue was a restriction to their (daily) lives and feelings of frustration were mentioned by almost all patients. Subsequently, severe fatigue had a major impact on the quality of life of patients with a systemic auto-immune disease. Even though some domains of quality of life were more affected than others, the reported impact that fatigue had on lives of patients regarded to personality, cognitive functioning, emotional functioning, social environment and leisure time, activities of daily living, employment status and voluntary work. Overall, cognitive functioning, activities of daily living and employment status were reported as most affected by fatigue.

3.2 Partners

3.2.1 General findings partners

The demographic characteristics of partners are presented in Table 1b. Of all partners, seven were living with a patient with SLE, sometimes combined with other auto-immune diseases. One partner had a spouse suffering from APS and one partner lived with a MCTD-patient. Most partners were low educated and either fully employed or retired. Despite the fact that the Fatigue Severity Scale (FSS) is intended to use for patients, partners were asked to fill in the survey for the fatigue level of the patient to get a perception of possible dissimilarities. A score above 4 indicates severe fatigue. All partners reported fatigue levels for patients above 4.

3.2.2 Partner's experience of patient's severe fatigue

Partners were asked to describe their experience of their partners' fatigue. Initially they described what effect fatigue had on their partner instead of the effect it had on their personal life. After asking the same question with an emphasis on what their partners' fatigue did to themselves, most partners had difficulties give an answer. All answers to this question were separated into three categories, i.g., daily structure, activities and emotional aspects.

Daily structure

The majority of the partners mentioned they adjusted - if possible - to the activity level of their partner, which is more slowly than their own activity level. For some partners slowing down was slightly difficult at first but eventually they adjusted to their partner.

> *"During the week or in the weekends she gets up at eight o'clock an at Saturdays to me it is, I like to sleep late. But I also enjoy watching television at Friday night, have a drink, eat some chips. That bothers me sometimes. But now she has, I tend to go with her more, if she goes to sleep I'll go to sleep as well (PR1)"*

One partner had to switch between work and home in a way that activities at work were going more quickly as they did at home. The feeling of living in two worlds was predominate.

> *"Yes, I had a hard time with that in the beginning because you have to slow things down. You always slow down, right, you want to go faster but after a while you do take it into account. You adjust the pace … yeah, you know, you actually live in, to me it's kind of two worlds because I have a fulltime job so at work I have my own pace, my own things. And when you're*

Table 1b. Partner Demographic Characteristics (*N*=9)

Participant (Nr.)	*Partners' disease*	*Gender (M/F)*	*Age (years)*	*Education level*[3] *(Low/Middle/High)*	*Employment status*	*Voluntary work (Yes/No)*	*Together with Partner*[2] *(years)*	*Children*	*Partner's FSS-score about patient's fatigue (max. 7)*
PR1	SLE	M	43	High	Fulltime employment	No	B	3	5,4
PR2	SLE	M	57	Low	Fulltime employment	No	D	2	6,2
PR3	SLE	M	64	Low	Retired	Yes	E	2	4
PR4	APS	M	69	High	Retired	No	E	1	5,7
PR5	SLE	M	66	Low	Retired	Yes	E	2	6,1
PR6	SLE	M	43	High	Part-time employment	No	B	2	5,6
PR7	SLE/Sjögren/Hashimoto's disease	F	48	Low	Fulltime employment	No	A	1	5,7
PR8	MCTD	M	71	Low	Retired	No	E	3	4,9
PR9	SLE/Sjögren/Hashimoto's disease/ fibromyalgia/COPD	M	53	Low	Fulltime employment	No	A	4	6,8

[1] Low: No education, primary school or lower vocational education
Middle: High school and middle vocational education
High: High vocational education and university

[2] A= 0-10; B=11-20; C=21-30; D=31-40; E=>41

at home, you really have to switch and the rhythm becomes differently, a different pace (PR2)"

Activities

Partners described the experience of fatigue as an obstacle and that they had to adapt to the needs and activities of their partner. First, they felt that their partners' fatigue was an obstacle because of the inability to spontaneously do things and the urge to plan most activities ahead. One participant answered to the question 'how do you experience your partners' fatigue' by the following words:

"Well, pretty much a huge inhibition to what we could have done and what we would like to do. I don't know if she told you, but I really love to travel and going out, etcetera. And if we're traveling, we are doing it a lot, I really have to hold myself back, which I always had to do for her, I have to say. Traveling is actually my pride and joy and if I am somewhere, I want to see as many as possible … But yeah, but that has became really unpleasant yeah, that it limits me and that actually causes problems for me as well (PR4)"

Even though not all patients responded to the question by identifying fatigue as an obstacle, throughout the interview it was an common subject. In addition, the adjustment to their partner was a extensive theme.

"Change of life. Adjustments. Not being able to do everything spontaneously. Planning everything. Things that need to be cancelled. Still more things that we would normally do together, did become to me more. So actually, I do the most part, yes, of everything at home (PR7)"

Emotional aspects

While nearly none of the partners spontaneously reported patients' fatigue having an emotional impact on them, four participants were occasionally struggling with their partner being fatigued. One partner was bothered by the patient's irascibility.

"Sometimes she can be really grumpy or heavily irritated about nothing. That probably the most important thing I'm disturbed by. Because it's about nothing, she can be so unreasonable when we're discussing. Small things can become really major. And that, yeah well, it depends on if you have worked all day and you come home and there is just some little thing, well, you're not waiting for that, for whining or whatever. Five years ago this was

not the case, right. So I do typically relate it to, call it fatigue, or the combination between medication and fatigue which we discussed earlier. It makes your personality different, it makes you more irritable (PR1)"

Another partner was tremendously dissatisfied by the way his partner had became due to fatigue. Of all participants, this partner was most struggling with the fact that his partner was suffering from fatigue. He felt fatigue was a major obstacle in life.

"Traveling is actually my pride and joy and if I am somewhere, I want to see as many as possible … But yeah, but that has became really unpleasant yeah, that it limits me and that actually causes problems for me as well. To be able to cope with that, because at times I feel like a caged lion, well that's exaggerated, but I do feel pretty, I thought to myself, kidnapped. That's the felling. Yes, that's all I can say (PR4)"

Two partners did feel their partners' fatigue was a burden at times:

"What it means to me? My wife's fatigue, yes … that's hard sometimes. I come home late and then you feel like going for a short walk, but that's not possible anymore. That stops you, those are the limitations that are there. And you still try to go to bed early … yes, pretty tough (PR9)"

3.2.3 The impact of patient's severe fatigue on partner's quality of life

When asking partners about the impact of their partners' fatigue, answers mainly referred to impact on daily activities or fatigue does not even have an impact at all. After probing, some themes were recognized as being affected by their partners' fatigue, whereas some partners still did not find there were consequences as regards to the theme. Domains were represented in figure 2b.

Impact on partner relationship

Most partners initially mentioned that fatigue has no consequences on their relationship. However, after additional questions during the interview, most partners had various examples of fatigue affecting their relationship. Two partners experienced difficulties in their relationship because the feeling of inability to freely do what they would like to do or feeling angry towards their partner having a disease.

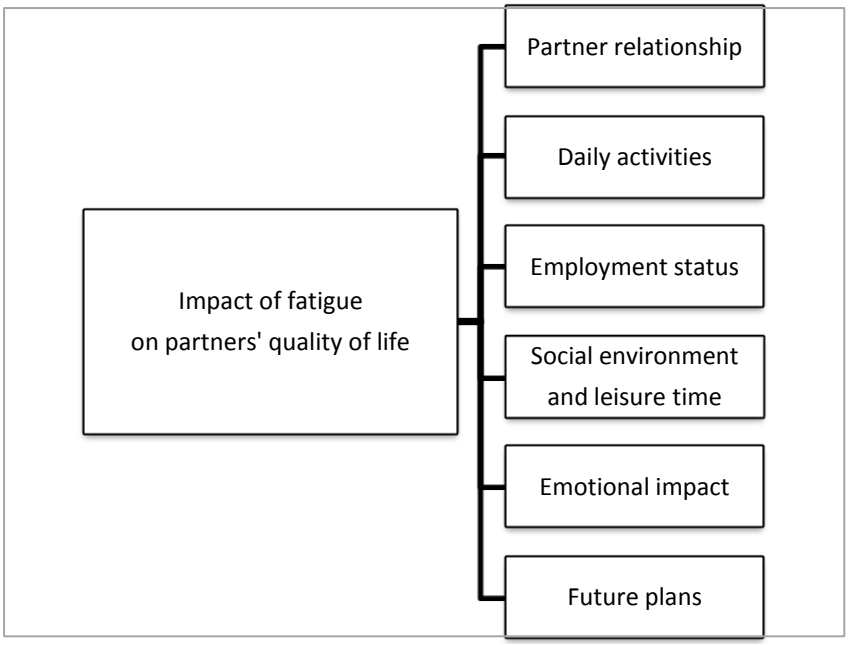

Figure 2b. Visual reproduction of impact of patient's fatigue on partner's quality of life

> *"It became worse, back then as well, but I hear her talking about it and thought yes I am extreme, so, you know, you're going to tone it down, right, even in marriage it's constantly mediating. But now it's starting to get a little out of hand, where I have to say yes, it's because of you that I can do a lot less and that also puts a strain on it (PR4)"*

Regarding to the impact on partner relationship, most partners mentioned the importance of communication in order to keep a good relationship. Most partners described about their coping with their partners' fatigue, generally in a positive way.

> *"Yes, it's limiting yeah. Look, if you look forward to something and it's been cancelled, that's not always nice, no. But I can handle it very well. Were together on the same page. We support each other in this. It's not like I'm having a hard time with it, with things being cancelled. We just changed our way of thinking, like, this is how we are dealing with it (PR7)"*

Sexuality became a less important theme since the presence of fatigue according to one partner.

> *"PR: yes, sexually it changed a little. That could be an example. In a certain way, that's how it went since last half year. INT: That you just don't feel like it or that it just doesn't happen anymore, that's also possible? PR: Yes, exactly. INT: Does fatigue play a role there? PR: Yes, without a doubt. And it's not only her, really. But there's not that much interest in it. Well, you think about it so now and then but I'm not sure what it is. I mean, if you ask me what has changed, yes I can't argue it myself, I still have to figure it out myself (PR1)"*

Besides negative consequences, a few participants felt they emotionally got closer to their partner. However, this was not only related to fatigue, but also related to the seriousness of the disease in general.

Daily activities

Daily activities was one of the most mentioned themes by partners. Questions in relation to the influence of fatigue on daily activities, showed a diversity of answers. Making plans, taking over tasks and participating alone in activities were reported. One partner clearly reported that making plans was one of the consequences.

> *"Yes, planning well haha. Iron on Sunday morning, haha. Strict, yes you have to, at least, to me it's more like when having to do more things, you have to schedule them well, plan well. Yes. And also really disciplined, but yeah, I'm not the kind of person that leaves it all, leave it for two weeks, that makes it only harder (PR2)"*

Almost all partners mentioned they provided support by taking over tasks, especially tasks in house holding.

> *"Yes, house holding. That's something I do now and then. Certain things, that are troublesome for her, I try to do it – if I'm there … when she's gardening and I'll continue. She has always loved to garden, but that became less now. Then I just pick up where she left (PR5)"*

> *"Sometimes I come home and the table, from this morning or so, is still laid. Or, vacuuming. Now she did a nice job, you know. But sometimes she can't do it. Practical things. Like giving our children a bath. Manage cooking is still ok, but reluctantly. And if it doesn't work, I'll do it. But basically you could, as far as I can see, still be vacuuming and doing the dishes and so and doing it all. But that just doesn't always work. When cleaning, of five things, she can only do two. So certain things, when I come home, I still have to do them (PR6)"*

Participating more often alone in activities was called by a few partners. Conversely, some partners did feel there were no consequences.

> *"INT: Are your daily activities also influenced by your partner's fatigue? PR: well, not really, no. My wife still knew, even when being tired, she knew her way around. Doing groceries by*

car, so she doesn't have to lift that much weight and all those kinds of things … but she does have fatigue as a complaint, of course (PR8)"

Employment status

Five partners were employed and four partners were retired. Two employed partners adapted their working hours, so that they could better plan household tasks and adapted working hours to better adjust to the daily fatigue cycle of the patient.

"I do adjust my working hours to her. To her fatigue too. Because I'm home all day. Because if I were about to work in the afternoon, from nine to five or something, she has a lot to do on her own. Bringing our children to school, pick them up again. And then at five o'clock she has to start preparing dinner. While if I were home at on o'clock, she has done something in the morning and I can help with groceries or picking up the children in the afternoon, cooking and so on. So in that way it certainly has an influence, yes (PR6)"

Two partners also reported a decline of income since their partner stopped working due to the consequences of fatigue or the disease. Other partners did not change anything towards their employment status, either they were retired or it did not affect work.

"No, no influence. No. I can separate work from home really well. It doesn't influence each other. I did call her today, just to see how she's doing (PR9)"

Social environment and leisure time

Almost all partners reported consequences on their social environment and leisure time, even though they initially said fatigue had no impact on this theme. As well as in other themes, planning was a recurrent concept. Regarding to social environment, planning was mostly referred to making plans with friends.

"Yes, you make plans now, you divide things more than you used to, way more checking the agenda, what did we plan, sometimes we do notice it. Sometimes you just make a mistake, when a weekend is fully planned or in a month, three weekends are full (PR1)"

Few partners had less or different contact with family or friends because of their partners' fatigue.

"No, everything goes well with visits, yes, oh, one thing we cut back on and that's a thing I've

been working on, is that we're not longer going out for dinner with friends that often. She's just too tired. We sometimes do but only with real close friends, but, and mostly at home. But really going out, which I find pretty regrettable, we were always having a good time when eating with friends but nowadays when eating at home it's also really nice and we're, we changed dinner with some friends, yes, into a nice lunch, a big lunch (PR4)"

Four partners referred having little time to unfold or participate in hobbies or in other leisure activities.

"Limiting, limiting. Well, no. Not limiting like that. It is limiting, but I do not experience it like that. Maybe now and then, yes. Lately I do realize again. I got my drums. I'm a man, I'm not a caregiver or something like that. I've got my hobby's, but which? I'm trying to find myself. That's because, since the last ten years, we were mainly focusing on her, to be honest I think (PR6)"

"INT: And does fatigue also leads to having less leisure time? Less time for yourself? PR: yes, to me of course. Because you have to do more after work. So that entails, somewhere it costs time, so yeah, that's what it seems like (PR7)"

Regarding to vacation, the lack of energy and the inability to spontaneously plan vacations as they used to, caused a change in type of destination and a less active vacation.

"Yes, for example, we were on vacation. Normally we would explore everything, see everything, but that's not possible anymore. So you have to do everything by taxi, right, traveling. Spontaneously follow a route to anywhere, that's not possible anymore … so, those are the things that have been changed. Biking. Biking, walking, that's no longer there. Just a little, it's not like it's not possible at all. But it's way more limiting than we were used to (PR7)"

One partner felt in addition to negative consequences a positive outcome regarding fatigue and his leisure time alone or with kids.

"Well, yeah. Sometimes it has its benefits, I can go swimming by myself or do other things. Often, I can leave and do nice things with the kids or something like that (PR6)"

After probing, one partner still did not find there were consequences to his social environment or leisure time.

> *"PR: Well, for that matter, we're well adjusted to each other. I, if she indeed has a period of being fatigue, well, I'll go gardening or something and she joins when she can. INT: Or for example with family? Do you do less since she feels fatigued? PR: No, no, not really, we found our way … we do what we can actually (PR3)"*

Emotional impact

Emotions were often not spontaneously mentioned, but after asking additional questions, some partners found that fatigue had a negative emotional impact, some felt there were positive emotions and some did not have specific emotions towards their partners' fatigue. Overall, most partners were able to report a negative emotion but put it into perspective by giving examples. For the most part, partners' fatigue did not have a large emotional impact, but was to some extent bothersome. More than half of the partners mentioned a negative emotional impact. Most of them missed their old life, found it hard to give up certain activities, a few got frustrated, angry or irritated and even feelings of jealousy.

> *"But if she's really tired, it's only hard when I'm tired myself, let me put it like this. If I'm fit, it doesn't bother me. But if I'm tired myself – working all day or don't feel like it, want to do something for me – and she tired too, then it's hard for me. Then I can get angry about it. I don't get angry towards her, but towards the fatigue. That's also an emotion, I get angry sometimes (PR6)"*

One partner quoted having positive emotions in a way of feeling more positive instead of worrying about insignificant things.

> *"I could worry about the little things, but I just don't anymore. I handle it, you think differently. A lot of things aren't that important anymore. They are, but not worth worrying about (PR7)"*

Future plans

Fatigue caused for two partners an influence on having future plans, as they felt cancellation of their initial plans was needed. They felt fatigue, as well as the disease, was already an obstacle to their plans for future or will become one.

"You're young, you've got kids, kids leaving the house, oh, we're going to travel, we're going to this, that. So those things are obviously, well, that is an ideal and doesn't always come true but yeah, you've had them once (PR2)"

"No, not yet. But I do worry sometimes, like where is it taking us. But yeah, I've learned, you can worry all the time. You can fear for everything or getting upset but that's not it (PR1)"

3.2.3 Paragraph summary

Partners from patients with a systemic auto-immune disease experience the patient's severe fatigue in terms of adjustments in daily structure and slowing down daily activities. They also reported that planning activities instead of spontaneously participate in activities became more important. Partners sometimes were struggling with their partner being fatigued because of the change in personality and the obstacle that fatigue can be in participating in activities. Patient's severe fatigue had for some partners a major impact on their quality of life. Some lives of partners as well as some domains between partners were more affected than others. Partners mentioned that the patient's fatigue played a role in their partner relationship, daily activities, employment status, social environment and leisure time, emotional impact and future plans. The most mentioned and affected domains were daily activities and the partner relationship.

3.3 Couples

3.3.1 General findings couples

Most couples dealt with one partner being fatigued for more than 10 years, whereas two couples less than 4 years. Within all couples, differences were found in FSS-scores, where mostly the partner scored higher on the FSS than patients (patients' average was 5.3; partners' average on patient's fatigue was 5.6). There was no relationship between FSS-scores and content of the interview that could explain these differences within couples. Interestingly, partners almost always mentioned health concerns regarding to the disease in general, instead of fatigue only.

3.3.2 The interference of fatigue within lives of couples

Couple 1

(Years together: 15; first symptoms: 9 years ago; official diagnosis SLE: 9 years ago; PT: female; FSS: PT6/PR5.4)

The interviews among this couple showed that perspectives towards the disease were different. The patient reported fatigue as the most invalidating symptom of the disease which caused the inability to work. On the contrary, the partner reported that fatigue was one of the three most disabling symptoms but not the largest. This might be explained by the patient masquerading the problems due to fatigue. By communicating about the disease, more understanding about the consequences existed.

> *"And maybe he's like, you can't help it either, that he accepts it … no, that's fine. I mean, when we're on holiday and I'll say 'I have to sleep right now', it's not a problem at all (PT1)"*

What is striking is the fact that only the partner reported having some relational problems. More arguing was mentioned because of patients' change in personality, i.e., being more uptight. Along the way, the partner found a way to cope with this by ignoring irrational behavior.

> *"Small things can become really major. And that, yeah well, it depends on if you have worked all day and you come home and there is just some little thing, well, you're not waiting for that, for whining or whatever. Five years ago this was not the case, right. So I do relate it typically to call it fatigue or the combination between medication and fatigue which we discussed earlier. It makes your personality different, it makes you more irritable (PR1)"*

In addition, the patient communicated more open about the changes due to fatigue which leads to more satisfaction, according to the partner. In order to accommodate to fatigue, planning and slowing down activities was needed and even brought them closer to each other. The partner

supported the patient by participating in different research activities, also because of the health concerns about the patients' flares and progress of fatigue. Partner's concerns about patients' reduced social activity and participation did also exist.

Couple 2

(Years together: 35; first symptoms: 15 years ago; official diagnosis SLE: 15 years ago; PT: female; FSS: PT6/PR6.2)

This couple reported that fatigue has a major impact on their daily activities, especially for household chores and also for leisure time they spent together. Even though the patient does not mention how fatigue interferes with their lives, the partner described spontaneously the interaction between them, in where the partner takes over all chores the patients is unable of. Patients' fatigue had a major impact on the partners' life and even though the partner sometimes wishes things were different. Looking at the positive side was a main theme within this couple.

> *"Yes, you do miss it, sometimes you see, acquaintances, colleagues, they tell you stories about this and that and you think to yourself, yes, I would have wanted that. You might catch yourself thinking that but I must say I'm not really bothered by that, let me put it that way … you far more enjoy things from up-close, plants, nature. That is what you'll learn (PR2)"*

As the partner reported, finding positive things were possible by accepting the consequences of fatigue and other symptoms of the disease. For both patient and partner, enjoying things from up-close, having less demands for life and living more consciously were reported as positive outcomes to the disease and fatigue. The partner mentioned providing mostly instrumental support and played a role in stimulating patients' preserved activities. This couple reported that they gave each other freedom to maintain social contacts and leisure time. Especially the seriousness of having SLE, whereas the possibility of the patient dying when flares are present, caused a greater depth in their relationship, as the partner reported.

Couple 3

(Years together: 46; first symptoms: 29 years ago; official diagnosis SLE: 29 years ago; PT: female; FSS: PT5.4/PR4)

This couple did not let fatigue affect their lives, mainly from the patient's perspective. On the one hand, the patient reported feelings of disappointment to the partner and therefore masqueraded symptoms of fatigue, even if they would worsen the day after. On the other hand, both patient and partner accepted the disease as well as the feelings of fatigue. The patient reported receiving instrumental and emotional support and having respect and understanding towards each other.

"PT3: We didn't make a big deal out of it, what you're asking about the relationship, no, it has actually only become better, yes. But if you specifically ask about fatigue, that is, yes you don't want to talk about. My husband notices something and yeah, well, what I mentioned earlier, I'll lie down for a while. And yeah, that's not something, it does occasionally happen on Sunday mornings. PR3: She always tries to get over it. So she actually never gives up, she doesn't want to accept it. And I'll say just take it easy, sit down for a while or lay down"

Looking forward and making the best out of it was mentioned by the patient. The partner accomplished that by giving emotional and instrumental support because of the health concerns in general for the patient.

Couple 4

(Years together: 45; first symptoms: 4 years ago; official diagnosis APS: 4 years ago; PT: female; FSS: PT5.2/PR5.7)

This couple dealt relatively short with the consequences of APS. They reported the most negative relational consequences of fatigue, which affected their partner relationship tremendously. Both mentioned that accepting the disease as well as symptoms of fatigue was difficult and caused frustration from both sides. Overall, both mentioned an incomprehension of the content and symptoms of the disease. The developed strain on their relationship due to the disease made the patient reporting feelings of guilt towards the partner.

"Yes, I think about him way more than about myself. Because he's the big organizer of everything and that has been restored because of the protection for my sake. And I don't like that, annoying to him actually (PT4)"

The partner felt frustrated about not being able to arrange and plan activities together. Neither of them mentioned communication about the consequences of fatigue. Furthermore, tensions were running high which caused more arguments.

"PT4: Yes … not that much, we do have fights every now and then and that's because, it all pens-up and suddenly there's a release, because of, yeah, that tasks have been changed and maybe .. [silence], yeah, what he said, it's about taking over things from me that I always did effortlessly. And that annoys me. PR4: But now it's starting to get a little out of hand, where I have to say yes, it's because of you that I can do a lot less and that also puts a strain on it "

Especially the partner explained the relational problems by denoting the differences in personality which previously existed and gotten worse since the presence of fatigue. The partner reported being unsure about the continuity of their relationship and preferred being active separately from each other. On the other hand, the partner felt sorry for the patient and worried about the decline in patient's cognitive ability.

Couple 5

(Years together: 44; first symptoms: 10 years ago; official diagnosis SLE: 5 years ago; PT: female; FSS: PT5.3/PR6.1)

In this couple the feeling of commitment and loyalty were most outspoken. Both patient and partner were willing to obtain more knowledge on the disease and on fatigue by visiting doctors and participating in activities arranged by the patient association, together. From partners' perspective, getting more knowledge on the consequences of fatigue and being aware of the needs of his spouse was important in order to give instrumental support.

> *"Still … you always have to take it into account. And again, assisting, keeping an eye on where you can assist … Back in the days you would go on a vacation with your kids. Now you have to be attentive to your wife. Especially in the evenings when the grandchildren are here, after all you have to do it together. Something she previously would do on her own, at least, that's how I see it (PR5)"*

Besides instrumental support, the patient also perceived emotional support in where the partner showed his understanding about the occurrence fatigue and could adapt to it.

> *"And when the grandchildren come over, you want to play a game or something … my husband is always in the background. If I can't do it, he'll say: 'Go and lay down'. And he will take them to see ducks or something and I can catch a breath and recover (PT5)"*

Even though the patient feels supported by the partner, feelings of guilt arise at times. The partner reported the urge to accept the situation because of the feeling of loyalty and commitment towards each other. Both patient and partner gave up some joint social contacts because of the lack of understanding from friends and family. This couple reported having no relational problems due to fatigue and even though not mentioned specifically, relational satisfaction existed by both trying to accept fatigue and supporting each other if needed.

Couple 6

(Years together: 13; first symptoms: 12 years ago; official diagnosis SLE: 5 years ago; PT: female; FSS: PT5.7/PR5.6)

This young couple reported that fatigue, as well as the disease itself, had a major impact on their lives. Even though both patient and partner mentioned being overjoyed by love for each other and their children, the fluctuation of the patient being independent to being dependant on the partner caused feelings of guilt from the patients' perspective. On the other hand, the partner felt sorry for the patient because of the consequences of fatigue and had major fears regarding to patients' health. These health concerns were causing the partner to play a large role in controlling patients' activities, so that fatigue would not worsen and possible flares would be prevented.

> *"She can't manage doing two things on a day. She has to deliberate everything in advance … and I'm holding her back, I'll say: 'Darling, you shouldn't do that'. Oh, that's something in where I'm responsible for. So … I hold her back sometimes. That's something I've taken on. I have to hold her back at times and be careful or something, because otherwise it would go wrong all again (PR6) "*

Since the onset of the disease and fatigue, habituation and coping came gradually. By communicating, the partner proved to know a lot about what the disease and fatigue entails. For both patient and partner, the awareness of not being a modal family was present, by means of financial setback and one parent having a disabling disease. However, both agreed on rearranging life in order to achieve a more meaningful way of living with a disease by finding a positive side of life with their children.

> *"The bed is just next to the living room, so yes, I'm just still a part of the family. So as a family, we can cope well with it. So I always say to my kids: 'When something's going on, just lay down with me' and we can talk in bed. It became more and more a part of our daily living, instead of it overwhelming me. I just got to know it a little bit better. And just the awareness that I would like to fill in life meaningfully. That also gives me strength (PT6)"*

That said, the partner reported that self development was an issue. This interacts with the patients' feeling of guilt towards the partner. Due to attention towards the patients' disease, the partner's self development and leisure time were reported for not gaining attention in the past few years.

Couple 7

(Years together: 8; first symptoms: 2 years ago; official diagnosis SLE/Sjögren/Hashimoto: 1 year ago; PT: male; FSS: PT5.2/PR5.7)

This couple deals with symptoms of fatigue since two years and since the onset, exploring the possibilities that are influenced by fatigue, was mentioned as a large theme. Both patient and partner mentioned that they were able to accept the consequences of the disease, including fatigue, even though activities had to be arranged differently.

> *"INT: And did you accept the fact that you can't work anymore? PT7: In the meantime yes, you have to, I have to, I don't have a choice. PR7: As I said, I can cope with it really well. I've got … I'm not sad. Of course I hate what happened, but I can handle it. We just made adjustments"*

This couple felt that fatigue had no consequences on their relationship and the partner reported that in order to cope with fatigue, communication, support and putting yourself second were important tools.

> *"Look, if you look forward to something and it's been cancelled, that's not always nice, no. But I can handle it very well. Were together on the same page. We support each other in this. It's not like I'm having a hard time with it, with things being cancelled. We just changed our way of thinking, like, this is how we are dealing with it … look, you're not putting yourself first. And if you don't [put yourself first] and take a step back, you don't end up arguing … we always talk to each other, yes, we're very open towards each other. We know where we stand (PR7)"*

The partner reported that thinking along with the patient at times was needed in order to control patients' activities to prevent overuse of energy. By both mentioned as positive outcome of the disease, was having less worries about the little things and having less priorities.

Couple 8

(Years together: 46; first symptoms: 27 years ago; official diagnosis MCTD: 25 year ago; PT: female; FSS: PT3.9/PR4.9)

This couple reported being little influenced by fatigue as a symptom of MCTD and were therefore the couple that were least affected by fatigue.

> *"PR8: Yeah, I mean. Since I've been retired, - in fact, also when I wasn't – on Saturdays I vacuum and those kinds of things and occasionally do groceries. Carrying things, carrying*

bags and stuff … but what I think, my wife still knew, even when being tired, she knew her way around. It's not like she's not doing anything. PT8: I'll do everything, but yeah, you just put a strain on everything"

Besides symptoms of fatigue affecting their lives, both patient and partner reported decline in leisure activities due to their age. Undertaking activities together became less while time went on, as they reported. The struggle with fatigue and other health issues were not frequently discussed topics according to the patient, besides, there was a lack of communication about it. Mostly, they dealt with health concerns individually. Nonetheless, they both felt that fatigue did not affect their relationship. Especially the partner reported that dealing with the disease by accepting it was the only way to avoid relational problems. Both patient and partner reported that they had joint leisure activities, but also the importance of having own hobbies and spending time on these individual interests was a mentioned subject.

Couple 9

(Years together: 6; first symptoms: 14 years ago; official diagnosis SLE/Sjögren/Hashimoto: 11 year ago; PT: female; FSS: PT5.4/PR6.8)

The patient and partner in this couple are both dealing with a chronic disease, which existed prior to the start of their relationship. Besides systemic auto-immune diseases, the patient also suffers from COPD and fibromyalgia; the partner suffers from tinnitus. As both reported, they have learned to know each other with the presence of fatigue which leads to understanding each other and their shortcomings. The patient reported talking openly about fatigue and showing frailty, alternated with moments of not willing to show weaknesses.

"No, it's not easy. I don't want to show it, certainly not when I made plans for the weekend with [my husband]. And I certainly won't be the one [causing us] not to go, because I'm tired … but he knew I was sick from the beginning. So there are still things that have become less. Vacuuming and cleaning windows, I did all of that, but I had to force myself doing that. Then, at a certain point in time I had to say: 'I shouldn't do this'. I'm only falling deeper down, I need those breaks and not being stubborn (PT9)"

Getting to know each other with the existence of the disease was mentioned by the partner as a reason for being able to cope with fatigue and other symptoms of the diseases. Therefore fatigue did not cause relational problems, according to the partner. From the partner's perspective, learning to live with fatigue and giving instrumental support, came over time. Also providing emotional support because of the interest towards the well-being of each other was given.

" No. I can separate work from home really well. It doesn't influence each other. I did call her today, just to see how she's doing. Yesterday she was really tired and went to bed early. Today at work, I did call her, just listening how she's doing (PR9)"

3.3.3 Paragraph summary

Recurrent themes in the interviews among couples were communication, acceptance and getting more knowledge on the disease. Whilst a minority did not mention these themes or perceived them as negative, all agreed that they were important in order to cope with fatigue and the disease as a couple. A common view amongst couples was that the consequences of fatigue and the disease made them to look at the positive side of life and it eventually gave more meaning to their lives. Some couples mentioned that they did not often communicated about fatigue, whereas one couple suffered from this lack of communication and a lack of knowledge on the disease which caused relational dissatisfaction. Partners sometimes related fatigue to disease activity and flares, meaning that they believed that flares could be prevented when the level of fatigue would be regulated and declined. They expressed their health concerns about the patient and would like to regulate patients' activities in order to decline worsening of fatigue and therefore causing a lower chance of developing flares.

4. Discussion

This study aimed to investigate the experience of severe fatigue and its impact on quality of life of patients with a systemic auto-immune disease, and their partners as individuals and as a couple. To our knowledge, this is the first study that examined patients' fatigue in partners and also the first study that explored the quality of life within couples, suffering from a systemic auto-immune disease. This chapter can be divided into five paragraphs. Findings regarding to patients, partners and couples will be discussed in the first three paragraphs. After that, strengths and limitations of this study will be denoted and finally, the chapter will end with a general conclusion and recommendations for future research.

4.1 Patients

The results in this study reflect the complexity of fatigue in patients with a systemic auto-immune disease. Patients experienced fatigue in terms of symptoms, frequency, emotions and aspects of daily living and reported that it affects personality, cognitive functioning, emotional functioning, social environment and leisure time, activities of daily living, employment status and voluntary work.
This study produced results which support the findings of a great deal of the previous work in this field, conducted by Sterling et al. (2014). Remarkably, they found also a variety in severity of fatigue, especially during flares and after being more active. In contrast to these findings, participants in the current study did not report disease activity as being instigator of severe fatigue. Furthermore, most patients in this study reported a 'standard' or 'baseline' level of fatigue and felt a worsening after exhausting activity. In accordance with the present results, previous studies (e.g. De Groot et al., 2003) on other chronic diseases have demonstrated that patients with severe fatigue could differentiate between 'normal' and 'pathological' fatigue.

Besides pain and uncertainty about development of the systemic auto-immune disease, severe fatigue limits social and physical functioning and was found to be one of the largest problems of the disease in general (Sterling et al., 2014). Moreover, the invisibility of symptoms of fatigue and the complexity of the disease in general caused a lot of misunderstanding and a lack of empathy from others. In this study, patients' fatigue was mentioned as having an influence on social environment, yet none of the patients reported being socially isolated. This is a rather contradictory result compared to the study of Petterson et al. (2010) and Sutanto et al. (2013), who have previously discussed that patients are in danger of social isolation. These differences are hard to explain but might be related to the fact that all patients in the current study have a partner in contrast to previous mentioned studies. It is likely that single patients are more in danger of feeling

socially isolated since emotional and instrumental support, given by a spouse, is lacking which might lead to social inactivity (Coyne & Fiske, 1992).

It is interesting to note that in the current study the severity of fatigue, based on FSS-scores, was almost equal to all patients, except for one patient with MCTD (scoring a 3.9 on the FSS). This one lower score might be explained by the type of disease, although these diseases show large similarities. Also, it should be stated is that cognitive functioning was in almost all patients, affected. Even though most patients felt it was due to fatigue, it is likely that the only patient with APS was also suffering from cognitive malfunction due to brain damage (Muscal & Brey, 2010). In contrast to earlier findings, the mean FSS-score in this study was 5.3, which slightly differed from mean scores in other studies. Omdal et al. (2003) found an average FSS-score of 4.6 and Tayer et al. (2001) found an average of 4.8. It seems possible that differences in mean scores are due to the fact that patients in this study were included if being fatigued, in contrast to previous studies in where patients were recruited for having SLE. Results from this current study can therefore only be applied to severe fatigued patients with a systemic auto-immune disease.

The impact of severe fatigue in this study shares similarities in clinical comparable diseases such as rheumatoid arthritis (e.g. Repping-Wuts, Uitterhoeve, Van Riel, Van Achterberg, 2008). They found that fatigue in rheumatoid arthritis affected role functioning, relationships, leisure time, adaptation to daily activities and emotional functioning. Outstanding is the fact that Gallop et al. (2012) and Sutanto et al. (2013) found similar domains of quality of life to be influenced by SLE in general, in contrast to the current study that searched for domains to be influenced by severe fatigue as a symptom of the disease. It can be assumed that fatigue as a symptom plays a major role in reduced quality of life, separately from other symptoms of the disease. Coping with severe fatigue as a concept was not subject of this study, nonetheless most patients reported that they had to learn to cope with fatigue over time by trial and error but still find it difficult at times. Moreover, some patients mentioned the need for more professional help. Therefore, future research should focus on developing self-management programs based on the results of this study in order for patients to cope with fatigue since curing fatigue is still not possible up till now.

4.2 Partners

Results of this study showed that partners' experience and impact of patient's fatigue on their quality of life varied extensively. Reported domains dealt with partner relationship, daily activities, employment status, social environment and leisure time, emotional impact and future plans. The findings observed in this study mirror those of the previous studies in other chronic diseases that have examined the effect of a chronic disease on partners (Årestedt et al., 2014; Giffords, 2003; Wadhwa et al., 2013; Bohnen et al., 2011; Eghlileb et al., 2007). Indeed, Baanders and Heijmans

(2007) found an impact on partners' quality of life, especially when the chronic disease was accompanied with symptoms of fatigue. As been mentioned previously, former research in other chronic diseases shows that a partner suffers just as well from patient's disease. Giving instrumental and emotional support became more relevant to partners, as well as having more concerns about the patient's health. Meanwhile, partners' own well-being might be put aside for longer period whereas all attention goes out to the patient's disease (Coyne & Fiske, 1992). Especially the complexity of finding the diagnose of systemic auto-immune diseases, adjusting to patient's disease and having concerns about the unexpected and abrupt presence of flares requires lots of energy from patient's spouse (Kuenzler et al., 2011). However, little research incorporating the views of partners from patients with a systemic auto-immune disease has been conducted. Overall, apart from the disease in general, the symptom of severe fatigue was often present at a daily basis in patients participating in this study, which required the partner to make adjustments from daily life to future activities.

The current study is the first that has given insights in how fatigue in patients with a systemic auto-immune disease affects the quality of life of partners. Even though the patient has to live with the symptom of fatigue, experiences the negative physical consequences from being fatigued and mentioned it as the most invalidating symptom, partners experienced also disadvantages from the patient's fatigue. However, more than the patient's fatigue, partners found the erratic uncertainty of the disease in general the most difficult to cope with. This has also been found in research on other chronic diseases such as cardiac diseases (Dalteg, Benzein, Fridlund & Malm, 2011), traumatic brain injuries (Jumisko et al., 2007) and cancer (Kim & Given, 2008). Partners in this study feared for the recurrence of flares and the life-threatening consequences of the disease, which was a greater burden or concern to them than consequences they experienced from their partner being fatigued. Especially after hospitalization of the patient, spouses can get more anxious or depressed (Moser & Dracup, 2004). One of the issues that emerges from findings in research in the field of cancer (Brandão et al., 2014; McCaughan et al., 2013) is that patients with a chronic disease in general depend on the emotional and practical support from their partners. Given that this study found that patient's fatigue has an impact on quality of life of partners, the need for an intervention to improve partner's quality of life needs to be further investigated. Evidence for the effectiveness of interventions for partners was found in research in patients with cancer (e.g., Badger et al., 2011), where they found that interventions for partners from prostate cancer survivors were effective in improving quality of life.

4.3 Couples

The main findings in this study were that communication, acceptance and acquiring more knowledge of the disease leads to better coping with the disease and less relational problems. Prior studies that have noted the importance of accounting interaction within couples on outcomes of quality of life, mainly focused on research in other chronic diseases, for example in cancer and cardiac diseases. To our knowledge, this is the first study that compared and explored how fatigue in systemic auto-immune diseases affects quality of life of couples. A major advantage of this study method was the ability to compare the impact of fatigue between patients and partners and to explore the interference of fatigue within the lives of them as a couple.

The results in this study match those observed in previous research by Druley, Stephens & Coyne (1997), who found that women with SLE experienced more emotional intimacy and satisfaction when disclosing more information about illness symptoms and emotions. According to Brandão (2014), challenges due to the presence of a chronic disease could lead to difficulties in couples' communication, which was apparent in a few couples in the current study. Hagedoorn et al. (2011) further supported the idea of spousal active engagement being positively associated with relational satisfaction for patients with colorectal cancer as well as their partners. In this study, good communication and openness about the consequences of fatigue was among several couples vital to keep a healthy relationship. However, disclosing information about symptoms of fatigue by the patient did not necessarily lead to fully understanding the physical burden of fatigue as can be concluded by the fact that some couples showed major differences in FSS scores. These conclusions must, however, be interpreted with caution because assessing partner's idea of patient's fatigue has not been validated. Partners namely tend to score higher on the FSS, meaning that partners think that fatigue affects patient's life more than patients report. Moreover, some partners even claimed that when the patient was more fatigued, the chance of developing flares increased. As a result, they showed overprotective behavior (Joekes, Van Elderen & Scheurs, 2007), e.g., behaving in a more intrusive and restrictive manner (Joekes et al., 2007). For patients, severe fatigue is mostly the worst symptom of the systemic auto-immune disease, whereas partners reported more anxiety for aggravation of fatigue causing a exacerbation of the disease in general.

All patients who felt their partner was overprotective did acknowledge their spouse's good intentions, which makes it more solicitous behavior which appears when being confronted with own anxiety and fear. Their behavior is then directed towards the patients as well as towards themselves (Gallant, 2003). As mentioned before, couples that reported having no or little relational problems felt that good communication, acceptance and acquiring knowledge about the disease was very important. This study proved that the presence of fatigue and the disease in general causes dyadic

challenges, therefore future research should focus on exploring 'good communication', acceptation and acquiring knowledge on illness within couples.

4.4 Strengths and limitations

This study gave more insights in not only how fatigue is experienced but also in how fatigue affects the quality of lives of couples. As compared to the study of Petterson, Möller, Svenungsson, Gunnarsson and Welin Henriksson (2010), that also aimed to find patients' experiences of fatigue, the current study gives a more detailed description of the impact of fatigue in different domains. Moreover, most studies only refer to selected domains such as daily life (Bauernfeind et al., 2009), work, family and health (Robinson et al., 2010; Almehed, Carlsten, H., & Forsblad-d'Elia, 2010), whereas this study gave a more general view of the aspects of life that are influenced by fatigue.

For the purpose of this study patients and partners were interviewed separately. Even though this setting knows its shortcomings, the absence of a spouse enables the participant to freely speak without inhibition. When interviewing couples separately, the depth and quality of the interview augment on a personal level (Taylor & De Vocht, 2011). Especially the patients and partners in this study that did not communicate often about fatigue with their spouse, would never reveal personal thoughts when interviewing couples together. However, most partners in the current study did not express themselves of being remarkably emotionally affected by fatigue. For some partners it seemed unnatural to talk about emotions. On occasion, partners put their emotions into perspective because they reported some kind of guilt about expressing negative emotions. Furthermore, some partners were quite closed when asking about fatigue affecting their relationship. The impression of defensiveness sometimes arose when opening the subject. In order to maintain the willingness of the partners' participation, no additional questions were asked to further explore the impact of fatigue on the relationship. This lack of information might cause an underestimation of how far partners' problems with fatigue reach. It is important to bear in mind the possible bias in these responses. Nonetheless, this further supports the preference of interviewing couples separately since it was hard for partners to express negative feelings, let alone in the presence of their spouse. Moreover, the chance of getting socially desirable answers would probably have been higher when interviewing couples together which could have made these study results rather unreliable.

Although the study has successfully demonstrated that fatigue has a major impact on patients' and partners' quality of life, individually as well as a couple, it has certain limitations in terms of the research design. For instance, domains of quality of life were sometimes not spontaneously mentioned by participants but after asking, fatigue played a role in almost all

domains. A reason for this might be that the setting of the interviews, in where patients were directly asked for the impact of fatigue in their lives and tended to respond immediately. More time for participants to think could lead to more spontaneously mentioning domains. Another reason could be that some domains are more obvious to think of spontaneously than others because patients have to cope with them at a daily basis. On the other hand, in-depth interviews give far more insights to how fatigue is experienced and to what extend fatigue is invalidating patients' lives than other research methods.

Another limitation to the study is the fact that two researchers collected the data. Although a joint interview scheme was used and evaluation between interviews took place, both researchers had a different research interest and might therefore be more focused to questions regarding their subject. Complementary questions were therefore, depending on interviewer and on subject, more used in some interviews. However, sufficient and useful information was attained in order to answer the research questions.

In this study, The FSS was used since it had a good reliability and the use of it in patients with a systemic auto-immune disease. And even though the FSS was solely used to get more insight in the severity of patients' fatigue, the Dutch version of the FSS has not been validated. Nonetheless, the inventory in Dutch is used in The Netherlands for clinical purposes. If used in the future and for quantitative research purposes, a pilot study among patients with a systemic-auto immune disease needs to be undertaken.

The generalizability of these results is subject to certain limitations, for instance, the scope of this study was limited to mostly patients with SLE. It is unfortunate that the study did not include more different types of systemic auto-immune diseases, with regards to the research question. Findings therefore need to be interpreted with caution, nonetheless, the inter-rater reliability of this study method was sufficient so findings can, especially for SLE-patients who are fatigued, be generalized. On the one hand, an underestimation could have taken place because of the fact that more severe fatigued patients were not able to join at the Wereld Lupus Dag because of the enabling consequences of fatigue. So this study might miss out the patients who were extremely fatigued. On the other hand, an overestimation of the impact of severe fatigue could have taken place. The sample of this study was derived by asking patients to subscribe for this research at the Wereld Lupus Dag. Patients who were more fatigued are more likely willing to join in any research regarding fatigue, meaning that patients who were less fatigued could have been missed.

4.5 Conclusion and future directions

Returning to the research question posed at the beginning of this study, it can be clearly stated that fatigue has a major impact on the lives of patients with SLE and related diseases, and their partners as individuals and as a couple. The findings of this study have a number of important implications for future studies. Firstly, future research should focus on developing self-management programs based on the results of this study in order for patients to better cope with fatigue and secondly, for partners it is important to investigate whether a self-management programme would be relevant to them. Finally, future research should focus on exploring 'good communication', acceptance and acquiring knowledge on illness within couples.

5. References

Ad hoc committee on systemic lupus erythematosus response criteria for fatigue (2007). Measurement of Fatigue in Systemic Lupus Erythematosus: A Systematic Review. *Arthritis & Rheumatism (Arthritis Care & Research), 57*(8), 1348-1357. doi: 10.1002/art.23113

Ahn, G.E. & Ramsey-Goldman, R. (2012). Fatigue in systemic lupus erythematosus. *International Journal of Rheumatology, 7*, 217-227.

Almehed, K., Carlsten, H., and Forsblad-d'Elia, H. (2010). Health-related quality of life in systemic lupus erythematosus and its association with disease and work disability. *Scandinavian Journal of Rheumatology, 39(1)*, 58-62. doi: 10.3109/03009740903124408

Årestedt, L., Persson, C., & Benzein, E. (2014). Living as a family in the midst of chronic illness. *Scandinavian Journal of Caring Sciences, 28,* 29–37. doi: 10.1111/scs.12023

Baanders, A.N. & Heijmans, M.J.W.M. (2007). The Impact of Chronic Diseases: The Partner's Perspective. *Family & Community Health, 30*(4), 305-317.

Baarda, D.B., De Goede, M.P.M., & Kalmijn (2000). *Enquêteren en gestructureerd interviewen.* Houten: Educatieve Partners Nederland BV.

Badger, T.A., Segrin, C., Figueredo, A.J., Harrington, J., Sheppard, K., Passalacqua, S., … Bishop, M. (2011). Psychosocial interventions to improve quality of life in prostate cancer survivors and their intimate or family partners. *Quality of Life Research, 20,* 833–844. doi: 10.1007/s11136-010-9822-2

Balsamo, S. & Santos-Neto, L.D. (2011). Fatigue in systemic lupus erythematosus: An association with reduced physical fitness. *Autoimmunity Reviews, 10*, 514–518. doi: 10.1016 /j.autrev.2011.03.005

Bauernfeind, B., Aringer, M., Prodinger, B., Kirchberger, I., Machold, K., Smolen, J., and Stamm, T. (2009). Identification of Relevant Concepts of Functioning in Daily Life in People With Systemic Lupus Erythematosus: A Patient Delphi Exercise. *Arthritis & Rheumatism, 61(1)*, 21-28. doi: 10.1002/art.24165

Blazquez, A. & Alegre, J. (2013). Family and Partner Facing a Chronic Disease: Chronic Fatigue Syndrome. *The American Journal of Family Therapy*, *41,* 46–62. doi: 10.1080 /01926187.2011.642651

Bohnen, M., Shea, J., Michaud, G., John, R., Stevenson, M., Epstein, L. … Koplan, B. (2011). Quality of Life with Atrial Fibrillation: Do the Spouses Suffer as Much as the Patients? *PACE, 34,* 804-809. doi: 10.1111/j.1540-8159.2011.03111.x

Brandãoa, T., Schulz, M., and Matosa, P. (2014). Psychological intervention with couples coping with breast cancer: A systematic review. *Psychology & Health, 29(5)*, 491–516. doi.org/ 10.1080 /08870446.2013.859257

Brod, M., Tesler, L.E., & Christensen, T.L. (2009). Qualitative research and content validity: developing best practices based on science and experience. *Quality of Life Research, 18*, 1263–1278. DOI 10.1007/s11136-009-9540-9

Brooks, J., King, N., & Wearden, A. (2014). Couples' experience of interacting with outside other in chronic fatigue syndrome: a qualitative study. *Chronic illness, 10(1),* 5-17. doi: 10.1177 /1742395312474478

Carlson, L.E., Bultz, B.D., Speca, M., & St. Pierre, M. (2000). Partners of Cancer Patients Part 1: Impact, Adjustment, and Coping Across the Illnes Trajectory. *Journal of Psychosocial Oncology, 18(2),* 39-63. doi: http://dx.doi.org/10.1300/J077v18n02_03

Cohen, D.J. & Crabtree, B.F. (2008). Evaluative Criteria for Qualitative Research in Health Care: Controversies and Recommendations. *Annals of Family Medicine, 6*, 331-339. doi: 10.1370/afm.818

Coyne, J.C. & Fiske, V. (1992). Couples coping with chronic and catastrophic illness. *Families and illness, 9*, 129-149.

Crosby, R.A., DiClemente, R.J. & Salazar, L.F. (2006). *Research methods in health promotion*. San Francisco: John Wiley & Sons.

Dalteg, T., Benzein, E., Fridlund, B., & Malm, D. (2011). Cardiac disease and its consequences on the partner relationship: A systematic review. *European Journal of Cardiovascular Nursing, 10*, 140-149. doi: 10.1016/j.ejcnurse.2011.01.006

De Groot, M., Phillips, S.J., & Eskes, G.A. (2003). Fatigue associated with stroke and other neurologic conditions: implications for stroke rehabilitation. *Archives of Physical Medicine and Rehabilitation, 84*, 1714–1720.

De Ridder, D.T.D., Scheurs, K.M.G., & Kuijer, R.G. (2005). Is spousal support always helpful to patients with asthma or diabetes? A prospective study. *Psychology & Health, 20*, 497-508.

Dorros, S.M., Card, N.A., Segrin, C., & Badger, T.A. (2010) Interdependence in Women with Breast Cancer and their Partners: An Inter-Individual Model of Distress. *Journal of Consulting and Clinical Psychology, 78(1),* 121–125. doi:10.1037/a0017724

Druley, J. A., Stephens, M. A. P., & Coyne, J. C. (1997). Emotional and Physical Intimacy in Coping with Lupus: Women's Dilemmas of Disclosure and Approach. *Health Psychology*, 16(5), 506-514.

Eghlileb, A.M., Davies, E.E.G, & Finlay, A.Y. (2007). Psoriasis has a major secondary impact on the lives of family members and partners. *British Journal of Dermatology, 156,* 1245-1250. doi: 10.1111/j.1365-2133.2007.07881.x

Gallant, M. (2003). The influence of social support on chronic illness selfmanagement: a review and directions for research. *Health Education & Behavior, 30*, 170- 195.

Gallop, K., Nixon, A., Swinburn, P., Sterling, K.L., Naegeli, A.N., & Silk (2012). Development of a conceptual model of health-related quality of life for systemic lupus erythematosus from the patient's perspective. *Lupus, 21,* 934-943. doi: 10.1177/0961203312441980

Giffords, E. (2003). Understanding and Managing Systemic Lupus Erythematosus (SLE). *Social Work in Health Care, 37(4)*, 57-72. doi: 10.1300/J010v37n04_04

Guest, G., Bunce, A., & Johnson, L. (2006). How Many Interviews Are Enough?: An Experiment with Data Saturation and Variability. *Field Methods, 18*, 59-82. doi: 10.1177/1525822X05279903

Goodwin, S.S. (2000). Couples' perceptions of wives' CFS symptoms, symptom change, and impact on the marital relationship. *Issues in Mental Health Nursing, 21*, 347-363.

Hagedoorn, M., Dagan, M., Puterman, E., Hoff, C., Meijerink, J.W.J.H., DeLongis, A., & Sanderman, R. (2011). Relationship satisfaction in couples confronted with colorectal cancer: the interplay of past and current spousal support. *Journal of Behavioral Medicine, 34*, 288–297. doi: 10.1007/s10865-010-9311-7

Harden, J., Sanda, M.G., Wei, J.T., Yarandi, H.N., Hembroff, L., Hardy, J., & Northouse, L. (2013). Survivorship After Prostate Cancer Treatment: Spouses' Quality of Life at 36 Months. *Oncology Nursing Forum 40*(6), 567-573. doi: 10.1188/13.ONF.567-573

Hatfield-Timajchy, K.S. (2007). *Delayed Diagnosis: The Experience of Women with Systemic Lupus Erythematosus in Atlanta, Georgia* (Doctoral dissertation). Retrieved from http:// pid.emory.edu/ark:/25593/13qkr

Hilton, B.A., Crawford, J.A., Tarko, M.A. (2000). Men's perspectives on individual and family coping with their wives' breast cancer and chemotherapy. *West Journal of Nursing Research, 22*, 438–459.

Joekes, K., Van Elderen, T., & Schreurs, K. (2007). Self-efficacy and overprotection are related to quality of life, psychological well-being and self-management in cardiac patients. *Journal of Health Psychology, 12*, 4 -16.

Jumisko, E., Lexell, J., & Söderberg, S. (2007). Living With Moderate or Severe Traumatic Brain Injury: The Meaning of Family Members' Experiences. *Journal of Family Nursing, 13,* 353. doi: 10.1177/1074840707303842

Kim, Y. & Given, B.A. (2008). Quality of Life of Family Caregivers of Cancer Survivors. *Cancer, 112*(11), 2556-2568.

Kozora, E., Ellison, M.C., Waxmonsky, J.A., Wamboldt, F.S., & Patterson, T.L. (2005). Major life stress, coping styles, and social support in relation to psychological distress in patients with systemic lupus erythematosus. *Lupus, 14*, 363 – 372. doi: 10.1191/0961203305lu2094oa

Krupp, L.B., LaRocca, N.G., Muir-Nash, J. and Steinberg, A.D. (1989). The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Archives of Neurology, 46*, 1121-1123.

Kuenzler, A., Hodgkinson, K., Zindel, A., Bargetz, M., & Znoj, H.J. (2011). Who cares, who bears, who benefits? Female spouses vicariously carry the burden after cancer diagnosis. *Psychology and Health, 26(3),* 337–352. doi: 10.1080/08870440903418877

Lechner, L., Mester, I & Bolman, C. (2010). *Gezondheidspsychologie bij patiënten*. Assen, Netherlands: van Gorcum.

Lerdal, A., Wahl, A.K., Rustoen, T., Hanestad, B.R. & Moum, T. (2005). Fatigue in the general population: A translation and test of the psychometric properties of the Norwegian version of the fatigue severity scale. *Scandinavian Journal of Public Health, 33,* 123. doi: 10.1080 /14034940410028406

Lupus Nederland (2014). Geraadpleegd op http://www.lupusnederland.nl/wat-is-lupus.html

McCaughan, E., Prue, G., McSorley, O., Northouse, L., Schafenacker, A., & Parahoo, K. (2013). A randomized controlled trial of a self-management psychosocial intervention for men with prostate cancer and their partners: a study protocol. *Journal of Advanced Nursing*, *69*(11), 2572–2583. doi: 10.1111/jan.12132

Mertens, D.M. (1998). *Research methods in education and psychology.* California: Sage Publications.

Moret, M., Reuzel, R., Van der Wilt, G., & Grin, J. (2007). Validity and Reliability of Qualitative Data Analysis: Interobserver Agreement in Reconstructing Interpretative Frames. *Field Methods, 19(1)*, 24–39. doi: 10.1177/1525822X06295630

Moser, D.K. & Dracup, K. (2004). Role of spousal anxiety and depression in patients' psychosocial recovery after a cardiac event. *Psychosomatic Medicine, 66*, 527 -32.

Muhr, T. (1991). A Prototype for the Support of Text Interpretation. *Qualitative Sociology, 14*, 349-371

Muscal, E. & Brey, R.L. (2010). Antiphospholipid syndrome and the brain in pediatric and adult patients. *Lupus, 19*, 406. doi: 10.1177/0961203309360808

Nationale Vereniging voor Lupus, APS, Sclerodermie en MCTD (NVLE; z.j.). Geraadpleegd op http: //www.nvle.org/ziektebeelden/sle

Nederlandse Federatie van Universitair Medische Centra (z.j.). Geraadpleegd op http://www.nfu.nl /trf/index.php?id=9&hoofdstuk=13&trf=138

Nederlanse Vereniging Sjögren Patiënten (NVSP, 2014). Geraadpleegd op http://www.nvsp.nl /syndroom-van-sj%C3%B6gren.html

Omdal, R., Waterloo, K., Koldingsnes, W., Husby, G., and Mellgren, S. (2003). Fatigue in patients with systemic lupus erythematosus: the psychosocial aspects. *Journal of Rheumatology, 30*, 283-287.

Pettersson, S., Möller, S., Svenungsson, E., Gunnarsson, I., and Welin Henriksson, E. (2010). Women's experience of SLE-related fatigue: A focus group interview study. *Rheumatology, 49*, 1935-1942. doi: 10.1093/rheumatology/keq174

Pitceathlya, C. & Maguirea, P. (2003). The psychological impact of cancer on patients' partners and other key relatives: a review. *European Journal of Cancer, 39,* 1517–1524. doi: 10.1016 /S09598049(03)00309-5

Repping-Wuts, H., Uitterhoeve, R., Van Riel, P., & Van Achterberg, T. (2008). Fatigue as experienced by patients with rheumatoid arthritis (RA): A qualitative study. *International Journal of Nursing Studies, 45,* 995–1002.

Reumafonds (2014). Geraadpleegd op http://www.reumafonds.nl/informatie-voor-doelgroepen /patienten/vormen-van-reuma/lupus-erythematodes

Rijksinstituut voor Volksgezondheid en Milieu (2013). Zeldzame aandoeningen samengevat. In: Volksgezondheid Toekomst Verkenning, Nationaal Kompas Volksgezondheid. Geraadpleegd op http://www.nationaalkompas.nl/gezondheid-en-ziekte/ziekten-en- aandoeningen/ zeldzame-ziekten/zeldzame-aandoeningen-samengevat/

Robinson, D., Aguilar, D., Schoenwetter, M., Dubois, R., Russak, S., Ramsey-Goldman, R., . . . Weisman, M. (2010). Impact of systemic lupus erythematosus on health, family, and work: The patient perspective. *Arthritis Care & Research, 62*, 266–273. doi: 10.1002/acr.20077

Smit, J.A. (2008). *Qualitative Psychology: A Practical Guide to Research Methods*. London: SAGE Publications Ltd.

Somers, T.J., Kurakula, P.C., Criscione-Schreiber, L., Keefe, F.J., & Clowse, M.E. (2012). Self-efficacy and pain catastrophizing in systemic lupus erythematosus: Relationship to pain, stiffness, fatigue, and psychological distress. *Arthritis Care & Research (Hoboken), 64*, 1334–1340.

Streiner, D.L. & Norman, G.R. (1991). *Health measurement scales: A practical guide to their development and use*. Oxford: Oxford University Press.

Sterling, K.L., Gallop, K., Swinburn, P., Flood, E., French, A., Al Sawah, S., . . . Nixon, A. (2014). Patient-reported fatigue and its impact on patients with systemic lupus erythematosus. *Lupus, 23,* 124-132.

Sutanto, B., Singh-Grewal, D., McNeil, H.P., O'Neill, S., Craig, J.C., Jones, J., & Tong, A. (2013). Experiences and Perspectives of Adults Living With Systemic Lupus Erythematosus: Thematic Synthesis of Qualitative Studies. *Arthritis Care & Research, 65*(11), 1752-1765. doi: 10.1002/acr.22032

Tani, C., Carli, L., Vagnani, S., Talarico, R., Baldini, C., Mosca, M., & Bombardieri, S. (2014). The diagnosis and classification of mixed connective tissue disease. *Journal of Autoimmunity, 48-49*, 46-49. doi:10.1016/j.jaut.2014.01.008

Tayer, W.G., Nicassio, P.M., Weisman, M.H., Schuman, C., Daly, J. (2001). Disease status predicts fatigue in systemic lupus erythematosus. *Journal of Rheumatology, 28*, 1999–2007.

Taylor, B. & De Vocht, H. (2011). Interviewing Separately or as Couples? Considerations of Authenticity of Method. *Qualitative Health Research, 21(11*), 1576-1587. doi: 10.1177/1049732311415288

Wadhwa, D., Burman, D., Swami, N., Rodin, G., Lo, C., & Zimmermann, C. (2013). Quality of life and mental health in caregivers of outpatients with advanced cancer. *Psycho-Oncology*, 22, 403-410.

Wagner, C.D., Bigatti, S.M., & Storniolo, A.M. (2006). Quality of life of husbands of women with breast cancer. *Psycho-Oncology, 15*, 109–120.

Wang, M., Gladman, D.D., Ibañez, D., & Urowitz, M. (2012). Long-term outcome of early neuro-psychiatric events due to active disease in systemic lupus erythematosus. *Arthritis Care & Research, 64*, 833–837.