

The burden of multimorbidity in patients with systemic lupus erythematosus – single-centre analysis

Marketa Dudkova, Martina Skacelova, Pavel Horak, Jakub Videman, Adela Skoumalova

Aims. Multimorbidity is a growing problem in the general population as well as in patients with rheumatic diseases like systemic lupus erythematosus (SLE). However, patients with SLE have twice the risk of developing multimorbidity than non-SLE patients. The aim of this study was to determine the prevalence of multimorbidity in patients with SLE treated in a university hospital.

Methods. This was a cross-sectional single-centre study and included patients diagnosed and treated with SLE fulfilling the EULAR/ACR 2019 classification criteria. Multimorbidity was defined as the co-occurrence of at least two chronic diseases in an individual. The multimorbidity status was determined by a simple count of associated diseases, as well as using the Rheumatic Disease Comorbidity Index (RDCI) and the Multimorbidity Index (MMI).

Results. A total of 122 patients with SLE were included in the study. Multimorbidity was found in 94% of the participants. The median comorbidity score, as measured by RDCI, was 1.5, while the MMI score was 4. The most prevalent comorbidities as measured by the RDCI were hypertension (37%), other cardiovascular disease (28%), pulmonary disease (18%) and depression (9%). No correlation was found for the RDCI and MMI scores and current disease activity as measured by the SLEDAI-2K scoring system. However, there was a marked increase in the multimorbidity indices with increasing patient age.

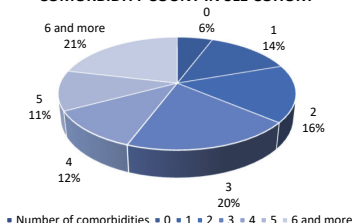
Conclusion. This study confirmed the high prevalence of the serious and often overlooked issue of multimorbidity in SLE patients. The RDCI and MMI were used to quantify comorbidities, as indices validated for usage in autoimmune rheumatic diseases, especially SLE. Due to the cross-sectional design of the study, it was not possible to determine the frequency of multimorbidity prior to diagnosis and its evolution with disease duration and activity. Nevertheless, the high prevalence of multimorbidity in this cohort underscores the importance of this issue.

THE BURDEN OF MULTIMORBIDITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS SINGLE-CENTRE ANALYSIS

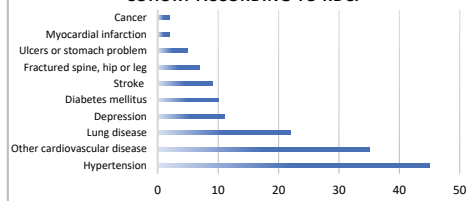
- The term 'multimorbidity' is used to describe the co-occurrence of two or more chronic conditions in an individual.
- An increasing amount of research data indicates significantly increased rates of multimorbidity among patients with rheumatological conditions in comparison to the general population.
- The aim was to determine the prevalence of multimorbidity and evaluate its impact on disease activity.
- The comorbidities were evaluated using the Comorbidity Count, the Rheumatic Disease Comorbidity Index (RDCI) and the Multimorbidity Index (MMI).

- A cross-sectional study was conducted, including 122 patients diagnosed with SLE who fulfilled the EULAR/ACR 2019 classification criteria, comprising both inpatients and outpatients.
- Multimorbidity was present in 94% of participants.
- The mean Comorbidity Count was 3.6, with a median comorbidity score of 1.5 as measured by RDCI and the MMI score of 4.
- Our findings revealed no statistically significant correlation between the current disease activity and the multimorbidity indices.

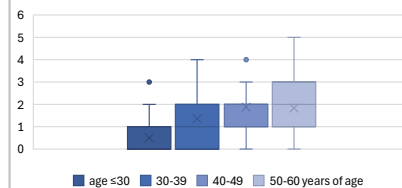
COMORBIDITY COUNT IN SLE COHORT



PREVALENCE OF ASSOCIATED DISEASES IN SLE COHORT ACCORDING TO RDCI



PREVALENCE OF MULTIMORBIDITY, AS MEASURED BY THE RDCI, INCREASES WITH AGE



We confirmed the high prevalence of multimorbidity in SLE patients. Increased attention to this concept is warranted because of its effect on patient's quality of life, treatment options, prognosis and healthcare utilization.

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Graphical Abstract

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Key words: systemic lupus erythematosus, comorbidity, rheumatic disease comorbidity index, multimorbidity index, disease activity, cross section study, prevalence of multimorbidity

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INTRODUCTION

In recent decades, the association between rheumatic diseases and other medical conditions has been extensively researched. A wide range of manifestations has been documented for rheumatoid arthritis (RA), ankylosing spondylitis (AS) and systemic lupus erythematosus (SLE), including links with various other clinical conditions. SLE is a chronic inflammatory autoimmune disease characterized by multiple organ involvement due to both the disease and the frequent comorbidities associated with it. The most encountered comorbidities are osteoporosis¹, cardiovascular², pulmonary³, and gastrointestinal diseases⁴. Further, there is an increased prevalence of infections⁵, malignancies⁶ and mental health disorders⁷. Multimorbidity is defined as the presence of at least two chronic diseases^{8,9}. The concept of multimorbidity aims to focus attention on the patient's burden of two or more chronic conditions. This is a more comprehensive and patient-centred approach than the mere coexistence of several diseases¹⁰. Further, it considers the potential interconnections and interactions of distinct diseases based on their pathophysiological link, with the aim of individualising treatment strategies^{10,11}. Multimorbidity has an impact on the quality of life, treatment options, healthcare utilisation, and overall patient prognosis¹¹⁻¹⁵.

A population-based study from the USA revealed that over 80% of patients with established SLE suffered from multimorbidity, with substantial multimorbidity in more than 50% of cases. The risk of developing multimorbidity in SLE patients was 78.5% within 5 years and 92.8% within 10 years. Compared to non-SLE participants, patients with SLE had twice the risk of developing multimorbidity than non-SLE comparators¹⁶.

Measurement of comorbidity

There are a number of comorbidity indices used to quantify the overall burden of co- and multimorbidity^{17,18}. As the impact of the diseases on patient outcome varies, different indices are used to select and weigh specific illnesses. These facilitate the identification of patients with a poor prognosis in terms of functional ability, decline in health-related quality of life, increased mortality and increased risk of hospitalisation^{13,15,17,18}. The aim of this study was to determine the prevalence of multimorbidity in patients with SLE treated at a university hospital in a real-world setting, to establish multimorbidity indices validated for use in patients with autoimmune rheumatic disease, and to evaluate the most common comorbidities.

MATERIALS AND METHODS

Study subjects

This cross-sectional single-centre study included patients who met the EULAR/ACR 2019 classification criteria for SLE (ref.²⁰) and were either outpatients or hospitalised for the primary diagnosis at the Department of Rheumatology, University Hospital Olomouc. The exclusion criteria were age over 60 years and the presence of the cutaneous form of lupus without evidence of systemic disease. The primary objective was to determine the overall prevalence of multimorbidity in the SLE cohort. The secondary objectives were to determine multimorbidity indices, to ascertain the frequency of the most common associated diseases and to compare current disease activity and the effect of age and sex on the multimorbidity index values.

The depersonalized, anonymous data were collected following the acquisition of informed consent from the patients. The study was approved by the Ethics Committee

Table 1. Demographic and Clinical Characteristics of the Enrolled Patients together with MMI and RDCI scores.

SLE cohort	Number of participants		
	SLE cohort	Women	Men
Total number of participants with SLE	122		
Number of participants newly diagnosed with SLE	7		
Ethnicity: White race/Asians/Hispanics	97.6%/1.6%/0.8%		
Women/Men	108/14		
Average age (years) (min-max)	42 (22–60)	41.3 (22–60)	47.6 (32–57)
Average duration of follow-up with dg. SLE (years) (min-max)	13 (0–32)	13.53 (0–32)	12 (0–30)
SLEDAI-2K (mean) (min-max)	4.2 (0–22)	4 (0–22)	5.4 (0–18)
RDCI (mean) (min-max)	1.61 (0–6)	1.53 (0–6)	2.07 (0–5)
RDCI (median) (min-max)	1.5 (0–6)	1 (0–6)	2 (0–5)
MMI.weight (mean) (min-max)	6.26 (0–29)	5.93 (0–29)	9.17 (0–25.5)
MMI.weight (median) (min-max)	4 (0–29)	3.5 (0–29)	7 (0–25.5)
MMI.count (mean) (min-max)	2.1 (0–7)	2 (0–6)	3.2 (0–7)
MMI.count (median) (min-max)	2 (0–7)	2 (0–6)	3.5 (0–7)
Comorbidity count according to ICD-10 in SLE cohort (mean) (min-max)	3.6 (0–11)	3.47 (0–11)	5.07 (0–11)

The table above illustrates the primary demographic and clinical characteristics of the enrolled participants. The cohort was then divided into groups according to gender.

of the University Hospital Olomouc and the Faculty of Medicine of Palacky University, Olomouc and was conducted in accordance with the latest Declaration of Helsinki.

The demographic data are presented in Table 1. Multimorbidity was defined as the presence of at least 2 chronic diseases, one of which was SLE. The term “substantial multimorbidity” was defined as the presence of at least 4 additional chronic diseases. Multimorbidity was quantified by enumerating the associated diseases in accordance with the International Statistical Classification of Diseases and Related Health Problems-10 (ICD-10) (ref.²¹) and referred to as the “Comorbidity count” (ref.²²). Additionally, the Rheumatic Disease Comorbidity Index (RDCI) (Table 2) (ref.¹⁷) and the Multimorbidity Index (MMI) (Table 3) (ref.¹⁸) were utilised. The MMI was assessed as both a counted index (MMI.count) and a weighted index (MMI.weight) (Table 3) (ref.¹⁸). The current disease activity was determined using the SLEDAI-2K scoring system²³.

Statistical analysis

IBM SPSS Statistics for Windows, Version 23.0 Armonk, NY: IBM Corp. statistical software was used for the statistical processing. Descriptive statistics, Spearman’s correlation coefficient, and non-parametric statistical tests were used for the data analysis. All tests were performed at the 0.05 level of significance.

RESULTS

A total of 122 participants were enrolled in the study. The study cohort consisted of 108 women (88.5%) and 14 men (11.5%), mean age 42 years. The mean follow-up period for the diagnosis of SLE was 13 years, with only 7 patients (5.7%) being newly diagnosed. As defined above,

multimorbidity was found in 94% of patients. The mean comorbidity score as measured by RDCI was 1.5 (range 0-6), while MMI.weight was 6.5, with median of 4 (range 0–25.5) and MMI.count ranged from 0 to 7, with a median of 2 and a mean value of 2.1 (Fig. 1). The comorbidity count in the SLE cohort is presented in Table 2, Fig. 2. Substantial multimorbidity was present in 53 cases (43%). The most prevalent comorbidities as determined by the RDCI were hypertension (38%), other forms of cardiovascular disease excluding hypertension (29%), pulmonary disease (18%), and depression (9%) (Table 2, Fig. 3). According to the MMI, the most prevalent comorbidities were hypertension (38%), chronic kidney disease (28.7%), thyroid disease (22%) and obesity (21%) (Table 3, Fig. 3). There was no correlation between the RDCI and MMI values and the current disease activity as measured by the SLEDAI-2K scoring system (Fig. 4). However, there was a significant increase in the comorbidity count (2.5 vs. 4.37, $P<0.01$), as well as in the MMI.weight (4.7 vs. 7.6, $P<0.01$) and RDCI (1.02 vs. 1.85, $P<0.01$) indices with age when comparing the patients under and over 40 years of age (Fig. 5).

It was evident after dividing the cohort into sex-specific groups that men had a higher mean age (47.6 vs. 41.3, $P<0.01$), a shorter duration of SLE (12 vs. 13.5 years, ns.) and a higher overall comorbidity count (men vs. women 5.07 vs. 3.47, $p=0.03$) as well as a higher MMI.weight (9.17 vs. 5.93, $p=0.058$), MMI.count (3.2 vs. 2, $P<0.01$) and RDCI (2.07 vs. 1.53, ns) compared to their female counterparts. The predominant comorbidities in the female cohort were hypertension (35.2%), chronic kidney disease (27.8%), and thyroid disease (22.2%), as determined by the MMI. In men, the most prevalent comorbidities were hypertension (57%), obesity (43%), chronic kidney and liver disease (36%), osteoporosis (28%) and diabetes (21%) (Table 3).

Table 2. Rheumatic Disease Comorbidity Index (RDCI) for the assessment of multimorbidity of rheumatic diseases.

Disease	Points	Prevalence in SLE cohort
Lung disease	2	18%
Myocardial infarction	2	1.6%
or		
Other cardiovascular diseases	2	29%
or		
Stroke	2	9%
or	or	
Hypertension	1	38%
Diabetes	1	8.2%
Fracture (prox. femur/vertebral body/lower limb)	1	5.7%
Depression	1	9%
Malignancy	1	1.6%
Ulcer disease or other stomach disorders (e.g. reflux, hernias)	1	4%

The Rheumatic Disease Comorbidity Index (RDCI) was developed as a self-administered questionnaire for patients with rheumatoid arthritis (RA), osteoarthritis (OA), SLE or fibromyalgia. The final score includes 11 comorbid illnesses, with a range of 0-9. The RDCI has been demonstrated to be an effective predictor of the death and physical disability¹⁶.

Table 3. Multimorbidity Index (MMI) and the prevalence of comorbid conditions in the SLE cohort

Comorbid condition	Points	Prevalence in SLE cohort	Prevalence in women	Prevalence in men
Glaucoma	0.5	2.4%	2.8 %	-
Irritable bowel syndrome	0.5	-	-	-
Schizophrenia, bipolar disorder	0.5	-	-	-
Learning disabilities	0.5	0.8%	-	7%
Anorexia/bulimia	0.5	-	-	-
Migraine	0.5	10.6%	10.2%	7%
Prostate diseases	0.5	-	-	-
Diverticulitis	0.5	2.4%	1.9%	7%
Chronic sinusitis	0.5	3.3%	2.8%	7%
Hypertension	0.5	38%	35.2%	57%
Malignancy	0.5	1.6%	1.9%	-
Diabetes mellitus	0.5	8.1%	6.5%	21%
Atrial fibrillation	0.5	-	-	-
Constipation	0.5	-	-	-
Multiple sclerosis	1	-	-	-
Substance Abuse	1	-	-	-
Osteoporosis	1	16.3%	14.8%	28%
Cutaneous psoriasis	1	2.4%	1.9%	7%
Ischemic heart disease	1	1.6%	1.9%	-
Hearing loss	1	0.8%	0.9%	-
Stroke/Transient ischemic attack	2	9%	9.3%	7%
Ischaemic disease of the lower limbs	2	-	-	-
Chronic kidney disease	2	28.7%	27.8%	36%
Idiopathic intestinal inflammation	3	0.8%	0.9%	-
Diseases of the thyroid gland	3	22%	22.2%	21%
Asthma	3	4%	4.1%	-
Obesity	4	21.3%	18.5%	43%
Chronic liver disease	5	11.5%	8.3%	36%
Heart failure	5	0.8%	0.9%	-
Bronchiectasis	5	1.6%	-	14%
Depression	6	7.4%	7.4%	7%
Anxiety/neurotic disorders	8	7.4%	8.3%	-
Alcohol addiction	9	-	-	-
Blindness or severe visual impairment	10	0.8%	0.9%	-
Parkinson's disease	10	-	-	-
Dyspepsia	10	3.3%	2.8%	7%
Chronic obstructive pulmonary disease (COPD)	10	-	-	-
Hepatitis (viral)	10	-	-	-
Epilepsy	20	5.7%	5.6%	7%
Dementia	20	-	-	-

The multimorbidity index contains a list of 40 chronic conditions. It can be used as a counted MMI (MMI.count) with a range of 0–40 or a weighted MMI (MMI.weight) with a range of 0–153. MMI.weight showed the highest correlation with the Health-related quality of life (HRQoL), physical function, and fatigue compared to other indices. Both indices are able to predict HRQoL after 1 year¹⁷.

DISCUSSION

The relationship between rheumatic diseases and other disorders has been the subject of extensive study in the recent decades. In the context of rheumatic diseases, not only have the manifestations of the disease itself been described, but also the links to other conditions. The term "comorbidity" is used to describe the co-occurrence of one or more diseases in addition to the disease of interest²⁴. This term requires the indexing of a certain condition as a primary disease, to which other, secondary

conditions are added. The focus is predominantly on the primary condition²⁴. In contrast, the recently emerging concept of multimorbidity seeks to shift attention to the patient's burden of two or more chronic conditions¹⁰. This approach aims to individualise treatment strategies⁹. Multimorbidity is a condition prevalent in the general population, affecting approximately 37% of individuals²⁵. However, regional variations in prevalence have been observed. A meta-analysis of 126 studies revealed that the prevalence of multimorbidity was 45.7% in South America, 43.1% in North America, 39.2% in Europe and

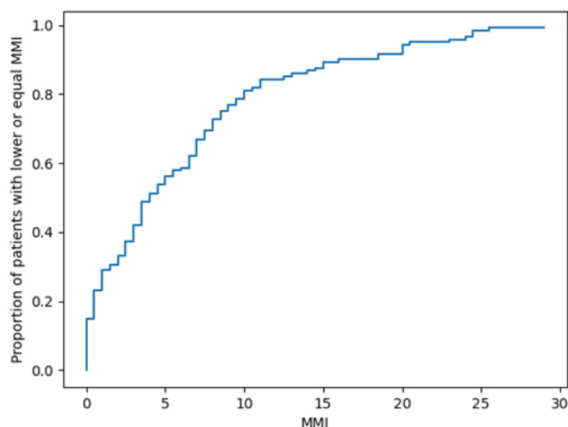


Fig. 1. The distribution of MMI.weight in the SLE cohort. Half of the patients have MMI.weight between 1 and 8.5, with a median of 4. No comorbidities were observed in 15% of the SLE cohort, 15% of patients have MMI.weight of 12.5 and higher.

35% in Asia. A higher prevalence was associated with female sex (39.4% vs. 32.8% in males) and increasing age²⁵. Additionally, a low socioeconomic standard was also identified as a risk factor²⁶.

Patients with multimorbidity are exposed to a multitude of potential risks, including polypharmacy (the simultaneous administration of multiple drugs), which can result in reduced compliance and the emergence of adverse drug reactions^{27,28}. Frequent interactions with health services can result in a failure to coordinate care delivery. Therefore, there is a need for clear communication and the individualisation of care, with a focus on the patient and his or her needs^{10,29}. Patients become more vulnerable due to poor health, older age, reduced cognitive abilities, limited health literacy as well as the prevalence of depression and anxiety^{19,29}.

The main factor contributing to the development of multimorbidity in chronic rheumatic diseases is systemic inflammation³⁰. This is followed by general factors such as ageing, smoking, obesity, sedentary lifestyle and factors associated with the adverse effects of treatment. Furthermore, evidence indicates that patients with multimorbidity may exhibit a more advanced stage of underlying disease and they may have lower odds of achieving low disease activity or complete remission^{13,15,30,31}. Additionally, there is frequently a discrepancy between the patient's subjective perception of disease activity and the clinical assessment¹⁵. The multimorbidity also affects the treatment. Multimorbid rheumatic patients are significantly less likely to undergo targeted therapy, despite exhibiting elevated disease activity^{13,15,17}. Conversely, appropriate selection and implementation of intensive treatment for rheumatic disease can have a beneficial impact on comorbidities, including cardiovascular disease, metabolic syndrome, osteoporosis and infections^{32,33}.

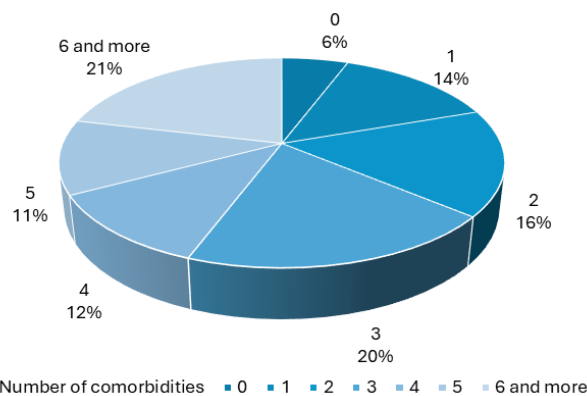


Fig. 2. Comorbidity count according to the ICD-10 in SLE cohort. The comorbidity count in the SLE cohort was determined by enumerating the number of comorbidities according to the ICD-10 present in SLE patients, expressed as a prevalence rate. The presence of at least one additional chronic disease in conjunction with SLE is indicative of multimorbidity.

As evidenced by research, the prevalence of multimorbidity among SLE patients may be up to 3 times the prevalence observed in the general population of similar age. Further, the risk of multimorbidity is twofold greater among SLE patients than a demographically comparable cohort without SLE (ref.³⁴).

In clinical practice, a variety of scoring systems are employed for the assessment of multimorbidity. In the general population, the most commonly used indices are the CCI (Carlson Comorbidity Index) (ref.^{35,36}) and ECI (Elixhauser Comorbidity Index) (ref.²⁴). The RDCI and MMI are employed for patients with rheumatic diseases^{17,18}. Both indices correlate very well with patients' functional disability and mortality^{17,18}.

The results of our study are in accordance with the high prevalence of multimorbidity observed in patients with this rheumatic disease⁹. A comparison of the original RA cohort used for MMI validation with our SLE cohort reveals that the latter is more polymorbid. While the median MMI.count is similar, there are notable differences in the overall multimorbidity, as well as in the comorbidity count and MMI.weight¹⁸. This suggests that the patients in our cohort may be more severely affected by comorbidities with greater impact on their quality of life and prognosis. As in previous studies, a high prevalence of metabolic-related diseases was observed in our cohort, including hypertension, obesity, diabetes and chronic liver disease^{37,38}. Additionally, a high proportion of cardiovascular disease was identified, characterised by a high prevalence of thromboembolic events and a minimal proportion of ischaemic heart disease or heart failure. Further, a notable proportion of both autoimmune and non-autoimmune thyroid diseases (AITD) was documented in the cohort. Although our results indicate a lower prevalence of AITD than previously reported in the

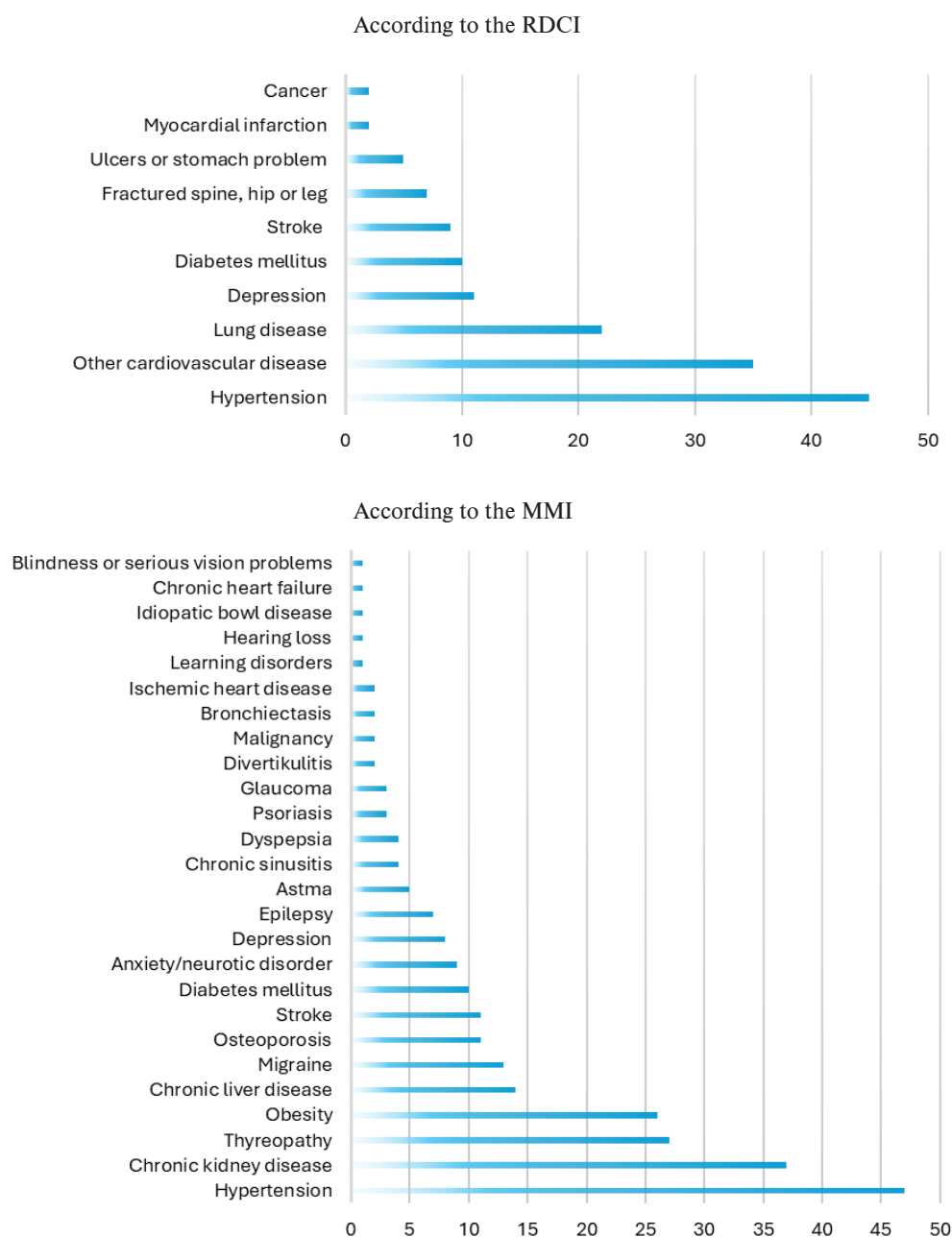


Fig. 3. The distribution of associated diseases according to the RDCI and MMI.

The most prevalent associated diseases in the SLE cohort, as identified by the RDCI and MMI were hypertension (present in 46 participants), chronic kidney disease (n=37), thyreopathy (n=27), obesity (n=26) and other cardiovascular diseases (n=35).

literature³⁹, the co-occurrence of these diseases has been documented for over six decades⁴⁰. The high prevalence of autoimmune thyroiditis in rheumatic disorders is well documented; it is a consequence of the fact that autoimmune diseases tend to cluster together. The prevalence of anti-thyroid antibodies has been documented to be between 20 and 25% in SLE patients, compared to 10% in the general population⁴¹. Additionally, certain gene polymorphisms have been identified that predispose individuals to the co-occurrence of SLE and AITD (ref.⁴²). Moreover, a higher prevalence of both nodules and tumours has been documented in SLE patients⁴³. The concomitant occurrence of AITD and rheumatic disease warrants attention, particularly during pregnancy. Alterations in fT3 and T4 levels

have been observed in pregnant women patients⁴⁴, and there may be differences in implantation, miscarriage and perinatal outcomes. Additionally, there may be a higher rate of preterm birth compared to that observed in SLE patients without AITD (ref.⁴⁵). The overall prevalence of malignancy in our cohort was low, and no case of thyroid cancer was diagnosed.

Chronic kidney disease (CKD) was present in one third of the patients in the cohort. CKD was defined as a condition in which, despite adequate treatment of lupus nephritis (LN), increased albuminuria or decreased renal function persisted after three months of therapy⁴⁶. Similarly, patients with other causes of chronic kidney disease were included in the cohort. Only two patients

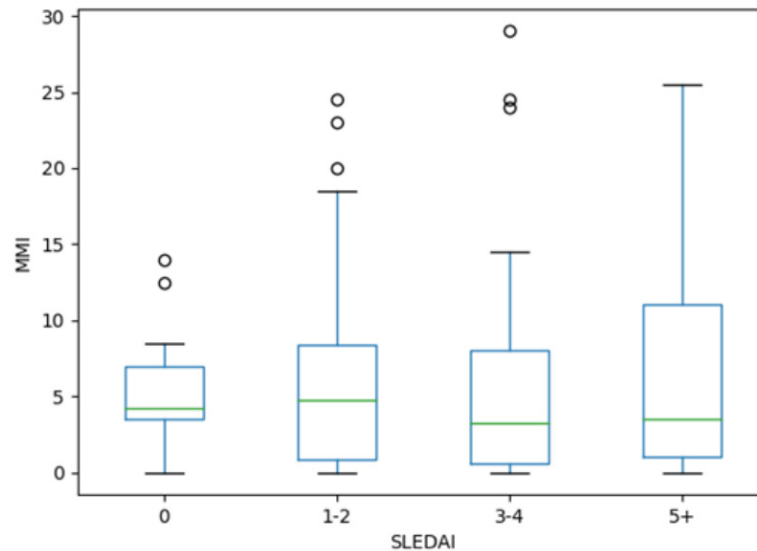


Fig. 4. Multimorbidity indices in comparison with current disease activity. Our findings revealed no statistically significant correlation between the current disease activity, as measured by the SLEDAI-2K, and the multimorbidity indices. To gain insight into the impact of multimorbidity on disease activity and treatment outcomes, it is essential to collect data over an extended period of time.

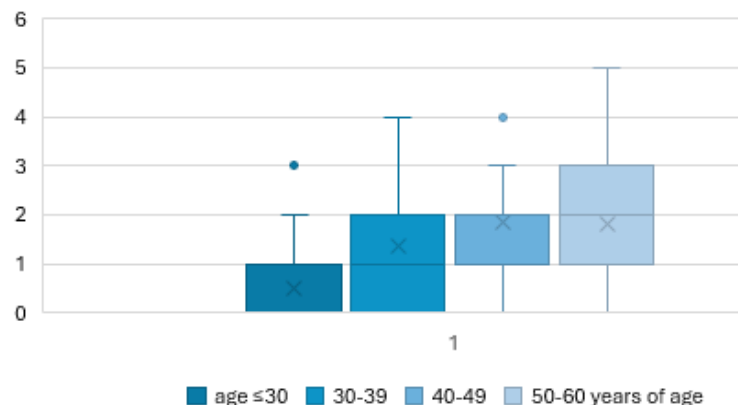


Fig. 5. The impact of age on RDCI in a cohort of SLE patients. The prevalence of multimorbidity was found to increase significantly with age. The same findings were observed for all multimorbidity indices, namely RDCI as well as for MMI.count and MMI.weight.

(1.6%) reached the end-stage renal disease (ESRD) and underwent successful cadaveric kidney transplantation. These results are consistent with those reported in the literature. However, the prevalence of LN is highly variable, with the literature reporting prevalence rates between 20 and 65% in SLE patients⁴⁷.

Mental health disorders are also frequently diagnosed in patients with SLE. Depression and anxiety, the most commonly reported disorders, are twice as prevalent in these patients as in the general population, and often have a profound impact on patients' health and well-being^{7,48}. This includes an increased incidence of cardiovascular disease, myocardial infarction, suicidal ideation, reduced quality of life, and higher risk of premature death⁷. In our cohort, approximately 14% of patients exhibited pre-existing depression, anxiety, and neurotic disorders. The co-occurrence of these conditions with fibromyalgia is

relatively common in SLE, as fibromyalgia has also been linked to mental health disorders⁴⁹. However, our study did not focus on this issue. Nevertheless, collaboration with a clinical psychologist or a psychiatrist appears to be very beneficial and often necessary.

The authors are aware of the limitations of the study, including the relatively small number of patients and the fact that the study was conducted at a single rheumatology centre. The study was designed as a cross-sectional study, including patients in different stages of disease activity from an ethnically nearly homogeneous population of the Central Moravia region. Furthermore, the study did not include information on the socioeconomic status of the patients or data on their highest level of education. The impact of disease activity and multimorbidity on the results was limited by the duration of the study, which would have necessitated data collection over a longer pe-

riod of time. The prevalence of certain diseases among male patients is influenced by two factors: the limited number of male patients in the cohort and the characteristic predisposition for SLE in females. The MMI and RDCI indices are limited by their broader representation of each diagnosis. For instance, osteoporosis was identified in 16.3% of the cohort according to the MMI index, whereas the RDCI index considered only the occurrence of osteoporotic fracture, which was identified in 5.7% of the patients. Conversely, a bone metabolism disorder in the level of osteopenia with a potential association with both the chronic disease itself and the therapy, was observed in additional 15% of the SLE patients at the time of the study. Nevertheless, studies have indicated that 20–26% of SLE patients may experience asymptomatic vertebral fractures, with up to another 32% developing them within 8 years of follow-up despite satisfactory bone mineral density (BMD) (ref.^{50,51}). The incidence of asymptomatic fractures was not assessed in our study.

In view of the aforementioned factors, it is necessary to adopt a comprehensive approach to the care of rheumatology patients, as this approach is likely to bring significant benefits. However, a key question remains: is such complex care readily available in the context of our current healthcare system? In the outpatient sector, the availability of complex care can be a challenge, particularly in the context of increasing waiting times for outpatient specialists. Our aim is to provide comprehensive care, particularly within the inpatient rheumatology department, which offers a wide range of consultative examinations, imaging and laboratory testing, physiotherapy and psychotherapy. Nevertheless, only a minority of patients are hospitalised, particularly those with a severe course of illness and high disease activity.

CONCLUSION

The prevalence of multimorbidity is increasing globally as a consequence of three factors: the ageing population, enhanced diagnostic capabilities and advances in treatment. Patients with chronic inflammatory autoimmune disease who are affected by multiple comorbidities are often undertreated, which may have a negative impact on their rheumatic disease activity and prognosis. This study aims to highlight the importance of monitoring and treating comorbidities in individuals with chronic inflammatory disease. A comprehensive and patient-centred approach to treatment recommendations can have a significant impact on the overall quality of life in individuals and their families, as well as on the healthcare systems and society-wide socioeconomic aspects.

ABBREVIATIONS

ACR, American College of Rheumatology; AITD, Autoimmune thyroid diseases; BMD, Bone mineral density; CCI, Carlson Comorbidity Index; CKD, Chronic kidney disease; ECI, Elixhauser Comorbidity Index; EULAR,

European Alliance of Associations for Rheumatology; ESRD, End-stage renal disease; HRQoL, Health-related quality of life; LN, Lupus nephritis; OA, Osteoarthritis; SLE, Systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; RA, Rheumatoid arthritis; RDCI, Rheumatic Disease Comorbidity Index; MMI, Multimorbidity Index.

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Author contributions: MD: patient selection, data collection, obtaining informed consent, major contributor in writing the manuscript; JV, AS: data collection; PH: study design, secondary contribution to the writing of the manuscript; MS: secondary contribution to the writing of the manuscript. All authors read and approved the final manuscript.

Conflict of interest statement: None declared.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Footnote: The findings in this manuscript were presented as a poster at the 14th European Lupus Meeting, Bruges, Belgium, 19.–22. March 2024.

REFERENCES

- Mendoza-Pinto C, Rojas-Villarraga A, Molano-González N, Jiménez-Herrera EA, León-Vázquez ML, Montiel-Jarquín Á, García-Carrasco M, Cervera R. Bone mineral density and vertebral fractures in patients with systemic lupus erythematosus: A systematic review and meta-regression. *PLoS One* 2018;13(6):e0196113. doi: 10.1371/journal.pone.0196113
- Lu X, Wang Y, Zhang J, Pu D, Hu N, Luo J, An Q, He L. Patients with systemic lupus erythematosus face a high risk of cardiovascular disease: A systematic review and meta-analysis. *Int Immunopharmacol* 2021;94:107466. doi: 10.1016/j.intimp.2021.107466
- Shin JI, Lee KH, Park S, Yang JW, Kim HJ, Song K, Lee S, Na H, Jang YJ, Nam JY, Kim S, Lee C, Hong C, Kim M, Choi U, Seo J, Jin H, Yi B, Jeong SJ, Sheok YO, Kim H, Lee S, Jeong YS, Park SJ, Kim JH, Kronbichler A. Systemic Lupus Erythematosus and Lung Involvement: A Comprehensive Review. *J Clin Med* 2022;11(22):6714. doi: 10.3390/jcm11226714
- Frittoli RB, Vivaldo JF, Costallat LTL, Appenzeller S. Gastrointestinal involvement in systemic lupus erythematosus: A systematic review. *J Transl Autoimmun* 2021;4:100106. doi: 10.1016/j.jtauto.2021.100106
- Pego-Reigosa JM, Nicholson L, Pooley N, Langham S, Embleton N, Marjenberg Z, Barut V, Desta B, Wang X, Langham J, Hammond ER. The risk of infections in adult patients with systemic lupus erythematosus: a systematic review and meta-analysis. *Rheumatology (Oxford)* 2021;60(1):60–72. doi: 10.1093/rheumatology/keaa478
- Clarke AE, Pooley N, Marjenberg Z, Langham J, Nicholson L, Langham S, Embleton N, Wang X, Desta B, Barut V, Hammond ER. Risk of malignancy in patients with systemic lupus erythematosus: Systematic review and meta-analysis. *Semin Arthritis Rheum* 2021;51(6):1230–41. doi: 10.1016/j.semarthrit.2021.09.009
- Zhang L, Fu T, Yin R, Zhang Q, Shen B. Prevalence of depression and anxiety in systemic lupus erythematosus: a systematic review and meta-analysis. *BMC Psychiatry* 2017;17(1):70. doi: 10.1186/s12888-017-1234-1
- World Health Organization. Multimorbidity: Technical Series on Safer Primary Care. World Health Organization; Geneva, Switzerland: 2016.
- Dey M, Busby A, Elwell H, Pratt A, Young A, Isaacs J, Nikiphorou E.

- The use and context of the term 'multimorbidity' in rheumatoid arthritis: a systematic literature review. *Rheumatology (Oxford)* 2021;60(7):3058-71. doi: 10.1093/rheumatology/keab214
10. Skou ST, Mair FS, Fortin M, Guthrie B, Nunes BP, Miranda JJ, Boyd CM, Pati S, Mtenga S, Smith SM. Multimorbidity. *Nat Rev Dis Primers* 2022;8(1):48. doi: 10.1038/s41572-022-00376-4
 11. Radner H, Yoshida K, Smolen JS, Solomon DH. Multimorbidity and rheumatic conditions-enhancing the concept of comorbidity. *Nat Rev Rheumatol* 2014;10:252-6. doi: 10.1038/nrrheum.2013.212
 12. Soley-Bori M, Ashworth M, Bisquera A, Dodhia H, Lynch R, Wang Y, Fox-Rushby J. Impact of multimorbidity on healthcare costs and utilisation: a systematic review of the UK literature. *Br J Gen Pract* 2020;71(702):e39-e46. doi: 10.3399/bjgp20X713897
 13. Radner H, Yoshida K, Frits M, et al. The impact of multimorbidity status on treatment response in rheumatoid arthritis patients initiating disease-modifying anti-rheumatic drugs. *Rheumatology (Oxford)* 2015;54(11):2076-84. doi: 10.1093/rheumatology/kev239
 14. Bloom DE, Chatterji S, Kowal P, Lloyd-Sherlock P, McKee M, Rechel B, Rosenberg L, Smith JP. Macroeconomic implications of population ageing and selected policy responses. *Lancet* 2015;385(9968):649-57. doi: 10.1016/S0140-6736(14)61464-1
 15. Radner H. Multimorbidity in rheumatic conditions. *Wien Klin Wochenschr* 2016;128(21-22):786-90. doi: 10.1007/s00508-016-1090-x
 16. Figueroa-Parra G, Meade-Aguilar JA, Hulshizer CA, Gunderson TM, Chamberlain AM, Thanarajasingam U, Greenlund KJ, Barbour KE, Crowson CS, Duarte-García A. Multimorbidity in systemic lupus erythematosus in a population-based cohort: the Lupus Midwest Network. *Rheumatology (Oxford)* 2024;63(11):3056-64. doi: 10.1093/rheumatology/kead617
 17. England BR, Sayles H, Mikuls TR, Johnson DS, Michaud K. Validation of the rheumatic disease comorbidity index. *Arthritis Care Res (Hoboken)* 2015;67(6):865-72. doi: 10.1002/acr.22456
 18. Radner H, Yoshida K, Mjaavatten MD, Aletaha D, Frits M, Lu B, Iannaccone C, Shadick N, Weinblatt M, Hmamouchi I, Dougados M, Smolen JS, Solomon DH. Development of a multimorbidity index: Impact on quality of life using a rheumatoid arthritis cohort. *Semin Arthritis Rheum* 2015;45(2):167-73. doi: 10.1016/j.semarthrit.2015.06.010
 19. Payne RA, Abel GA, Guthrie B, Mercer SW. The effect of physical multimorbidity, mental health conditions and socioeconomic deprivation on unplanned admissions to hospital: a retrospective cohort study. *CMAJ* 2013;185(5):E221-8. doi: 10.1503/cmaj.121349
 20. Aringer M, Costenbader K, Daikh D, Brinks R, Mosca M, Ramsey-Goldman R, Smolen JS, Wofsy D, Boumpas DT, Kamen DL, Jayne D, Cervera R, Costedoat-Chalumeau N, Diamond B, Gladman DD, Hahn B, Hiepe F, Jacobsen S, Khanna D, Lerström K, Massarotti E, McCune J, Ruiz-Irastorza G, Sanchez-Guerrero J, Schneider M, Urowitz M, Bertsias G, Hoyer BF, Leuchten N, Tani C, Tedeschi SK, Touma Z, Schmajuk G, Anic B, Assan F, Chan TM, Clarke AE, Crow MK, Czirják L, Doria A, Graninger W, Halda-Kiss B, Hasni S, Izmirly PM, Jung M, Kumánovics G, Mariette X, Padjen I, Pego-Reigosa JM, Romero-Diaz J, Rúa-Figueroa Fernández Í, Seror R, Stummvoll GH, Tanaka Y, Tektonidou MG, Vasconcelos C, Vital EM, Wallace DJ, Yavuz S, Meroni PL, Fritzler MJ, Naden R, Dörner T, Johnson SR. 2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus. *Arthritis Rheumatol* 2019;71(9):1400-12. doi: 10.1002/art.40930
 21. World Health Organization, International statistical classification of diseases and related health problems. - 10th revision, Fifth edition, 2016, Available from: <https://icd.who.int/browse10/2019/en> [accessed March 10, 2023]
 22. Butterly EW, Hanlon P, Shah ASV, Hannigan LJ, McIntosh E, Lewsey J, Wild SH, Guthrie B, Mair FS, Kent DM, Dias S, Welton NJ, McAllister DA. Comorbidity and health-related quality of life in people with a chronic medical condition in randomised clinical trials: An individual participant data meta-analysis. *PLoS Med* 2023;20(1):e1004154. doi: 10.1371/journal.pmed.1004154
 23. Gladman DD, Ibañez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. *J Rheumatol* 2002;29(2):288-91.
 24. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care* 1998;36(1):8-27. doi: 10.1097/00005650-199801000-00004
 25. Chowdhury SR, Chandra Das D, Sunna TC, Beyene J, Hossain A. Global and regional prevalence of multimorbidity in the adult population in community settings: a systematic review and meta-analysis. *E Clinical Medicine* 2023;57:101860. doi: 10.1016/j.eclinm.2023.101860
 26. Barnett K, Mercer SW, Norbury M. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet* 2012;380(9836):37-43. doi: 10.1016/S0140-6736(12)60240-2
 27. Aggarwal P, Woolford SJ, Patel HP. Multi-Morbidity and Polypharmacy in Older People: Challenges and Opportunities for Clinical Practice. *Geriatrics (Basel)* 2020;5(4):85. doi: 10.3390/geriatrics5040085
 28. Calderón-Larrañaga A, Poblador-Plou B, González-Rubio F, Gimeno-Feliu LA, Abad-Diez JM, Prados-Torres A. Multimorbidity, polypharmacy, referrals, and adverse drug events: are we doing things well? *Br J Gen Pract* 2012;62(605):e821-6. doi: 10.3399/bjgp12X659295
 29. Mair FS, May CR. Thinking about the burden of treatment. *BMJ* 2014;349:g6680. doi: 10.1136/bmj.g6680
 30. Surandran S, Ahmed S, Walton T, Nikiphorou E, Dey M. Multimorbidity in rheumatoid arthritis: common mechanistic links and impact and challenges in routine clinical practice. *Rheumatology (Oxford)* 2023;62(S13):SI260-SI270. doi: 10.1093/rheumatology/kead489
 31. Ranganath VK, Maranian P, Elashoff DA, Woodworth T, Khanna D, Hahn T, Sarkisian C, Kremer JM, Furst DE, Paulus HE. Comorbidities are associated with poorer outcomes in community patients with rheumatoid arthritis. *Rheumatology (Oxford)* 2013;52(10):1809-17. doi: 10.1093/rheumatology/ket224
 32. Costa L, Caso F, Atteno M, Del Puente A, Darda MA, Caso P, Ortolan A, Fiocco U, Ramonda R, Punzi L, Scarpa R. Impact of 24-month treatment with etanercept, adalimumab, or methotrexate on metabolic syndrome components in a cohort of 210 psoriatic arthritis patients. *Clin Rheumatol* 2014;33(6):833-9. doi: 10.1007/s10067-013-2369-1
 33. Dixon WG, Watson KD, Lunt M, Hyrich KL; British Society for Rheumatology Biologics Register Control Centre Consortium; Silman AJ, Symmons DP; British Society for Rheumatology Biologics Register. Reduction in the incidence of myocardial infarction in patients with rheumatoid arthritis who respond to anti-tumour necrosis factor alpha therapy: results from the British Society for Rheumatology Biologics Register. *Arthritis Rheum* 2007;56(9):2905-12. doi: 10.1002/art.22809
 34. Figueroa-Parra G, Meade-Aguilar JA, Hulshizer CA, Gunderson TM, Chamberlain AM, Thanarajasingam U, Greenlund KJ, Barbour KE, Crowson CS, Duarte-García A. Multimorbidity in systemic lupus erythematosus in a population-based cohort: the lupus Midwest network. *Rheumatology (Oxford)* 2024;63(11):3056-64. doi: 10.1093/rheumatology/kead617
 35. Charlson ME, Carrozzino D, Guidi J, Patierno C. Charlson Comorbidity Index: A Critical Review of Clinimetric Properties. *Psychother Psychosom* 2022;91(1):8-35. doi: 10.1159/000521288
 36. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40(5):373-83. doi: 10.1016/0021-9681(87)90171-8
 37. Barozet M, Le Tilly O, Bejan-Angoulvant T, Fesler P, Roubille C. Hypertension and Cardiovascular Outcomes in Inflammatory and Autoimmune Diseases: A Systematic Review and Meta-analysis. *Curr Hypertens Rep* 2024;26(11):419-29. doi: 10.1007/s11906-024-01311-6
 38. Gomez A, Hani Butrus F, Johansson P, Åkerström E, Soukka S, Emamikia S, Enman Y, Pettersson S, Parodis I. Impact of overweight and obesity on patient-reported health-related quality of life in systemic lupus erythematosus. *Rheumatology (Oxford)* 2021;60(3):1260-72. doi: 10.1093/rheumatology/keaa453
 39. Gergianaki I, Garantziotis P, Adamichou C, Saridakis I, Spyrou G, Sidiropoulos P, Bertsias G. High Comorbidity Burden in Patients with SLE: Data from the Community-Based Lupus Registry of Crete. *J Clin Med* 2021;10(5):998. doi: 10.3390/jcm10050998
 40. White RG, Bass BH, Williams E. Lymphadenoid goitre and the syndrome of systemic lupus erythematosus. *Lancet* 1961;277:368-73.
 41. Blich M, Rozin A, Edoute Y. Systemic lupus erythematosus and thyroid disease. *Isr Med Assoc J* 2004;6(4):218-20.
 42. Wu H, Cantor RM, Grahon DS, Lingren CM, Farwell L, Jager PL, Bottini N, Grossman JM, Wallace DJ, Hahn BH, Julkunen H, Hebert LA, Rovin BH, Birmingham DJ, Rioux JD, Yu CY, Kere J, Vyse TJ, Tsao BP. Association analysis of the R620W polymorphism of protein tyrosine

- phosphatase PTPN22 in systemic lupus erythematosus families: increased T allele frequency in systemic lupus erythematosus patients with autoimmune thyroid disease. *Arthritis Rheum* 2005;52:2396-402. doi: 10.1002/art.21223
43. Klionsky Y, Antonelli M. Thyroid Disease in Lupus: An Updated Review. *ACR Open Rheumatol* 2020;2(2):74-8. doi: 10.1002/acr2.11105
44. Moleti M, Trimarchi F, Vermiglio F. Thyroid physiology in pregnancy. *Endocr Pract* 2014;20(6):589-96. doi: 10.4158/EP13341.RA
45. Stagnaro-Green A, Akhter E, Yim C, Davies TF, Magder L, Petri M. Thyroid disease in pregnant women with systemic lupus erythematosus: increased preterm delivery. *Lupus* 2011; 20:690-9. doi: 10.1177/0961203310394894
46. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int* 2024;105(4S):S117-S314. doi: 10.1016/j.kint.2023.10.018
47. Hocco Lu M, Valenzuela-Almada MO, Dabit JY, Osei-Onomah SA, Chevet B, Giblon RE, Zand L, Ferverza FC, Helmick CG, Crowson CS, Duarte-García A. Incidence, Prevalence, and Mortality of Lupus Nephritis: A Population-Based Study Over Four Decades Using the Lupus Midwest Network. *Arthritis Rheumatol* 2023;75(4):567-73. doi: 10.1002/art.42375
48. Bachen EA, Chesney MA, Criswell LA. Prevalence of mood and anxiety disorders in women with systemic lupus erythematosus. *Arthritis Rheum* 2009;61(6):822–9. doi: 10.1002/art.24519
49. Wolfe F, Petri M, Alarcón GS, Goldman J, Chakravarty EF, Katz RS, Karlson EW. Fibromyalgia, systemic lupus erythematosus (SLE), and evaluation of SLE activity. *J Rheumatol* 2009;36(1):82-8. doi: 10.3899/jrheum.080212
50. Mendoza-Pinto C, García-Carrasco M, Sandoval-Cruz H, Muñoz-Guarneros M, Escárcega RO, Jiménez-Hernández M, Munguía-Realpozo P, Sandoval-Cruz M, Delezé-Hinojosa M, López-Colombo A, Cervera R. Risk factors of vertebral fractures in women with systemic lupus erythematosus. *Clin Rheumatol* 2009;28(5):579-85. doi: 10.1007/s10067-009-1105-3
51. Li EK, Tam LS, Griffith JF, Zhu TY, Li TK, Li M, Wong KC, Chan M, Lam CW, Chu FS, Wong KK, Leung PC, Kwok A. High prevalence of asymptomatic vertebral fractures in Chinese women with systemic lupus erythematosus. *J Rheumatol* 2009;36(8):1646-52. doi: 10.3899/jrheum.081337