What matters for lupus patients?

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ystemic lupus erythematosus (SLE) is a heterogeneous systemic autoimmune disease, whose diagnosis has a significant impact on patients’ life. In clinical routine, the impact on the patient is predominantly evaluated with regard to morbidity and mortality due to disease symptoms, co-morbidities and complications because of its immunosuppressive treatment. Advances in disease management have improved survival of lupus patients in the past decades [1] and shifted the focus to other outcome parameters measuring health related quality of life (HRQoL) and quality of life (QoL) that are of interest for use in clinical trials as well as clinical routine [2]. Furthermore, they are of growing importance for the pharmaco-economic evaluation of new drugs with implications for reimbursement and accessibility.

Material and methods

We conducted a search of English or German language publications related to SLE and the burden of illness, QoL and HRQoL using the Medline (PubMed) library. The following search terms were used: SLE, burden of illness, quality of life, health related quality of life, outcome, patient reported, self-reported, employment, work, work disability, work productivity, psychological impact, physical impact, fatigue, depression, anxiety, discordance, body image, self-image, work productivity, unmet needs, sleep disturbances, sleep quality, sleep disorder, sexual dysfunction, sexual function and pain. Furthermore, bibliographies of existing publications were reviewed as well as studies primarily relating to the development or evaluation of QoL or HRQoL instruments to identify additional factors that are of interest to QoL in SLE patients. We focused on prospective interventional and observational studies in adult SLE patients preferring Caucasian ethnicity and larger study population though this was not generally applicable. The abstracts were reviewed manually to identify studies of interest.

In addition, we present data from our “Lupus-(erythematodes)-Langzeit-Studie” (LuLa-Study). The LuLa-Study is a longitudinal cross-sectional survey of the German LE self-help community on a multitude of LE associated factors that is being conducted annually by means of a self-reported questionnaire since 2001 and is ongoing. It was shown that LuLa participants are representative of SLE patients in Germany [3]. HRQoL is measured since 2003 by the Short Form 12 Health Survey (SF-12 Mental Component Summary [MCS] and SF-12 Physical Component Summary [PCS]) with additional census of other disease characteristics regularly, including co-morbidities, lupus-specific medication, disease activity and a damage index. Additionally, annual focal topics, like depression, fatigue, sleep disturbances, work disability or work productivity have been
surveyed. The LuLa cohort was a closed cohort since the end of recruitment in 2004. In 2011, the LuLa-Study was reopened for new participants with disease duration of less than two years. During the closed cohort phase, we observed a decline from 866 participants in 2005 to 624 in 2010 but reached annual return rates between 84.4% and 93.4%. In 2011, 585 SLE patients participated of whom 34 had entered the reopened study in that year. We observed a steady proportion of female participants of 94.0–94.8%. Mean age and disease duration increased from 48.7 in 2005 to 53 years in 2010 and 11.8 to 18.3 years, respectively. Mean disease duration of the new recruited participants in 2011 was 0.7 years at a mean age of 34 years. Disease activity measured by the self-reported Systemic Lupus Activity Questionnaire (SLAQ) decreased from a mean of 14.7 to 12.8 (2005 until 2011), presenting significantly higher in the newly recruited patients in 2011 (SLAQ 18.1), while the self-reported damage index (Brief Index of Lupus Damage (BILD)) presented in 2011 higher accrued damage in the closed cohort participants (2.6 vs 1.6).

**Patients’ perspective on SLE and QoL**

Former studies have shown that the impact of perceived SLE symptoms might strongly differ from the physicians’ perspective. Studies by Neville et al. [4] and Yen et al. [5] observed significant differences in the scoring of global disease activity on a Visual Analogue Scale (VAS) between patients and physicians. Patients scored higher than their physician in 16 to 20.7% of cases whereas the physicians only scored higher in 6 to 7.2%. They concluded that patients score their disease activity based on their psychological and physical well-being, whereas physicians score disease activity based on the clinical and physical signs and symptoms of lupus. Pain [5] as well as SF-36 mental health and SLAM-R kidney [4] scores were identified as main factors contributing to a higher discordance between the patients’ and physicians’ assessment.

In our LuLa-study in 2010, we asked 621 lupus patients which manifestation of SLE has the highest impact on their well-being. Manifestations of the joints, skin and accompanying mental disorders were perceived as the three major compromising factors, followed by pulmonary, serological (cytopenia), renal, central nervous and cardiac manifestations. We further assessed whether they felt more compromised by any of the organic manifestations or by general symptoms (e.g. fatigue, fear, sleep disorders). The participants were able to grade from −5 (organic symptoms) to +5 (general symptoms) on an eleven item rating scale. Most patients were indecisive and rated 0 (32.4%), whereas 48.1% felt more compromised by their general symptoms (score 1 to 5) (figure 1).

To assess HRQoL, many studies have used the generic MOS 36-item Short Form Survey Instrument (SF-36) a patient reported instrument developed in the 1990s by Ware et al. to assess health status in diverse populations. The health status is represented by different domains (vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning and mental health) [6]. As it is a generic instrument, it is being used in different diseases and facilitates comparability between them. However, this advantage has also its drawback as the SF-36 lacks disease specific domains that are of importance in such a heterogeneous disease as SLE.

In a large cohort of 1316 SLE patients, Wolfe et al. documented that the mental component summary (SF-36 MCS) was lower in SLE (44.3) compared with rheumatoid arthritis (49.1) and other non-inflammatory rheumatic disorders (50.8), while the physical component summary showed comparable values between the disease (36.3–36.7). Within SF-36 domains, physical functioning was better, but general health perceptions, vitality, social role functioning, emotional role functioning, and mental health were more impaired in SLE compared with the other diseases [7]. In our LuLa cohort, we used the SF-12, a short version of the SF-36 that facilitates comparable assessments of mental and physical health [8]. We observed a comparable lower MCS (44.9–47.4) and PCS (39.5–40.6) over a 9-year observation period that presented significantly lower than in general German population (PCS 49.0 MCS 52.2 [9]). PCS was comparably decreased like in other disease conditions in German control groups while MCS presented lower than in most other chronic conditions (arthritis: PCS 39.7 MCS 49.8; cancer: PCS 41.5 MCS 49.7; heart attack PCS 37.4 MCS 44.7; COPD PCS 42 MCS 50.2; diabetes PCS 38.9 MCS 50.1 [9]). The particular limitation of the MCS compared to other disease conditions states the importance of the associated domains

### Glossary

- **BILD** Brief Index of Lupus Damage
- **CDS** Calgary Depression Score
- **CES-D** Center for Epidemiological Studies Depression Scale
- **FSS** Fatigue Severity Scale
- **HRQoL** Health Related Quality of Life
- **MCS** Mental Component Summary of the SF-36 resp. SF-12
- **PCS** Physical Component Summary of the SF-36 resp. SF-12
- **QoL** Quality of Life
- **SCL-90-R** Symptom Checklist-90-R
- **SF-12** Short Form 12 (subset of the SF-36)
- **SF-36** MOS 36-Item Short Form Survey Instrument
- **SLAM-R** Revised Systemic Lupus Activity Measure
- **SLAQ** Systemic Lupus Activity Questionnaire
- **SLE** Systemic lupus erythematosus
- **SLEDAs** Systemic Lupus Erythematosus Disease Activity Index
- **VAS** Visual Analogue Scale
vitality, emotional role functioning, social role functioning and mental health for patients’ quality of life. Since 2003, there has been much effort to develop disease specific instruments to assess QoL and HRQoL in SLE. As shown in table I, they focus on different aspects of SLE. Most of these instruments have been developed using feedback from patients or structured interviews with patients to determine items of importance. These instruments give us an idea, which problems are of great importance from a patient’s perspective. Furthermore, few studies surveyed SLE patients’ unmet needs concerning their disease and its management by using the SLE Needs Questionnaire in Australian and American cohorts. The questionnaire surveys up to 97 items in seven domains. Nearly all patients (94–100%) reported some kind of unmet need [15,16], most were reported in the physical (94–98) and psychological domain (91%) followed by daily living (72–90%), health services (78–80%), health information (74–78%), social support (79%) and employment/financial (54–62%). Predominant reported unmet needs were tiredness (81–90%), pain (73–80%), not being able to do things one used to (72–77%), fear of exacerbation (72–80%), sleeping problems (70–75%), anxiety/stress (69–79%), feeling worse after physical activity (71%), fears about physical disability (74%) and feeling down/depressed (68%). Increasing age presented as an independent predictors of greater unmet needs to physical and psychological symptoms as well as daily living. Furthermore, African-American patients as well as people who were born overseas in the Australian cohort presented higher unmet needs in the health service and health information domain [15,16]. In longitudinal analysis, unmet needs show a high persistency over time. Over a six-month observation period, overall level of unmet needs increased or stayed the same in 63% while the prevalence remained the same for 82 of the 97 items [17]. These results emphasize that many patients’ concerns are still not managed adequately. HRQoL, QoL and unmet needs want at least the same consideration as laboratory results, clinical examination and treatment decision. In the following, this article summarizes some of these essential points that influence QoL and matter to SLE patients.

Fatigue

Fatigue is a common symptom not only in SLE patients but also in other rheumatic or chronic conditions. Its impairing impact on patients’ quality of life is significant, affecting both mental and physical health [18–20] by debilitating the initiation and maintenance of activities as well as cognitive abilities. There are a multitude of patient reported instruments to assess fatigue. Therefore, the American College of Rheumatology systematically reviewed fatigue instruments in 2007 and recommended the use of the Fatigue Severity Scale (FSS) for future studies [21]. In our LuLa cohort, we used the FSS in 2011. We observed a mean FSS of 4.14 (median 4.33). A FSS score below 4 is considered normal whereas a score of more than five represents severe fatigue [22,23]. In the LuLa cohort, only 46% had FSS scores below 4.0 while 40% scored higher than 5.0. When analyzing the three groups (≤ 4, 4–5 and ≥ 5), we observed plural significant differences in disease activity, accrued damage, physical and mental health surveyed by the SF-12, number of co-morbidities and SLE-specific medications (all patient-reported) (see table II). The proportion of SLE patients...
with reported fatigue in our LuLa cohort (54%) is comparable to that reported in other cohorts with numbers ranging from 50–92% [19,20,24,25]. The importance of fatigue from a patient’s perspective was also documented in other research groups where patients rated their fatigue worse or on par with pain [26,27]. Studies have shown that increased fatigue is closely associated with sleep disturbances and depressed mood in SLE patients [20,26,28,29]. Other factors that are considered to be linked with severe fatigue are: fibromyalgia, lack of social support, marital status, pain, lack of exercise/physical activity, smoking, abnormal illness-related behaviours, feeling of helplessness, stress, constitutional symptoms, use of non-steroidal anti-inflammatory drugs, use of antidepressants and Caucasian ethnicity [19,26,28,30,31]. Some of these have been identified as independent predictors by multivariate analysis: fibromyalgia, depression, sleep quality, level of exercise participation, social support, abnormal illness-related behaviours, feeling of helplessness, stress, Caucasian ethnicity, constitutional symptoms (fever, weight loss), pain, organ damage and disease activity [19,26,28,29]. The influence of disease activity is controversial as some authors report a significant correlation [20] while others deny it [26,32], which might partly be reasoned by the use of different instruments for assessing disease activity. The Systemic Lupus Activity Measure (SLAM) applied by Tench at al. uses considerably more patient-derived information than the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) used in the other studies. This effect was similarly observed and discussed by Fortin et al. examining the influence of disease activity on health and quality of life in SLE patients [33]. Other co-existing conditions, like anemia, hypothyroidism or infectious diseases can be responsible for fatigue and should be considered as specific therapy might be helpful.

### Table 1

<table>
<thead>
<tr>
<th>QoL/HRQoL instruments</th>
<th>Instruments Domains (items in this domain)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLE Symptom Checklist (SSC) [10] 2003</td>
<td>Unidimensional (38 questions focussing on disease-related and therapy-related symptoms)</td>
</tr>
</tbody>
</table>
Burden to others (3)  
Emotional health (6)  
Fatigue (4)  
Intimate relationships (2)  
Pain (3)  
Physical health (8)  
Planning (3) |
| Systemic Lupus Erythematosus-Specific Quality Of Life Questionnaire (SLEQOL) [12] 2005 | Activities (9)  
Food (4)  
Physical functioning (6)  
Self-image (9)  
Symptoms (8)  
Treatment (4) |
| Systemic Lupus Erythematosus Quality Of Life Questionnaire (L-QoL) [13] 2009 | Unidimensional (25 questions focussing on different aspects, amongst others self-care, fatigue and emotional reaction) |
| Lupus Patient Reported Outcome tool (LupusPRO) [14] 2012 | Body image (5)  
Cognition (2)  
Coping (3)  
Desires-goals (4)  
Emotional health (6)  
Lupus medications (2)  
Lupus symptoms (3)  
Pain vitality (5)  
Physical health (5)  
Procreation (2)  
Satisfaction with care (4)  
Social support (2) |

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### Table II
Characteristics of the LuLa cohort split by fatigue severity

<table>
<thead>
<tr>
<th>FSS score</th>
<th>≤ 4</th>
<th>&gt; 4 and &lt; 5</th>
<th>≥ 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.9</td>
<td>52.0</td>
<td>50.6</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>17.9</td>
<td>18.3</td>
<td>16.3</td>
</tr>
<tr>
<td>SLAQ</td>
<td>9.2</td>
<td>12.5</td>
<td>17.6</td>
</tr>
<tr>
<td>BILD</td>
<td>2.2</td>
<td>2.6</td>
<td>2.9</td>
</tr>
<tr>
<td>SF-12 PCS</td>
<td>46.2</td>
<td>39.7</td>
<td>33.4</td>
</tr>
<tr>
<td>SF-12 MCS</td>
<td>50.9</td>
<td>47.3</td>
<td>41.2</td>
</tr>
<tr>
<td>No of co-morbidities</td>
<td>0.8</td>
<td>1.0</td>
<td>1.4</td>
</tr>
<tr>
<td>No of SLE medication</td>
<td>1.5</td>
<td>2.0</td>
<td>1.9</td>
</tr>
</tbody>
</table>

BILD = Brief index of lupus damage; FSS: Fatigue severity score; SF-12 MCS = Short Form 12 Mental component summary; SF-12 PCS = Short Form 12 Physical component summary; SLAQ = Systemic lupus activity questionnaire; SLE Systemic lupus erythematosus.

* Significant (P < 0.005) calculated by the Kruskal–Wallis one-way analysis of variance.

Over 8 to 12 weeks; walking, jogging, cycling, swimming or using Wii Fit) [31,34,35]. These can be implemented by the patients themselves and thereby enhance their individual responsibility and self-efficacy.

### Depression and anxiety

One of the top three mentioned problems of the LuLa participants was mood disorders that were reported by 41% in our cohort. In 2008, we used the Center for Epidemiological Studies Depression Scale (CES-D) to assess the prevalence of depressive symptoms: 19% of the participants scored higher than the cut-off point for significant symptomatology and the mean score was significantly higher than in normal population (18 vs 14). Involvement of the central nervous system in SLE is a common but often unrecognized manifestation. This has led to development of a nomenclature system for neuropsychiatric syndromes in SLE by the American College of Rheumatology in 1999 [36] where besides organic syndromes also a variety of psychiatric disorders (e.g. anxiety disorder, cognitive dysfunction, mood disorder) are listed. Classification of the latter is considered especially difficult as in a high number of cases a distinction between neuropsychiatric manifestations caused by SLE and psychological reactions to the stress of having a major chronic systemic illness is not possible.

Generally, the recognition of psychiatric disorders in SLE patients is to be considered unsatisfying. Petri et al. [37] included 111 US patients in their study with short disease duration (max. 9 months). Only 8% had an ACR neuropsychiatric case definition of mood disorder at inclusion but 32% scored higher than 6 in the Calgary Depression Score (CDS), which classified them as depressed. This result is in accordance to the statement of van Exel et al. [38] that only 7% of SLE patients with a major depression receive antidepressant treatment, which underlines that its recognition or its treatment might be insufficient.

The prevalence range of depressive symptoms in literature shows a broad range. Larger cross-sectional studies on US cohorts documented a major depression prevalence between 17 and 42% (Bachen et al. [39] 42% in 326 Caucasian SLE patients; Brey et al. [40] 28% major depressions and 19% mood disorders with depressive features in a multiethnic cohort of 128 patients; Julian et al. [41] 17% major depressions or 26% of any mood disorders with depressive features in a multiethnic cohort of 150 patients). Several studies with European populations (Finland [42] n = 46, Netherland [38] n = 102, Poland [43] n = 52, UK [44] n = 323) recorded comparable ranges between 12 and 43%. The prevalence of depression in SLE patients is considerably higher than in general population [38,39,45]. Julian et al. [41] calculated an annual incidence of 12% in her multiethnic cohort.

Predictors of depression are manifold and contain less formal education [38,41], higher levels of fatigue [37,38], less physical activity [38], lower quality of life (SF-36 subdomains) [45,46], socioeconomic status [45], Hispanic/Latino ethnicity [41], perceived illness stigma [47], higher anxiety scores [48], younger age [41,48], diabetes mellitus [41], fibromyalgia [37] and alopecia [38]. Several studies have examined the association between disease activity and depression in SLE. The results are inconsistent as some studies prove a significant association of depression in active disease [39,46,49], while others do not [37,38]. The type of disease activity instrument might also be accounted for this inconsistency. The often-used SLAQ is a patient reported instrument and implies a high number of items that are subjective. Therefore, the correlation of the SLAQ with (patient-reported) QoL instruments is to be considered higher than with other physician-reported instruments that assess disease activity. It was shown by Carr et al. [50] that a higher self-reported disease activity in the SLAQ correlated with depression, whereas the physician-reported SLEDAI did not.

A study in an Italian cohort by Doria et al. considered depression, anxiety and joint pain as independent major determinants of HRQoL. Thereby, the accrued damage deteriorated HRQoL by enhancing depressive symptoms [51]. The observed prevalence of anxiety in SLE patients is lower than the prevalence of depression ranging from 4 to 37% [37,39,40,42–45,48]. The highest rates were registered in a Thai (37%) [48], a Mexican American (24%) [40] and a Chinese (20%) [45] cohort, indicating that social factors or characteristics of the health care system might play an important role. Shen et al. [45] reported a significantly higher anxiety than in a healthy control group. Simultaneously, the affected SLE patients...
had a low socioeconomic status, worse disease status and lower quality of life. Hawro et al. [43] observed anxiety disorder in 8%. Shorter SLE duration and lower cumulative doses of corticosteroids were predictive of anxiety in this Polish cohort. The lack of acquired coping abilities and perceived social support in early stages of disease were the explanation for this observation. Depression and anxiety are considered to have a negative effect on the course of SLE and its co-morbidities, such as a higher incidence of cardiovascular disease [52,53], decreased QoL [54], decreases HRQoL [51], disability, and the loss of employment. It can even bring forth suicidal ideation as stated by Xie et al. and Zakeri et al. [55,56]. The documented rates of suicidal ideation were very high (34.4% and 10.5%) possibly due to other characteristics, like social and cultural domains in these Iranian and Chinese cohorts. Early recognition and effective treatment of psychiatric disorders are important considering their impact on the course of disease.

**Body image**

Body image defines the patients’ attitude to her own body respectively physical appearance. This subjective rating is affected by multiple factors, like perception, feeling, aesthetic perception and functioning of the body. In a chronic disease, such as SLE many possible factors, like disease manifestations, disease activity, accrued damage and co-morbidities may influence the body image. Jolly et al. reported a significantly worse body image-related QoL in SLE patients than age-matched non-SLE controls. Especially younger patients and those with cutaneous disease activity or damage, or depression were more likely to have poor body image-related QoL [57]. Comparable, a study among 84 adolescents showed that appearance concerns were predictive of depression in SLE [58]. Important concerns for SLE patients with change in appearance are the visibility of the change in public, society’s knowledge of SLE and received disease information and explanation. Several strategies are used to overcome this problem, like cosmetic concealment, clothing to cover-up or social withdrawal [59]. This emphasizes the importance of non-medical treatment and interventions in patients with SLE. Support can be given by patient education by health care professionals or self-help groups.

**Sexual functioning, intimate relationship**

Impaired sexual functioning is a common problem in SLE patients. Sexual problems often are unrecognized as inquiry of this subject is frequently being avoided by health care professionals [60]. The rates of impaired sexual functioning in SLE patients is reported between 22 and 49% [61–63] and is reported significantly higher than in healthy controls [63,64] or in other chronic diseases (e.g. arthritis related conditions, muscular illnesses, neurological related illnesses, blood or bone marrow transplanted leukaemia) [61]. This indicates that SLE has a greater impact on sexual functioning than other chronic conditions. SLE patients have higher rates of abstention [64] and pain [63], and lower frequency of sexual activity [64], vaginal lubrication [63,64], general sexual adjustment [64], desire [63], arousal [63], orgasm [63], sexual esteem and body esteem [61]. Daleboudt et al. found that sexual functioning in SLE patients was negatively affected by treatment, even more than by treatment in a cohort of bone marrow transplanted patients. However, they discovered that the individual illness perceptions were an even stronger predictor of impaired sexual functioning [61]. Further reported influences are greater disease severity, age, relationship status, weight concerns, pre-morbid sexual attitude, and depression [64]. García Morales et al. documented an association with most of the psychological problems and symptoms of the Symptom Checklist-90-R (SCL-90-R) (somatisation, obsessive-compulsive behaviour, interpersonal sensitivity, depression, hostility, paranoid ideation, higher scores in the Positive Symptom Total and Positive Score Discomfort Index) and some HRQoL domains measured by the SF-36 (vitality, social function, emotional role and mental health) while none of the specific disease or clinical characteristics (e.g. disease duration, activity or damage) of SLE were found to be associated with sexual problems or sexual distress [63]. As the majority of patients with SLE are receptive to inquiry and education about sexual problems [64], rheumatologists and other health care professionals should be encouraged to routinely address this topic.

**Employment, productivity loss, disability**

Morbidity, due to high disease activity, damage, as well as co-morbidities in SLE patients lead to impairments and disabilities, limiting productivity and activities of daily living. In Germany, compensations for persons with disabilities or impairments according to the charter of fundamental rights of the European Union are complex. The prerequisite for compensation is an official governmental approval of the disability, which grades severity from 30 to 100%.

In our LuLa cohort, 76% had made an application for disability which was approved in 41 years with mean disease duration of 6 years. This matches a physician-reported study from the German Collaborative Arthritis Centers that showed that the employment rate dropped after disease duration of 5 years and was comparably lower than in general population [65]. Other studies support this observation that work disability accumulates and employment rates decline with an increase of disease duration [65–69]. Data from the US Lupus Outcomes Study (n = 982) showed that the proportion of employed patients with SLE dropped from 74% at diagnosis to 54% after two years. A Kaplan–Meier analysis estimated a cessation of work...
among patients employed at diagnosis of 15% after 5 years, 36%, 51% and 63% after 10, 15 and 20 years, respectively. In another analysis of the German Collaborative Arthritis Centres (n = 3465), employment declined from 53% in patients with a disease duration of ≤ 2 years to just 25% in those with a disease duration of more than 20 years [69]. With regard to causation, 92% of the patients in the Carolina Lupus Study reported health problems as the main reason for cessation of work, which was much higher than in the controls (40%) [67]. A Dutch study observed a comparable high number (75%) of SLE patients that attributed their withdrawal from work at least in part to disease-related factors [70]. Details of factors that were identified to be associated with work loss, work disability or employment status are listed in Table III. The high number of work cessation in SLE patients is the main reason for productivity loss. A productivity loss due to a reduction of working hours is minimal in the people who stay employed [68]. The chance of getting employed after diagnosis of SLE is significantly worse than in controls (18% vs 37%) [67]. Less disease activity, fewer lung manifestations, better physical functioning, and shorter time since last employment are predictive of work entry [71].

| Table III |
| Factors associated with different employment status |

<table>
<thead>
<tr>
<th>Employment status</th>
<th>Factors associated</th>
<th>References</th>
</tr>
</thead>
</table>
| Work loss/unemployment | Low educational attainment  
Older age  
Longer disease duration  
Female gender  
Neuropsychiatric organ damage  
Lower cognitive and physical functioning  
Co-morbid depression  
Co-morbid diabetes mellitus  
Arthritis, pleurisy or gonadal failure  
Reduced HRQoL  
Work characteristics (high physical/psychological/cognitive demands of the job and low levels of job control)  
Region of residence/labour market conditions | [65,67,68,70,71] |
| Work incapacity or disability | Memory impairment  
Low educational attainment  
Depression  
Not being married/living with a partner  
Co-morbid fibromyalgia, hypertension or arthralgia  
Male gender  
A high number of diagnostic criteria for SLE  
Renal involvement  
Being unable to work at diagnosis  
Fatigue  
Pain  
Low self-efficacy  
Abnormal illness-related behaviours  
Feeling of helplessness  
Low levels of social support  
Low performance of vigorous activity  
Higher disease activity  
Lower HRQoL  
Younger age at diagnosis  
Low household income or poverty | [66,72–74] |
| Being employed | Lack of memory impairment  
Lack of depression  
Being employed at diagnosis  
Male gender  
High educational attainment | [74] |

HRQoL: Health Related Quality of Life.
Due to the chronic nature of the disease and its recurrent flares, sick leave is commonly reported by SLE patients. In our LuLa cohort, 29% of the employed participants reported a sick leave during the prior 12 month of which 20% was longer than one week (mean 12.3 weeks, range 1–56 weeks). We observed that the proportion of longer sick leave (> 1 week) was significantly higher (59% vs 16%) in the in 2011 new recruited participants with short disease duration (mean 0.7 years, maximum 2 years) than in a group with longer standing disease (mean 18.3 years, minimum 7 years). A Dutch study observed 61% of 114 patients who were absent from work for at least 6 consecutive weeks in the last 12 months of whom 31% had not resumed work even after 6 months [75]. In comparison, in the study from Campbell et al., 21 of 100 SLE patients missed 15 or more days of work with a median of 10 days [67]. The difference in rate and length of sick leave between the cohorts is mostly explained by differences in the health care system. The continuation of payments is warranted by law in Germany (6 weeks, afterwards sickness benefit from the health insurance company for up to 78 weeks) and the Netherlands (104 weeks). Nonetheless, work disability and productivity loss or unemployment has a great importance for QoL in the individual patient as financial independence might be at risk, which implicates further problems not only in health care but also in social life.

Sleep disorders

Sleep is an essential factor for health and quality of life. Sleep disorders are quite common in the general population and include insomnia with inadequate sleep quantity or quality. They are frequently reported in SLE patients with proportions between 56 and 81% [20,76–82]. In our German LuLa cohort, we observed sleep disorders in up to 61% of the SLE patients of whom 22% suffered from chronic sleep disorders. Compared to healthy controls sleep disturbances are more common and significantly worse in patients with SLE [78–83].

Daytime sleepiness is reported in up to 51% of the patients accompanied by daytime dysfunction, fatigue and somnolence, which are more frequently, observed in SLE patients than in general population [78,83]. Polysomnographic data shows that SLE patients’ sleep is often characterized by respiratory (sleep apnoea or abnormal respiration) or movement disorders (periodic limb movement) in up to 50% [78,81]. Many patients with SLE relate their poor sleep to pain and vegetative symptoms as breathlessness, sweating and palpitations [79].

In our German LuLa cohort, predictors of severe sleep disorders were age, working state, general health, pain, osteoporosis and psychotropic drugs. Further identified factors that are associated with poor sleep quality are pain [20,80,83,84], depression [20,80,83,84], anxiety [20,80,83], fatigue [20], lack of exercise [80], high disease activity [20,76,80], cumulative organ damage [80], poor functional ability [80] and prednisolone usage [80,83]. The detection of associated factors was inconsistent between different studies. For example, some studies were not able to show a linkage to prednisolone usage [20,84] or disease activity [83,84]. Amongst others, these differences might be due to different cohort characteristics. Nonetheless, the mentioned factors offer treatment options to improve sleep in patients with SLE. Kasitanon et al. [84] investigated the effect of psychological treatment, including supportive psychotherapy, psycho-education, advice for practice of meditation and medication. After treatment for three consecutive months, the patients showed an improvement of sleep quality and quantity as well as depression, anxiety, pain and overall quality of life [84].

Pain

Pain is commonly reported by patients with SLE. In the 1000 faces of Lupus cohort, only 11% reported “no pain” on a visual analogue scale (VAS, 0–100 mm) [85]. In our LuLa cohort, the annual proportions of patients reporting pain (2005 until 2009) fluctuated between 78 and 82%. Mean pain level was between 3.1 and 3.4 on a numerical rating scale (0–10). Causes for pain in SLE are manifold. Most frequently observed pain reasons are arthralgia, headaches and myalgia [86]. Other possible sources are abdominal pain, serositis, neuropathic pain or pain due to accrued damage and co-morbidities. In early stages of disease, pain might be accentuated due to higher disease activity [86] though in longer standing disease the risk for co-morbidities as well as damage and thereby inflicted pain increases. Another factor facilitating pain in early stages of disease is the incapability of effective coping and catastrophizing. For fibromyalgia, it has been shown that catastrophizing as a measure of coping was a better predictor of pain perception than demographic variables (e.g. age, duration of illness) [87]. A study on SLE patients revealed that a lower self-efficacy for pain control as part of a coping strategy and higher pain catastrophizing went along with higher levels of pain, stiffness, fatigue and reduced mood [88].

As pain affects most domains of quality of life, including above-mentioned sleep, anxiety, depression, work incapacity, sexual functioning and fatigue, an effective treatment of pain is mandatory. Due to the above-mentioned interference of coping and catastrophizing on pain, perception psychological intervention should be considered amendatory to medical treatment.

Treatment

Many of the above-mentioned factors that influence QoL and HRQoL in SLE patients are interconnected and show a high dependency on each other. Optimized treatment of disease activity and its symptoms, as well as avoidance of damage accrual and development of co-morbidities can partly improve some of the mentioned problems but often not to full extent. Psychological interventions, like psycho-education,
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Several publications have demonstrated the effectiveness of psychological interventions. Cognitive behavioural intervention can increase coping skills [89], reduce depression, anxiety and daily stress and improve QoL and even somatic symptoms [90]. A treatment of combined psycho-educative and psychotherapeutic elements was able to improve coping, depression, anxiety, and overall mental burden [91]. Even a generic self-management program for chronic diseases (Chronic Disease Self-Management Program [CDSMP]) was able to enhance the SF-36 physical health component summary, self-efficacy and several self-management behaviours (cognitive symptoms management, communication with physicians and treatment adherence) in SLE patients [92].

To improve family and social support, interventions that include family members are beneficial. A study on psychological intervention of SLE patients and their partner presented significant improvement for problem-focused coping, social support, self-efficacy, couples communication and fatigue [93].

Conclusion

In conclusion, while physicians mainly address parameters related to life expectancy their patients focus far more on quality of life. Many problems of SLE patients stay unnoticed or are not adequately taken into account as they do not evidently impact common clinical treatment goals, like disease activity, damage or laboratory values. Nonetheless, they have a vast impact not only on patients’ quality of life but also on physical components of the disease. Therefore, comprehensive medical and non-medical care exceeding the established medical treatment of disease symptoms and its consequences are of major importance to improve quality of life and outcome in all SLE patients.

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References

[22] Lerdal A, Wahl A, Rusten T, Hanesad BR, Mourn T. Fatigue in the general population: a translation and test of the psychometric properties of the Norwegian version of the


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[84] Bertoli AM, Fernández M, Alarcón GS, Vilá LM, Reveille JD. Systemic lupus erythematosus in...